Co-occurring Addictive and Psychiatric Disorders

A Practice-Based Handbook from a European Perspective

Geert Dom
Franz Moggi
Editors

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In honor of and gratitude to all patients and their families, who have shared some of their pathway to recovery with me.

Geert Dom

Dedicated to Marina, Anna-Chatrina, Nicolo, Laura, David, and Nikola.

Franz Moggi

Introduction to Dual Disorders: Co-occurrence of Psychiatric and Addictive Disorders

General Context

Dual Disorders (dual diagnosis) are defined as the co-occurrence of a psychoactive substance use disorder (or non-substance-related addiction) and another psychiatric disorder in the same individual (WHO 2010). The prevalence of patients with dual disorders is high and is suspected to rise. This accounts for general population samples, but is most evident within patients who present for treatment for either addictive or mental health problems. In recent European studies, the high prevalence of psychiatric comorbidity was a remarkably stable finding across very different regions (e.g., Southern and Nordic European countries), despite large differences in types of substances of abuse, severity, and routes of drug use (Reissner et al. 2012). Inversely, among patients presenting with a mental health disorder, a high prevalence of substance use disorder comorbidity can be found (European Monitoring Centre for Drugs and Drug Addiction, EMCDDA 2013). Consistent with these European studies, results from the US National Comorbidity Survey (NCS) indicate that about half of the individuals who suffer from a psychiatric disorder will develop a substance use disorder (SUD) sometime in their life (Kessler 2004) and that 15 % of them will do so within one year (Kessler et al. 1996).

Patients with dual disorders comprise a disproportionately large part of the disease burden and mortality compared to other single mental health conditions. Indeed, most of these patients can be described as individuals with multiple problems who are at a high risk for a variety of detrimental outcomes in all possible domains (e.g., social, legal, mental, and physical health outcomes).

In addition to their complexity, treatment compliance and effectiveness for patients with dual disorders are generally poorer when compared with other, less complex, patients with a single disorder. This may in part be related to the problems in care delivery for patients with dual disorders. At the heart of this issue is the traditional split between treatment for addictions and mental health care, a paradigm that is still highly influential in many European countries. Of note, mental health and addiction care organizations are very diverse across Europe. Great differences exist between countries and even between different regions within the same country. This is true for models of care, resources, methods of working or

training, and most importantly, the collaboration between addiction and psychiatric care.

Overall, there is a great need to improve the care for patients with dual disorders. In 2013, Europe introduced the European Mental Health Action Plan. If one compares the current, actual levels of care currently offered with the objectives proposed in this Action Plan (Table 1), patients with dual disorders clearly do not reach these targets. Specifically, domains such as accessibility and specific competencies (objective 3), provision of joint mental and somatic health (objective 5), and coordination of services (objective 6) are critically underdeveloped for patients with dual disorders, even compared with other patient types.

Table 1 Objectives of the European Mental Health Action Plan (2013)

Objective 1: Everyone has an equal opportunity to realize mental well-being throughout their lifespan, particularly those who are most vulnerable or at risk
Objective 2: People with mental health problems are citizens whose human rights are fully valued, respected, and promoted
Objective 3: Mental health services are accessible, competent, affordable, and available in the community according to need
Objective 4: People are entitled to respectful, safe, and effective treatment
Objective 5: Health systems provide good physical and mental health care for all
Objective 6: Mental health systems work in well-coordinated partnerships with other sectors
Objective 7: Mental health governance and delivery are driven by good information and knowledge

Helping to improve treatment standards, and ultimately, the quality of life for patients with dual disorders is at the heart of this book. We specifically focus on European contributions for two reasons. First, it is noteworthy that the bulk of both research and clinical textbooks originate from the USA. Indeed, there is no European country that spends more money on mental health and addiction research than the USA. Consequently, more than two-thirds of all papers in scientific journals on addictions, including those on comorbidity, are of US origin (Bramness et al. 2014). Thus, a European-grounded dual disorder textbook might provide an important and complementary addition to the existing works.

Second, in spite of the high quality of the US scientific and clinical contributions, an important question remains whether these findings can be implemented seamlessly into the broad variety of European contexts. Indeed, within Europe many differences exist in patient characteristics (and types of drugs used), organization and financing of care, attitudes toward patients with dual disorders, and also levels of stigmatization. Although US models are currently used frequently as the basis when developing treatment programs for patients with dual disorders, more and more interesting models are developed within many European settings, with each model providing their own emphases to take into account the cultural and local conditions. In addition, within the broader European psychiatry and mental health field, there is currently a powerful trend toward developing more homogeneity in standards and quality of care, training, and curriculum requirements, and joining research efforts. Many European organizations actively work toward better

integration and harmonization. This accounts both for psychiatry (e.g., European Psychiatric Association, EPA, www.europsy.net) and addiction care (e.g., European Federation of Addiction Societies, www.eufas.net). The editors and the contributors of this book hope that this edition will be a significant contribution to shared knowledge and increased awareness throughout the various European countries and will help to promote a European network of interested individuals and organizations that take the care for patients with dual disorders to heart.

Clinical and Research Problems

From a clinical perspective, it is important to know whether and how two or more disorders are etiologically related to each other because there are implications for treatment. For example, in the Environment Catchment Area Study (Regier et al. 1990), the authors found a risk close to 30 times higher for individuals with Antisocial Personality Disorder (ASPD) to have any SUD sometime in their lifetime; but for individuals with anxiety disorders, only about a twofold higher risk for a SUD. Thus, it is questionable whether ASPD and SUD are comorbid disorders or only a single disorder where substance abuse is one of its criteria. In contrast, the "comorbidity" of anxiety disorders and SUD is not necessarily a dual disorder, but rather anxiety symptoms could be a consequence of intoxication or substance withdrawal and, as such, could be a substance-induced anxiety disorder with corresponding implications for treatment. There is certainly more than one valid etiological model for dual disorders, as well as several models for specific comorbidities of psychiatric and substance use disorders. These are included in the chapters on specific dual disorders in this volume.

Even for experienced professionals, there are many difficulties in the clinical assessment of symptoms and making a diagnosis. Clinicians basically need to evaluate firstly whether there are enough symptoms with sufficient severity present for two or more disorders (i.e., meet the criteria of a diagnosis), secondly whether the symptoms are substance induced or independent of a SUD, and thirdly whether there are interaction processes between the two (or more) disorders. However, often it is not possible to observe patients in a stable psychiatric state while abstaining from substance use for a sufficient period of time to answer these three well-founded questions; thus, diagnoses are often tentative, and as a consequence, treatment is prone to errors.

The treatment of patients with dual disorders has been called a "mission impossible" for some time (Chow et al. 2012). Nowadays, integrated treatments are accepted as the first choice of treatment for patients with dual disorders. Treatment is characterized by the enhancement of motivation to behavioral change and adherence to the treatment; the concurrent integration of effective pharmacological and psychosocial interventions for both the psychiatric disorder and the substance

use disorder by the same professional(s) within the same care system; and a stepped approach to care with a long-term commitment, including relapse prevention. However, such programs are often hard to implement and maintain due to many problems, such as separated health care and social care systems, problems in financing treatment programs, or a lack of professionals trained in dual disorder treatment.

Finally, there are some research problems that can be summarized under the term "heterogeneity." Overall, the research literature has revealed great heterogeneity in study design characteristics (e.g., randomized controlled trials vs. observational studies), patient samples (e.g., diagnoses and sociodemographics), treatment strategies (e.g., evaluation of treatment systems, such as case management vs. evaluation of disorder-specific interventions, such as relapse prevention), settings (e.g., residential vs. outpatient), intensity (i.e., long- vs. short-term treatment), and outcomes (i.e., substance use, psychological symptoms, and social functioning). This heterogeneity makes it difficult to compare results and draw conclusions about the etiology, diagnostics, and treatment of patients with dual disorders.

Structure of the Book

As editors, we aim to make this a comprehensive textbook in which, in our view, the most important aspects of dual disorders are covered in a way that the contributions can be of interest for both the specialist in the field, as well as other clinical and scientifically interested professionals from the mental health and medical systems. All of the contributing authors have longstanding experience in both clinical and scientific work within their different specialized target patient groups. In their contributions, they offer, on the one hand, an overview of the current clinical and scientific state of the art in their field, but on the other hand, and most important, they make use of their own local context and/or European data to illustrate their domain. Thus, each of the chapters offers a rich overview of the field throughout a broad variety of European countries.

The book is classically structured with the different psychiatric disorders as a leading organizing principle at its core (Part II), framed by chapters on epidemiology, etiology, and healthcare systems (Part I), and subsequently assessment, integrated treatment systems and psychopharmacological and psychosocial interventions, and specific perspectives such as somatic disorders (Part III). In our view, one advantage of this book's organization is that the reader can easily find his or her way to their field of interest. However, we are aware that this structure is an artificial simplification. Indeed, as patients with dual disorders teach us every day, they are difficult to classify under one heading, and frequently display characteristics of many disorders and multiple needs, so the reader is invited to use the book accordingly.

Finally, the central thesis defended throughout the book is that the care for patients with dual disorders will not improve unless the mental health, addiction,

and medical care systems are combined. As editors we want to make a strong case for a full integration of all care systems. In our view, this will be the only way to provide real patient-centered care, allowing the targeting of treatment to all the many needs of these vulnerable patients.

Boechout, Belgium — Geert Dom
Bern, Switzerland — Franz Moggi
June 2014

References

Bramness JG, Henriksen B, Person O, Mann K (2014) A bibliometric analysis of European versus USA research in the field of addiction. Research on alcohol, narcotics, prescription drug abuse, tobacco and steroids 2001–2011. Eur Addict Res 20(1):16–22. doi: 10.1159/000348260

Chow CM, Wieman D, Cichocki B, Qvicklund H, Hiersteiner D (2012) Mission impossible: treating serious mental illness and substance use co-occurring disorder with integrated treatment: a meta-analysis. Mental Health Substance Use 1–19

European Monitoring Centre for Drugs and Drug Addiction (2013) Co-morbid substance use and mental disorders in Europe: a review of the data, EMCDDA Papers, Publications Office of the European Union, Luxembourg

Kessler RC (2004) The epidemiology of dual diagnosis. Biol Psychiatry 56(10):730–737. doi: 10.1016/j.biopsych.2004.06.034

Kessler RC, Nelson CB, McGonagle KA, Edlund MJ, Frank RG, Leaf PJ (1996) The epidemiology of co-occurring addictive and mental disorders: implications for prevention and service utilization. Am J Orthopsychiatry 66(1):17–31

Regier DA, Farmer ME, Rae DS, Locke BZ, Keith SJ, Judd LL, Goodwin FK (1990) Comorbidity of mental disorders with alcohol and other drug abuse. Results from the Epidemiologic Catchment Area (ECA) Study. JAMA 264(19):2511–2518

Reissner V, Kokkevi A, Schifano F, Room R, Storbjork J, Stohler R, Scherbaum N (2012) Differences in drug consumption, comorbidity and health service use of opioid addicts across six European urban regions (TREAT-project). Eur Psychiatry 27(6):455–462. doi: 10.1016/j.eurpsy.2010.10.001

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Part I

General Aspects

Epidemiological Perspectives on Comorbidity Between Substance Use Disorders and Other Mental Disorders

1

Roselind Lieb

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Abstract

Epidemiological studies all over the world could show impressive associations between different groups of substance use disorders and mental disorders, such as affective disorders or anxiety disorders. Most studies investigated cross-sectional associations. The Munich longitudinal population based Early Developmental Stages of Psychopathology (EDSP) Study reported predictive associations between alcohol and cannabis use disorders and nicotine dependence and other mental disorders. This study revealed associations in both directs: from substance use disorders to other mental disorders and vice versa. Explanation of comorbidity should take into account therefore both directions of causality.

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1.1 Introduction

The goal of this chapter is to discuss the comorbidity between substance use disorders and other mental disorders from an epidemiological perspective. An extensive literature has documented worldwide a strong association of problematic substance use (use and use disorders) with other mental disorders (for review see, e.g., Lieb and Isensee 2007; Moore et al. 2007; Lev-Ran et al. 2014). A review of European findings has recently confirmed the evidence for Europe (European Monitoring Centre for Drugs and Drug Addiction 2013a). Therefore, the chapter will not repeat these worldwide comorbidity findings but will instead focus on selected findings from European epidemiological studies that have examined comorbidity between substance use disorders and other mental disorders in European community samples. The aim is to demonstrate how epidemiological research can help us understand the phenomenon of comorbidity.

1.2 What Is Comorbidity?

The term comorbidity was introduced by Feinstein (1970) to "refer to any distinct additional clinical entity that has existed or that may occur during the clinical course of a patient who has the index disease under study" (pp 456–457). Or in other words: When two or more clinical conditions occur simultaneously or sequentially in the same person, they are said to be "comorbid."

But why is it interesting to study comorbidity? There are clinical concerns (i.e., diagnostic issues, treatment strategy) that have to be reconsidered in comorbid patients, but the phenomenon of comorbidity is also of scientific interest. Comorbidity of substance use disorders and other mental disorders may, for example, reveal gaps in current knowledge and become the basis for interesting hypotheses for future studies.

To explain comorbidity of substance use and other mental disorders, two basic scenarios can be used (assuming that the comorbidity findings cannot be explained by methodological shortcomings):

1. The two (or more) comorbid disorders are causally linked; for the comorbidity of substance use and other mental disorders, this means
   (a) The substance use disorder can cause the temporally secondary other mental disorder (e.g., through biological processes introduced by substance use);
   (b) The other mental disorder can cause the temporally secondary substance use or disorder (e.g., as a means of self-medication).
2. The substance use disorder(s) and the other mental disorder(s) share disease-related factors, for instance, risk factors, causal factors, triggers, or abnormalities in the same brain regions.

Comorbidity seems to be a very complex phenomenon that may help researchers detect etiological pathways to disorders or consequences of diseases. In evaluating

the complexity of comorbidity, epidemiologists focus first on determining if there is an association (cross-sectional) between substance use disorders and other mental disorders. If such an association can be shown, the next question addresses the longitudinal or predictive association: Does one (the primary) disorder (i.e., the disorder with the earlier onset) prospectively increase the risk (in terms of incidence) for the other (secondary) disorder? If yes, the primary disorder is said to be a risk factor for the development of the secondary one (see Kraemer et al. 1997). Risk means here the probability of developing the secondary disorder but does not imply a deterministic association. For a factor to be called a "risk factor," a statistically significant association between the predictor and outcome under consideration must be shown. In the search for causality of the association, such a risk association is one critical component but is not sufficient on its own. Other criteria for causal relationships have been proposed in the literature (e.g., Rothman and Greenland 2005) and must be reviewed for the each association (e.g., biological plausibility, coherence of existing empirical knowledge, dose–response relationship.

In the following, we focus on selected epidemiological studies that have addressed cross-sectional and longitudinal (predictive) associations between substance use/disorders and other mental disorders. We start with a brief look at the size of the problem, that is, on the prevalence of mental and substance use disorders in Europe.

1.3 Size of the Problem in Europe

The best and most valid information about the prevalence of mental and substance use disorders can be taken from a comprehensive review on the 12-month prevalence and disability burden estimate of a broad range of mental disorders in the European Union (EU) that was conducted by Wittchen et al. (2011). The authors systematically reviewed the existing literature, reanalyzed existing data and national surveys, and consulted experts. They included studies and data from all member states of the EU (EU-27) plus Switzerland, Iceland, and Norway. Using this method, they estimated that each year, 38.5 % of the adult EU population suffer from at least one mental disorder. Adjusted for age and comorbidity, this corresponds to 164.8 million people affected per year. Anxiety disorders (14.0 %; 61.4 million people affected) and major depression (6.9 %; 30.3 million people affected) are the most frequent mental disorders. Almost 15 million people (3.4 %) are affected by alcohol dependence. More than one million adult Europeans are affected by drug dependence (opioid or cannabis dependence; prevalence rates: 0.1–1.8 %). These findings underline impressively that neither mental nor substance use disorders affect "only" few people. Rather, they must be considered an important care challenge for the EU in the twenty-first century.

1.4 Comorbidity Findings from Selected European Population-Based Studies

1.4.1 Description of Comorbidity

Results of the German National Health and Examination Survey Mental Health Supplement (GHS-MHS) can be used to develop a preliminary description of comorbidity between substance use disorders and other mental disorders. The GHS-MHS was the first nationwide study to investigate the prevalence of a broad range of mental disorders as defined in the *Diagnostic and Statistical Manual of Mental Disorders* (American Psychiatric Association 1994) and their comorbidities and correlates in the community in Germany. The survey included a random sample of $N = 4{,}181$ people aged 18–65 years. Diagnoses of mental disorders were based on fully standardized computer-assisted interviews (the Munich-Composite International Diagnostic Interview, or M-CIDI; see Jacobi et al. 2004). This study presented rates for 12-month comorbidity between substance use disorders and other mental disorders as follows: Among people who fulfilled *DSM-IV* diagnostic criteria for alcohol abuse or alcohol dependence, about half (55.1 %) presented this as a "pure" disorder (i.e., did not fulfill criteria for any other mental disorder). More than 20 % fulfilled diagnostic criteria for one other mental disorder, 7.8 % the criteria for two other diagnoses, and 14.4 % the diagnostic criteria for three or even more additional diagnoses. Among people who fulfilled diagnostic criteria for drug abuse or drug dependence, even a higher proportion were comorbid (total 54.7 %). Here, 29.0 % fulfilled criteria for one additional diagnosis, 12.9 % for two additional diagnoses, and 12.9 % for three or more additional diagnoses (within the same 12-month interval).

Results additionally revealed that among mental disorders, substance use disorders are the less frequently treated disorders. Among people with substance abuse or dependence, only about a quarter (23.0 % for alcohol abuse/dependence to 25 % for illicit drug abuse/dependence) received at least a "minimal intervention" for their condition. In contrast to these low treatment rates, treatment was offered far more often to people suffering from other mental disorders (e.g., any affective disorder: 52.5 %; panic disorder: 75.4 %; any eating disorder: 47.0 %; see Jacobi et al. 2004). The study also found that across disorders people with comorbid disorders tended to report higher healthcare utilization rates than those with pure disorders.

Remarkably high comorbidity rates specifically for alcohol use disorders were found in the Copenhagen City Heart Study (Flensborg-Madsen et al. 2009). This study included 18,146 individuals randomly selected from the population. Among people who fulfilled study criteria for alcohol use disorders, more than the half (50.3 %) fulfilled criteria for another disorder. A closer inspection revealed that among these people, 18 % fulfilled criteria for an affective disorder, 24 % for personality disorder, 8 % for psychotic disorder, 7 % for anxiety disorder, and 16 % for drug abuse. Comparable findings were reported for nicotine dependence from the German Transitions in Alcohol Consumption and Smoking (TACOS) Study

(Schumann et al. 2004). This population-based study ($N = 4{,}075$ 18- to 64-year-olds) found that among people with *DSM-IV* nicotine dependence, 19.5 % fulfilled criteria for another substance use disorder (abuse/dependence). A comparable rate (19.2 %) fulfilled criteria for any affective disorder and almost one quarter the criteria for any *DSM-IV* anxiety disorder (24.4 %). Together, descriptive data from the three studies show that an impressive proportion of people affected by substance use disorders also fulfill diagnostic criteria for at least one other mental disorder within the same time interval (12 months).

To determine if people with a substance use disorder have a higher risk for another mental disorder compared to people without a substance use disorder, one needs to look into the associations. One measure for association is the "odds ratio" (OR). The OR is a quantitative measure of association and is defined as the ratio of two odds. It takes into account the base rates for each disorder under consideration. Cross-sectional associations describe associations without taking temporal sequence into consideration, while predictive (or longitudinal) associations evaluate associations between temporally primary and temporally secondary disorders (which is critical to evaluate the risk factor status of the first disorder).

1.4.2 Age of Onset

Several community surveys have collected retrospective information about age of onset of substance use and mental disorders. Their findings consistently revealed that the "adult" mental disorders mostly have their onset in adolescence and early adulthood. For example, the GHS-MHS showed that anxiety, bipolar, mood, somatoform, and substance use disorders reach a median age of onset by the age of 20, while depressive and possible psychotic disorders tend to manifest later (median age of onset = 31 and 37 years; Jacobi et al. 2004). These German findings match the average findings of the international cross-national ICPE results (Andrade et al. 2000). Median age of onset by age 20 clearly implies that the first three decades must be seen as an important risk period for the onset of substance use and other mental disorders.

1.4.3 Associations Between Substance Use Disorders and Other Mental Disorders

Cross-sectional comorbidity of substance use disorders and other mental disorders in adults has been studied extensively (see above). Taking the age-of-onset findings into consideration, the high-risk period for first manifestation of disorders may also be a high-risk period for the manifestation of comorbidity. In the following we focus therefore mainly on findings from a community study that investigated exactly this high-risk period: the Early Developmental Stages of Psychopathology (EDSP) Study (see Box 1.1).

Box 1.1. The Early Development Stages of Psychopathology Study
The prospective, longitudinal Early Developmental Stages of Psychopathology (EDSP) study assessed *DSM-IV* substance use and mental disorders and associated risk factors in a representative sample of 3,021 adolescents and young adults aged 14–24 years at baseline (T0) in Munich, Germany. The baseline assessment took place in 1995. The study also included three follow-up surveys (at T1, T2, and T3 in 1997, 1999, and 2005), a family history component (at T0, T2, and T3), and parent surveys (at T1 and T3; see Lieb et al. 2000; Zimmermann et al. 2008). Diagnostic assessment was based on the computer-assisted version of the Munich-Composite International Diagnostic Interview (DIA-X/M-CIDI). The DIA-X/M-CIDI allows for the standardized assessment of symptoms, syndromes, and diagnoses of *DSM-IV* disorders along with information about onset, duration, and severity. Highly trained clinical interviewers carried out the interviews face-to-face mostly in the homes of the participants.

1.4.4 Association Between Alcohol Use/Disorders and Other Mental Disorders

Based on the EDSP baseline data, Zimmermann et al. (2003) evaluated first *cross-sectional associations* between lifetime *DSM-IV* panic attack, panic disorder, agoraphobia, social phobia, specific phobia, and generalized anxiety disorder (GAD) and lifetime alcohol use (regular use, hazardous use) and alcohol use disorders (abuse, dependence). These analyses revealed even in this young sample consistently positive associations between all included *DSM-IV* anxiety disorders and the investigated alcohol outcomes. In the *predictive analyses*, only baseline social phobia and panic disorder predicted subsequent alcohol use disorders, while the other anxiety disorders (agoraphobia, specific phobia, GAD) did not (Zimmermann et al. 2003). Using the 10-year follow-up data, Behrendt et al. (2011) confirmed these predictive effects of primary anxiety disorders on secondary alcohol use disorders. Further EDSP analyses studied early separation anxiety disorder and revealed additionally a strong association between childhood separation disorder and the later onset of alcohol dependence, but not alcohol abuse (Brueckl et al. 2007).

The EDSP data were also included into the analyses of the International Consortium in Psychiatric Epidemiology (ICPE, Merikangas et al. 1998). The Consortium analyzed population based studies from different countries (USA, Germany, Mexico, Netherlands, Canada) regarding cross-sectional associations between substance use disorders (alcohol use disorders, drug use disorders) and a broad spectrum of mental disorders. For alcohol dependence, the group reported associations to any anxiety disorders, affective disorders, conduct disorder, and adult antisocial behavior.

1.4.5 Association Between Smoking, Nicotine Dependence, and Mental Disorders

Moylan et al. (2012) undertook a systematic review of population-based epidemiological studies that investigated the association between smoking, nicotine dependence, and anxiety disorders. In total, 47 studies met predefined inclusion criteria, with 12 studies providing information about predictive associations. The authors found evidence that smoking and nicotine dependence increase the risk specifically for subsequent panic disorder and GAD. Literature assessing anxiety disorders as a risk factor for the incidence of smoking and nicotine dependence reported inconsistent results. Isensee et al. (2003) categorized EDSP study subjects into nonsmokers, occasional smokers, nondependent regular smokers, and dependent smokers (i.e., fulfilled diagnostic criteria for *DSM-IV* nicotine dependence). Using lifetime information collected at baseline T0, rates for panic attacks and panic disorder increased with higher tobacco consumption status—all three smoking categories were significantly associated with panic attacks and panic disorder (ORs ranged from 3.0 to 28.0).

Another pattern was found for other *DSM-IV* anxiety disorders: With the exception of obsessive compulsive disorder (OCD), all other anxiety disorders (agoraphobia, social phobia, specific phobia, GAD, and posttraumatic stress disorder, or PTSD) were associated with nicotine dependence (ORs between 1.9 and 7.4), but in general not with lower smoking categories. Investigation of predictive associations between primary smoking and incidence of anxiety disorders revealed that primary nondependent and dependent smoking was associated with higher rates of incident panic attacks, and dependent smoking was also associated with higher rates of panic disorder. For other anxiety disorders, prior dependent smoking predicted the onset of agoraphobia, social phobia, specific phobia, and PTSD (ORs between 2.4 and 5.1). Point estimates were also elevated for OCD OR = 4.2) and GAD (OR = 3.6) but—probably due to the low cell sizes—failed to reach significance.

This study also evaluated the other direction, that is, the associations between primary anxiety disorders and the onset of secondary nondependent regular or dependent smoking. Using strict prospective information, no evidence was found that primary anxiety disorders predict onset of the different smoking categories. However, using Cox regressions that included the entire age range of the study subjects, associations were found between prior panic attacks (Hazard Ratio HR = 3.3) and prior panic disorder (HR = 3.3) as well as the subsequent onset of nicotine dependence. Using the same data set and smoking categories, Bronisch et al. (2008) showed that not only anxiety disorders but also suicide ideation and suicide attempts were strongly associated with occasional smoking, regular smoking, and nicotine dependence (ORs between 1.4 and 16.4). Bronisch et al. (2008) evaluated further whether primary smoking predicted subsequent onset of suicidal behavior. They revealed that both nondependent and dependent smoking increased the risk for suicidal ideation and suicide attempts (ORs between 1.6 and 4.5). However, no associations were found for the other direction: Primary suicidality did not increase the risk for the onset of the different smoking categories.

1.4.6 Associations Between Cannabis Use and Disorders and Mental Disorders

Cannabis is the most widely used illicit drug in Europe (European Monitoring Centre for Drugs and Drug Addiction 2013b). In the last decades, several epidemiological studies have reported comorbidity between cannabis use or cannabis use disorders and psychotic or affective outcomes. Even more, meta-analyses showed that use of cannabis increases prospectively the risk for psychotic and also depressive outcomes (Moore et al. 2007; Lev-Ran et al. 2014). The ICPE analyses confirmed associations between the overall group of drug dependence and affective disorders, anxiety disorders, conduct disorder, and adults' antisocial behavior (Merikangas et al. 1998). Using the 10-year longitudinal data set of the EDSP, Kuepper et al. (2011) confirmed cannabis use to be a risk factor for the development of incident subclinical psychotic symptoms. They also showed that continued cannabis use might increase the risk for psychotic disorder by impacting on the persistence of symptoms. Using the same data set, Wittchen et al. (2007) additionally found cross-sectional associations between cannabis use and cannabis use disorders (abuse, dependence) and other mental disorders (all affective disorders, panic attack/panic disorder and other substance use disorders). Interestingly, they also found evidence that the onset of cannabis use and use disorders were predicted by other substance use disorders as well as affective and anxiety disorders. These findings suggest that longitudinal associations seem to exist in both directions: Mental disorders seem to increase the risk for cannabis outcomes and conversely, cannabis use/disorder seems to increase the risk for mental disorders.

Conclusions

Epidemiological studies all over the world could show an impressive association between different groups of substance use disorders and mental disorders, such as affective disorders or anxiety disorders. Most studies investigated cross-sectional associations. On the basis of cross-sectional associations, however, we cannot draw conclusions about the temporal sequence of the onset of the comorbid disorders. If we want to learn more about the etiological implications of comorbidity, predictive associations are required. The Munich EDSP Study reported several predictive associations between substance use disorders and other mental disorders. So far, we cannot report a clear and conclusive pattern of predictive associations—as we have seen for the associations of mental disorders and cannabis use disorders, both directions (from substance use disorder to mental disorder and vice versa) seem to be plausible. This would mean that none of the two above discussed models should be excluded so far. Both, the risk factor model and the shared factor model must be considered in explanation models of the comorbidities.

References

American Psychiatric Association (1994) Diagnostic and statistical manual of mental disorders: DSM-IV, 4th edn. American Psychiatric Association, Washington, DC

Andrade L, Caraveo-Anduaga JJ, Berglund P, Bijl R, Kessler RC, Demler O et al (2000) Cross-national comparisons of the prevalences and correlates of mental disorders. Bull World Health Organ 78(4):413–426. doi:10.1590/S0042-96862000000400003

Behrendt S, Beesdo-Baum K, Zimmermann P, Hofler M, Perkonigg A, Bühringer G, Lieb R, Wittchen HU (2011) The role of mental disorders in the risk of speed of transition to alcohol use disorders among community youth. Psychol Med 41(5):1073–1085. doi:10.1017/S0033291710001418

Brückl TM, Wittchen HU, Höfler M, Pfister H, Schneider S, Lieb R (2007) Childhood separation anxiety and the risk of subsequent psychopathology: results from a community study. Psychother Psychosom 76(1):47–56

Bronisch T, Hofler M, Lieb R (2008) Smoking predicts suicidality: findings from a prospective community study. J Affect Disord 108(1–2):135–145. doi:10.1016/J.Jad.2007.10.010

European Monitoring Centre for Drugs and Drug Addiction (2013a) Co-morbid substance use and mental disorders in Europe: a review of the data (EMCDDA Papers). Publications Office of the European Union, Luxembourg

European Monitoring Centre for Drugs and Drug Addiction (2013b) European Drug Report 2013: trends and developments (European Drug Report package). Publications Office of the European Union, Luxembourg

Feinstein AR (1970) The pre-therapeutic classification of comorbidity in chronic disease. J Chronic Dis 23(7):455–468

Flensborg-Madsen T, Mortensen EL, Knop J, Becker U, Sher L, Gronbaek M (2009) Comorbidity and temporal ordering of alcohol use disorders and other psychiatric disorders: results from a Danish register-based study. Compr Psychiatry 50(4):307–314. doi:10.1016/j.comppsych.2008.09.003

Isensee B, Wittchen HU, Stein MB, Hofler M, Lieb R (2003) Smoking increases the risk of panic—findings from a prospective community study. Arch Gen Psychiatry 60(7):692–700. doi:10.1001/Archpsyc.60.7.692

Jacobi F, Wittchen HU, Holting C, Hofler M, Pfister H, Muller N et al (2004) Prevalence, co-morbidity and correlates of mental disorders in the general population: results from the German Health Interview and Examination Survey (GHS). Psychol Med 34(4):597–611. doi:10.1017/S0033291703001399

Kraemer HC, Kazdin AE, Offord DR, Kessler RC, Jensen PS, Kupfer DJ (1997) Coming to terms with the terms of risk. Arch Gen Psychiatry 54(4):337–343. doi:10.1001/archpsyc.1997.01830160065009

Kuepper R, van Os J, Lieb R, Wittchen HU, Hofler M, Henquet C (2011) Continued cannabis use and risk of incidence and persistence of psychotic symptoms: 10 year follow-up cohort study. Br Med J 342:d738. doi:10.1136/bmj.d738

Lev-Ran S, Roerecke M, Le Foll B, George TP, McKenzie K, Rehm J (2014) The association between cannabis use and depression: a systematic review and meta-analysis of longitudinal studies. Psychol Med 44(4):797–810. doi:10.1017/S0033291713001438

Lieb R, Isensee B (2007) Häufigkeit und zeitliche Muster von Komorbidität. In: Moggi F (ed) Doppeldiagnosen: Komorbidität psychischer Störungen und Sucht, 2nd edn. Verlag Hans Huber, Bern, pp 27–58

Lieb R, Isensee B, von Sydow K, Wittchen HU (2000) The Early Developmental Stages of Psychopathology Study (EDSP): a methodological update. Eur Addict Res 6(4):170–182. doi:10.1159/000052043

Merikangas KR, Mehta RL, Molnar BE, Walters EE, Swendsen JD, Aguilar-Gaziola S et al (1998) Comorbidity of substance use disorders with mood and anxiety disorders: results of the

International Consortium in Psychiatric Epidemiology. Addict Behav 23(6):893–907. doi:10.1016/S0306-4603(98)00076-8

Moore THM, Zammit S, Lingford-Hughes A, Barnes TRE, Jones PB, Burke M et al (2007) Cannabis use and risk of psychotic or affective mental health outcomes: a systematic review. Lancet 370(9584):319–328. doi:10.1016/S0140-6736(07)61162-3

Moylan S, Jacka FN, Pasco JA, Berk M (2012) Cigarette smoking, nicotine dependence and anxiety disorders: a systematic review of population-based, epidemiological studies. BMC Med 10:123

Rothman KJ, Greenland S (2005) Causation and causal inference in epidemiology. Am J Public Health 95:S144–S150. doi:10.2105/Ajph.2004.059204

Schumann A, Hapke U, Meyer C, Rumpf HJ, John U (2004) Prevalence, characteristics, associated mental disorders and predictors of DSM-IV nicotine dependence. Eur Addict Res 10(1):29–34. doi:10.1159/000070983

Wittchen HU, Frohlich C, Behrendt S, Gunther A, Rehm J, Zimmermann P et al (2007) Cannabis use and cannabis use disorders and their relationship to mental disorders: a 10-year prospective-longitudinal community study in adolescents. Drug Alcohol Depend 88:60–70. doi:10.1016/J.Drugalcdep.2006.12.013

Wittchen HU, Jacobi F, Rehm J, Gustavsson A, Svensson M, Jonsson B et al (2011) The size and burden of mental disorders and other disorders of the brain in Europe 2010. Eur Neuropsychopharmacol 21(9):655–679. doi:10.1016/J.Euroneuro.2011.07.018

Zimmermann P, Brueckl T, Lieb R, Nocon A, Ising M, Beesdo K et al (2008) The interplay of familial depression liability and adverse events in predicting the first onset of depression during a 10-year follow-up. Biological Psychiatry 63(4):406–414. doi:10.1016/J.Biopsych.2007.05.020

Zimmermann P, Wittchen HU, Hofler M, Pfister H, Kessler RC, Lieb R (2003) Primary anxiety disorders and the development of subsequent alcohol use disorders: a 4-year community study of adolescents and young adults. Psychol Med 33(7):1211–1222. doi:10.1017/S0033291703008158

Evolution of Mental Health and Addiction Care Systems in Europe

2

Jaap van der Stel

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Abstract

In all European countries there are institutions for mental health care and addiction treatment. The way in which they have developed, however, is different in each country. In addition, institutions for mental health care and substance abuse treatment have evolved mostly independently of each other. This hinders an integrated treatment for people with both addiction and other mental disorders.

This chapter gives an overview of the health-care systems in Europe in this area. Furthermore, a description of the European institutions that develop policies on this subject and monitor the developments in the various countries will be provided.

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2.1 History

2.1.1 Mental Health/Psychiatry

In the approach to mental disorders, including addiction, we can distinguish a number of waves. Such waves exist relating to the following topics:

- The approach of psychopathology (including addiction) from the perspective of disease (and therefore the involvement of doctors) versus sin (religion) or public disorder and crime (police and justice).
- The emphasis on a natural, biological (hereditary or 'organic') explanation for psychopathology versus pointing to (also) external, psychological, or social backgrounds of an issue. Historically also 'possessed by the devil' fell under the set of in life acquired forms of psychopathology.
- The focus on asylum, nursing, and care (often from churches or religious organizations) versus the attention focused on treatment.
- Regarding treatment: accent on purely medical-somatic treatment versus (also, or explicitly) an accent on a social psychological or psychotherapeutic therapy.

Many historians begin their history of psychiatry shortly before 1800, because only then there were, on a relatively larger scale, medical centres specifically for people with mental disorders. Moreover, only in that period there were doctors who were specialized in psychopathology. However, psychiatry is in fact of much older date and actually runs parallel to the history of medicine in general. The ancient Greek, Roman, Muslim, and Christian doctors focused both on physical and psychological symptoms. It is even questionable whether they—like we have become accustomed to—made such a distinction between mental and physical illnesses. See Sadock et al. (2009) for a compact but well-documented overview of the history of psychiatry.

Important events in the history of modern psychiatry are in the first place the humanization of the psychiatric centres and the 'moral' therapy that was brought into practice. As far as we can ascertain, the conditions in the still scarce psychiatric institutions in the eighteenth century, were pitiful. There was no or hardly any therapeutic policy. Patients were locked up as imbeciles, idiots, or insane people and more or less left to their own fate. This changed gradually around 1800. The establishments became more humane and a search for effective therapies began. This can partly be traced back to the works of Philippe Pinel (1745–1826) and Jean-Étienne Dominique Esquirol (1782–1840). Pinel is in our memory the symbol for the literal liberation of psychiatric patients from their chains. This took place at the end of the eighteenth century in the Parisian Hôpital Bicêtre. His commitment marks the development of psychiatry as a medical discipline: 'lunatics' became 'patients'. Of interest, this action is falsely attributed to Pinel. In fact, it was his assistant Jean Baptiste Pussin who did this historic act in 1797.

The 'moral therapy'—we would now speak of psychological treatment—was based on the idea that mental disorders were the result of genetic as well as

environmental influences. The treatment was focused on education and (on belief-oriented) conversations with patients. This therapy worked only modestly. Therefore, psychiatrists also sought refuge in other, in our eyes sometimes 'barbaric', methods. In this way, they tried to call agitated patients with bizarre, violent (or aggressive) behaviour to order. However, this did not have a truly therapeutic effect.

In the first half of the twentieth century, experiments were done with limited effective biomedical interventions. Examples are inducing fever using malaria infection to treat psychotic symptoms as a result of general paresis. Real results were only realized when, starting from the middle of the twentieth century, chemicals were discovered that proved efficacious for the treatment of mental disorders. Examples of disorders that could be treated with medications are schizophrenia, bipolar disorder (manic depression), depression, or anxiety disorders. The advent of antipsychotic drugs for the treatment of patients with schizophrenia contributed to a substantial decline in the number of psychiatric hospitalizations.

As a result of different views about the treatment of psychiatric patients and strong criticism on the large psychiatric hospitals (often far away from the population centres), a movement to de-institutionalize psychiatry arose. The aim was to reduce the number of inpatient admissions, to reduce the dependence on caregivers and to rehabilitate the social position of psychiatric patients. It was realized that it makes sense to help those affected to reintegrate in society and to increase their self-reliance, despite having a chronic mental illness. Psychiatric patients were people with a mental limitation, but with plenty of opportunities for a humane existence.

2.1.2 Biopsychosocial

In psychiatry, the biological dimension has from time to time been emphasized. An example of this is the German physician Wilhelm Griesinger (1817–1868) who stated that all mental disorders are 'brain diseases'. Therefore, psychiatry had to be a medical discipline. At the same time, there are people who have stressed the importance of the psychological and social dimensions (without neglecting the biological). Influential was the American Adolf Meyer (1866–1950), who developed the concept of psychobiology. In the wake of this, he introduced psychosocial treatments. Meyer also advocated that patients had to be treated as much as possible in their own environment.

In the 1970s, the American psychiatrist George Engel (1913–1999) proposed the biopsychosocial approach to illness, which he presented as an alternative to the traditional biomedical approach. This is focused on the treatment of diseases or on the related symptoms, but there was little attention for the psychosocial context in this approach (Engel 1977; Frankel et al. 2003). The biopsychosocial approach is based on system theory. It was a very important innovation and has been of immense significance, especially for psychiatry. Engel insisted on looking at different levels, from the perspective of different disciplines. He considered the

tangle of problems that often exist with different types of health problems, while stressing the importance of paying attention to the complexity of such problems. This was better than to reduce them to separate components or separate aspects. Apart from psychiatry, this way of thinking has especially taken hold in general practice.

Engel (who would have had no qualms to add also the cultural dimension to his biopsychosocial approach), made it clear that the biopsychosocial approach holds true for schizophrenia as well as for diabetes or addiction. He pointed out that regardless of what the aetiology is of a condition, a layered and multi- or interdisciplinary approach is always preferable compared to the traditional biomedical approach. Schizophrenia and diabetes are in this perspective both a 'somatic' condition as a 'mental' condition. And social problems can be part of both illnesses: when the course is chronic, the consequences of the condition are not limited to one level or domain.

Engel was far ahead of his time in theoretical terms and built on the insights of Adolf Meyer. In the practice of medicine in a broad sense, the consequences of his approach are far from being understood. Moreover, there is the continuous risk of a relapse in the classical biomedical approach. In this sense, his approach is still very 'modern'.

The relevance of the biopsychosocial approach is particularly reflected in the transition that currently takes place in mental health: the recovery-oriented care. Serious mental disorders take for a large part a chronic course. 'Healing' is not possible for this group. On the other hand, in biopsychosocial and cultural terms, there are many possibilities for those concerned to recover.

2.1.3 Based on Evidence

Under the name of evidence-based medicine there exists, from the end of the twentieth century, a movement to review medical procedures as much as possible by experimental, scientific research. Based on the outcomes are subsequently treatment recommendations and guidelines designed, which also happens in psychiatry or substance abuse treatment. Before, there were initiatives going on to test interventions in experiments, but there was still a lot of critique or doubts regarding the methods that were used. And there were no databases yet that could quickly determine whether an intervention or therapy was working, and that such a ruling was based on evidence. Nowadays, statements about the strength or weakness of a recommendation are based on the analyses of a series of experiments in a laboratory. Then, these are tested in practice. The randomized controlled trial (RCT), a randomized and controlled trial in which ideally the subjects do not know which treatment they undergo, now has the status of 'gold standard'. The evidence-based medicine has a long history. Philippe Pinel, one of the founders of modern psychiatry, advocated for more than 200 years ago the use of statistics for making statements about treatment methods.

2.1.4 Addiction Treatment

Substance abuse treatment is younger than the general mental health services or psychiatry, although there are many parallels with the description above.

In many cases, relatively independent of psychiatry or mental health care, separate institutions for addiction treatment have been established in most countries in Europe. There were initiatives from the nineteenth century when organisations for the temperance movement emerged. Just as in psychiatry, the attention was first focused on asylums or clinics for alcoholics, but also outpatient facilities arose gradually. Until the 1960s, the attention was concentrated mainly or exclusively on problems with alcohol. However, the rise of illegal drugs from the seventies of the twentieth century (such as heroin, amphetamine, cannabis, cocaine, and years later ecstasy) led to a boom in new centres. These were partly the same facilities targeted on alcohol problems, but a large number of facilities focused exclusively on issues related to drug use. This separation is understandable because the target groups, and their social backgrounds, were different from one another. The rise of the Human Immunodeficiency Virus (HIV) that causes Acquired Immune Deficiency Syndrome (AIDS) gave the drug services in the 1980s even more clearly its own distinct position: the discussion thrived on the question if *harm reduction*, by improving the sanitary conditions of drug users (distribution of condoms for safe sex, swap used syringes for clean ones), was not more important than achieving abstinence as the primary purpose of the care.

Finally, also the importance of a biopsychosocial-cultural approach is relevant to the substance abuse treatment. The same applies to working according to evidence-based guidelines.

2.1.5 Dual Disorder

For the treatment of people with addictions and a co-morbid or co-occuring mental disorder (or vice versa: dual disorder), it is of great importance that there are facilities available that are able to respond adequately to both problems. In no country, in Europe or elsewhere, this is the rule. In most countries there are—often already since the nineteenth century, or longer ago—psychiatric hospitals. After World War II, in the one country faster than in the other, ambulatory facilities emerged also. Even more recent is the closure of these hospitals or at least a reduction in the number of beds. But, as a rule, the attention to addiction problems was and is herein limited, or secondary. This has to do with the fact that addiction—to this day—is not nearly everywhere and by everyone recognized as a mental disorder. Indeed, the ICD and the DSM—in various editions—have listed addiction definitely as illness or disorder. In public opinion, but also by many clinicians, addiction is often approached as something special: for example as a form of deviant behaviour, as an expression of moral weakness, or as a form of crime. This has resulted in a situation where drug addicts or alcoholics were not—as a matter of course—admitted to psychiatric (ambulatory or clinical) facilities. That

does not mean that there were (and are) not a lot of people with addiction problems that were hospitalized. This has always been the case: the prevalence of use, abuse and dependence of people with a mental disorder is, compared to the general population, relatively high. This means that even though the policy was and is aimed to ward off people with addiction problems, it is unlikely that this really was successful.

Together, a landscape was created in which facilities for alcohol and drugs emerged relatively independently from each other, and often still function apart from each other. This has inevitably consequences for the organizational conditions of the treatment of people with dual disorder problems. Caring for people with addictions is—unfortunately—not a natural part of mental health institutions. And the reverse is also true: the treatment of co-morbid mental disorders in substance abuse treatment is not standard practice. Even if one would like to do this, there is often a lack the skills and resources. What often happens is that clients or patients will be referred between services for addiction and mental health. This happens as soon as a mental disorder of a client in substance abuse treatment is so severe that psychiatric intervention is necessary. Conversely, a patient can be referred to a service for addiction care when the substance use is so strong that this frustrates a psychiatric or psychological treatment.

From this point of view, the integration of these facilities should be obvious. To this end there are indeed initiatives in many places. This has been done by initiative of either addiction care or mental health care (or together) in the form of 'double disorder'-clinics. These provide a treatment specifically for people with dual disorder problems, and in which patients do not have to be concerned that they will be discharged because they do not meet the exact admission criteria. Also in the form of outpatient programs or projects there are many initiatives on dual disorder. Yet, taken together, the range of these services is limited. We can assume that roughly at least half of the people with a (severe) mental disorder are excessively taking substances or might be addicted (at least addicted to tobacco). And conversely, we can assume that perhaps half of the (seriously) addicts have an additional mental disorder, such as Attention Deficit-/Hyperactivity Disorder (ADHD), depression, personality disorder (borderline or antisocial personality disorder), or post-traumatic stress disorder. While this does not mean that both problems (addiction and the other disorder) always need to be addressed, or that they are always closely linked, it is plausible that this is often the case. In such a case, it is desired that organizations or treatment teams are able to deal with both problems—parallel or in series. To achieve this, projects are set up in many mental health and substance abuse treatment institutions to educate each other's expertise to staff. This diminishes the need for organizational changes (and eventually mergers). However, the chance that something is changing in favour of clients does increase with this approach.

In the literature, researchers, policy makers and professionals use the term co-morbidity or dual disorder to indicate the combination of addiction problems and another mental disorder. In this handbook, the term dual disorder will be used.

In the remainder of this chapter I give an overview of the main similarities and differences in Europe in the field of addiction treatment and mental health care. It focuses on a description of some of the major organizations that make periodic reviews in Europe: epidemiological data, policy developments and trends, and characteristics of the health-care providers. Unfortunately, the fragmentation described above is also present in the European institutions. As a result, it is difficult to describe the state of the art in the organization of the treatment of comorbid problems. The World Health Organization (WHO) is incidentally a good exception to this. This organization makes reviews in which somatic disorders, mental disorders and addiction to alcohol and drugs are discussed in conjunction. Nevertheless, there is a considerable lack of knowledge on how the approach of dual disorder problems in the different European countries could be improved.

2.2 Care Systems

2.2.1 Treatment Drugs-Related Disorders

With under-treatment we mean the functions aimed at people who because of substance (ab)use are in need of help. It concerns early detection, detoxification, provision of substitutes and other medication, psychotherapy, risk and harm reduction (prevention of the transmission of infectious diseases), rehabilitation, social reintegration, and recovery. Ideally, there is also attention to gender specific issues, problems of minorities, and age-specific differences.

The main source on drug use and drug policy in Europe is the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA; www.emcdda.europa.eu). It is established in Lisbon. The EMCDDA collects data from all EU countries plus Norway. Leading are the annual reports that are produced in co-operation of the member states. These give overviews of the state of affairs on drug use, drug policy, and treatment or rehabilitation. The EMCDDA also publishes thematically oriented reports. The centre is the focal point for the development and implementation of the EU drugs strategy. Recently, the new strategy for 2013–2020 has been made public (Council of the European Union 2012). In the first two decades since its founding, the EMCDDA was focused on reducing supply and demand. As a new policy issue, the 'reduction of the health and social risks and harms caused by drugs' has been added to this. This means that in the coming period the treatment of addiction the social integration and recovery of all drug users will receive increased attention. This applies both to those receiving voluntary assistance as to those in a forced framework (prisons). This recognises that the fixation on achieving abstinence has had insufficient results. Direct access to mental health services or psychiatry for addicts is not in the European Union (EU) strategy. Yet, this does not mean that the importance of dual disorder within the EMCDDA is not recognized. In 2004, this Centre published an overview of co-morbidities in which the relationship between drug use and mental disorders has been described (see below) (EMCDDA 2004a).

In addition to the EMCDDA, the Pompidou Group (www.coe.int/t/dg3/pompidou), connected with the Council of Europe, is active in the field of drug use and drug services. In 2010, it published an extensive review of the treatment systems in Europe (Muscat and members of the Pompidou Group treatment platform 2010). The review is divided into four blocks: North of Europe, Centre and East of Europe, West of Europe and South of Europe. It describes—per block—the epidemiology of drug use, and, briefly, the history of the drug treatment. The review makes clear that there are differences in the positioning of drug treatment: either under the umbrella of health care system or under social services. It can be presumed that attention to dual disorder is greater when drug treatment is seen as part of the (mental) health care.

The report of the Pompidou Group gives per country a quantitative and an as differentiated as possible description of the availability of facilities. Traditionally, it was focused on heroine use (and dispensing methadone); but now also other forms of drug abuse are addressed. It goes without saying that—partly as a result of epidemiological, cultural and financial characteristics—the countries differ in strengths and weaknesses. The Eastern European countries had in the 1990s lack of knowledge and facilities, but also there significant improvements have been made.

Unfortunately, the Pompidou Group has indicated that there are hardly any facilities in European countries for the dual disorder treatment.

2.2.2 Treatment for Alcohol-Use Disorders

There is no European institute that, similar to the EMCDDA, makes detailed annual reviews of the progress of the alcohol services in different countries. This has to do with the fact that, for the past 25 years, drugs (production, trade, and use) has been given a prominent place in government policies. Most drugs are illegal; the production and trade are linked to criminal organizations. And also the use of drugs is often classified as an offence or a criminal act. However, from a physical and mental health-point of view, the abuse of alcohol is a much bigger problem. Alcohol consumption in Europe is relatively high, though it has declined in recent years. Alcohol is causally related with over 60 different medical conditions (Room et al. 2005). Because of the relatively high consumption, the prevalence of these disorders in Europe is troubling. Additionally, numerous social problems are related to alcohol abuse. However, the gap of lacking a separate institute is compensated by the efforts that WHO Regional Office for Europe has been made to this theme (www.euro.who.int). Furthermore, with the support of the EU, there is the Amphora-project (www.amphoraproject.net), which develops and disseminates knowledge about alcohol policy and promotes its implementation.

From a number of recent publications a picture can be drawn of the alcohol problem in Europe and the available facilities to reduce the problem. WHO Regional Office for Europe recently published a very extensive status report on alcohol and health in 35 European countries (WHO Regional Office for Europe

2013). This report provides data on treatment of problematic alcohol use, but unfortunately, this information is very brief. The document is nevertheless important because of the various references.

Drummond et al. (2011) recently published a literature review of the range of facilities and questioned the possible gap with the needs for care. They concluded nevertheless that it is difficult to answer this question because of a lack of comparative data. This problem is also described by Drummond et al. (2013). The authors conclude the following on the basis of their comparison of six European countries (Austria, England, Germany, Italy, Spain, and Switzerland):

1. There is considerable variation in the implementation of alcohol interventions across Europe, partly related to national strategies and devolved responsibility.
2. There is a need for a more concerted effort across Europe to implement evidence-based alcohol interventions.
3. There is a lack of comparable high quality information on the prevalence of alcohol use disorders and access to interventions.
4. A Europe-wide system for estimating prevalence or alcohol use disorders and monitoring implementation of early identification and treatment is needed.

In the past few decades, a great deal of knowledge about effective treatment for alcohol problems has been developed. Rehm et al. (2013) made an overview of the availability of formalized guidelines that are formed on the basis of this knowledge. They found, however, that less than half the EU countries use a guideline. The analysis made clear that 'abstinence is the usual treatment goal', but in most guidelines there is nowadays also a focus on intermediate goals, such as reduction of drinking or controlled drinking. The overview also made visible that cognitive behavioural therapy, motivational interviewing, and family therapy are often mentioned for relapse prevention—this in combination with medication.

2.2.3 Mental Health Care

The prevalence of mental disorders in Europe and the adverse impacts on the social functioning are considerable. Yearly, over a third of the population has to do with a mental disorder. Noteworthy is that only a third of them receives aid (Wittchen et al. 2011).

The European Observatory on Health Systems published a sound and still useful overview of the policies and the relating practice in the European field of mental health care in 2007 (Knapp et al. 2007). This report provides insight into the history, recent developments and prospects. It gives further insight into the development of treatment strategies, financing, legislation, strengthening the role of primary care, decreasing the importance of psychiatric hospitals and ambulatory services, the fight against the rise of stigmas and social exclusion, the promotion of social integration (housing and employment), the meaning of the user and survivor movement, the role of carers and families, and the developments in former eastern

bloc countries. This report also deals with addiction and substance use, but unfortunately gives no attention to dual disorder.

A more practical view of the situation for policy makers of mental health and mental health care in Europe was published in 2008 by WHO-Europe (WHO Regional Office for Europe 2008). The WHO found that compared with 5 years ago, the countries had made significant progress, but there were also several weaknesses signalled. A weak point is the lack of consensus on definitions of concepts and the absence of a compatible data collection. Further, the wide variety of facilities and funding opportunities signalled the fact that the level of mental health in the various countries can differ significantly within Europe. The conclusion was: 'If one word could summarize this report, it would be diversity. Many sentences and tables in the chapters are characterized by various differences' (WHO Regional Office for Europe 2008, p. 79). Of course, it is not the case that diversity always points to shortages. Mental health care is most effective when it is closely connected to the particular characteristics of regions, target groups, and cultural conditions. The WHO concluded that there is also a trend to more convergence. The priorities of the Mental Health Declaration for Europe (WHO European ministerial conference on mental health Helsinki 2005) may be a guideline. These are:

1. Foster awareness of the importance of mental wellbeing.
2. Collectively tackle stigma, discrimination and inequality, and empower and support people with mental health problems and their families to be actively engaged in this process.
3. Design and implement comprehensive, integrated and efficient mental health systems that cover promotion, prevention, treatment and rehabilitation, care, and recovery.
4. Address the need for a competent workforce, effective in all these areas.
5. Recognize the experience and knowledge of service users and carers as an important basis for planning and developing mental health services.

The report further recommended prioritizing services for vulnerable groups, including people with dual disorder problems 'i.e. where mental health problems occur jointly with other problems such as substance misuse or physical illness' (WHO European ministerial conference on mental health Helsinki 2005, p. 81).

The European Commission has recently published the most comprehensive report on mental health systems in Europe (European Commission 2013). In addition to a review of the relevant European literature, the report includes systematic country profiles. On the basis of these, cross-country comparisons have been made. Important is that the country profiles also mention substance abuse treatment facilities and programs. This provides an important basis to examine the consistency and to stimulate cooperation in the future.

These three facilities for additional mental health data are important:

1. WHO European Health for All database (HFA-DB): www.euro.who.int/en/data-and-evidence/databases/european-health-for-all-database-hfa-db.
2. OECD Health Care Quality Indicators: www.oecd.org/health/health-systems/healthcarequalityindicators.htm.
3. Eurostat: http://epp.eurostat.ec.europa.eu/statistics_explained/index.php/Healthcare_statistics.

Another important source for knowledge about health care in Europe is the European Observatory on Health Systems and Policies (www.hspm.org). This institute works closely with WHO-Europe. It offers the possibility of looking into quantitative data from countries and compare these directly online. In addition, there is an extensive search function for documentation on health policy in the various European countries.

2.2.3.1 Dual Disorder Treatment

In a report released in 2004 by the EMCDDA on dual disorder (the EMCDDA uses in its documents the term co-morbidity), a series of obstacles for its treatment were signalled (EMCDDA 2004b):

1. Problem drug users, more often than not, suffer from mental disorders. Both psychiatric teams and drug services regularly fail to identify patients with dual disorder.
2. In the dual disorder treatment, there is no single psychosocial intervention for drug addiction that is superior to all others.
3. Dual disorder clients are often sent back and forth between psychiatric and drug services, not receiving proper assessment or treatment.
4. Treatment staff is often not trained to deal with dual disorder clients, since their training usually is specialised (medicine, psychology, social work, etc.).
5. Currently, dual disorder treatment is often not effectively organised and lacks quality management. This leads to inefficient treatment and high staff turnover.
6. Treatment of dual disorder patients involves different services over a long time.

In the international literature different forms of service delivery are described: (1) sequential or serial delivery, (2) parallel treatment, and (3) integrated treatment. While the last form is the most desirable in many cases, in 2004 facilities for such cases were only sporadically available in Europe.

The EMCDDA formulated the following policy considerations (ibid):

1. Dual disorder patients often have many mental, physical and social problems, which have to be identified and diagnosed.
2. Treatment is effective if delivered according to evidence-based practice, planned and managed individually.

3. Dual disorder patients need carefully coordinated and integrated services in order for treatment to be successful. Case management is a particularly effective approach for these patients.
4. Training at all levels of each involved organisation is necessary to enhance staff capacity to deal with dual disorder patients in a holistic way and increase treatment success.
5. Coordinated, integrated and flexible treatment services based on scientific evidence and with regular monitoring will reduce staff turnover and be cost-efficient.
6. Aftercare and social reintegration efforts are important in order to avoid relapse and renewed need for cost-intensive care.

Recently, the EMCDDA (2013) published an update. The focus of this document was on the available epidemiological data about dual disorder (co-morbid substance use and mental disorders) in Europe. The EMCDDA found that in Europe the most common combinations are:

- Alcohol use and depression or anxiety;
- Opioid use and personality or behavioural disorders;
- Cannabis use and schizophrenia;
- Amphetamines use and psychotic disorders.

The EMCDDA concluded that there is still a huge lack of uniform criteria for the sampling of national data on this subject. The national reports demonstrate a disputable variation in the quality and quantity of the available statistics. There is some progress in the way countries are collecting national data. However, to date, as a result of the fragmented way data are collected in Europe, it is impossible to compose a reliable and valid overview. As a consequence of that, North-American literature is frequently referred to in order to give an impression of the prevalence of dual disorder. The EMCDDA has announced to stimulate their partners to harmonise future data collection. This requires agreement on methodologies and criteria about the registration of disorders and substances. Of note, the EMCDDA focuses on illicit drugs, although it would be wise to include alcohol and tobacco.

General Findings and Conclusions

In general, we can state that in most European countries some general developments are taking place in mental health care: the importance of clinical facilities is decreasing, more ambulatory work is being done, the primary care is becoming more important, and the activities are better supported by scientific research (guidelines). But the differences between countries and even regions are great. It seems unlikely that this will change soon. The same trends apply also more or less for substance abuse treatment. However, moral standards and legal regimes play here an even bigger role than in mental disorders. This explains partly why countries differ so much from each other in this respect.

Organizationally, facilities for substance abuse treatment usually exist separately from those for mental health care. This is rarely expressed as a real problem, which points out that the attention to the dual disorder treatment is not central to the policies of international organizations and countries. This applies also to the question of how these can be better organized. The organizational conditions for the treatment of dual disorder problems are therefore not optimal. Yet, it cannot be concluded that this would not be possible. Mental health care and substance abuse treatment institutions can decide to adjust their treatment policy, which also applies to the professionals working there. The possibilities for this vary from country to country. Usually, the financiers limit the policy freedom.

A known issue is that national data collection is not uniform in Europe. However, after a few years the EMCDDA has shown that it is possible to change this. It yearly publishes in-depth reviews on drug use, drug policy, and drug services, which clarify the differences between countries and their background. Unfortunately, the EMCDDA does not make reviews about alcohol problems.

Another shortcoming is that the view on the outcomes of care is limited. Although there are data on inflows and outflows, whether treatments really work cannot be derived from these data. Also, there are no reviews showing whether in Europe—by country—evidence-based strategies are applied. And if so: which one.

The dual disorder treatment (substance abuse or dependence and mental illness) presupposes in the first place a sufficient overview of clinical-epidemiological data. These should answer the questions how many clients experience dual disorder problems, what combinations of disorders it concerns, and what the nature and the severity of their condition is. Secondly, there is a need for a collection of well-researched methods: biomedical and psychosocial techniques and strategies for rehabilitation and recovery. Ideally, these are brought together in a treatment-guideline. Thirdly, professionals need to have sufficient skills to be able to treat dual diagnosis problems effectively. They can develop this usually only when they are encouraged or challenged and that assumes that in the policy of their work organisation this theme is considered to be important. Fourthly, there is a need for integrated facilities: institutions for mental health care that work well together with institutions for addiction care, or institutions that have created integrated facilities internally. Sometimes, this arises only after external policy makers put pressure on the facilities. Finally, there is a need for sufficient funding. And there should be a procedure that guarantees patients access to integrated care.

The care is still diverse and fragmented in Europe. And there are still few policies designed to improve the care to people with dual disorder problems. Also international organisations in this field are not yet tightly integrated. However, a lot can change in the next decade. An important condition for change is that addiction is understood as a mental disorder and that the ‘status aparte’ will disappear.

References

Council of the European Union (2012) EU drugs strategy (2013–2020). Brussels
Drummond C, Gual A, Goos C, Godfrey C, Deluca P, Von Der Goltz C, Gmel G, Scafato E et al (2011) Identifying the gap between need and intervention for alcohol use disorders in Europe. Addiction 106(Suppl 1):31–36
Drummond C, Wolstenholme A, Deluca P, Davey Z, Donoghue K, Elzerbi C, Gual A et al. (2013) Chapter 9. Alcohol intervention and treatments in Europe. In: Anderson P, Braddick F, Reynolds J, Gual A (eds) Alcohol Policy in Europe: Evidence from AMPHORA, 2nd edn. The AMPHORA project, pp 72–101
EMCDDA (2004a) Co-morbidity. In EMCDDA 2004 Annual report on the state of the drugs problem in the European Union and Norway
EMCDDA (2004b) Co-morbidity—drug use and mental disorders. Drugs in focus
EMCDDA (2013) Co-morbid substance use and mental disorders in Europe: a review of the data, EMCDDA Papers. Publications Office of the European Union, Luxembourg
Engel G (1977) The need for a new medical model: a challenge for biomedicine. Science 196 (4286):129–136
European Commission (2013). Mental health systems in the European Union member states, status of mental health in populations and benefits to be expected from investments into mental health. Brussels.
Frankel RM, Quill TE, McDaniel SH (eds) (2003) The biopsychosocial approach: past, present, future. University of Rochester Press, Rochester, NY
Knapp M, McDaid D, Mossialos E, Thornicroft G (2007) Mental health policy and practice across Europe. The future direction of mental health care. Open University Press, Berkshire
Muscat R and members of the Pompidou Group treatment platform (2010) Treatment systems review. Council of Europe, Strasbourg
Rehm J, Rehm MX, Alho H, Allamani A, Aubin H, Bühringerm G, Daeppen J, Frick U, Gual A, Heather N (2013) Alcohol dependence treatment in the EU: a literature search and expert consultation about the availability and use of guidelines in all EU countries plus Iceland, Norway, and Switzerland. International Journal of Alcohol and Drug Research 2(2):53–67
Room R, Babor T, Rehm J (2005) Alcohol and public health. Lancet 365(9458):519–530
Sadock BJ, Sadock V, Ruiz P (2009) Kaplan and Sadock's comprehensive textbook of psychiatry, 9eth edn. Lippincott, Williams & Wilkins, Philadelphia
WHO European ministerial conference on mental health Helsinki (2005). Mental Health Declaration for Europe. Facing the challenges, building solutions. Finland 12–15 January 2005
WHO Regional Office for Europe (2008). Policies and practices for mental health in Europe: meeting the challenges. WHO Regional Office for Europe: Copenhagen
WHO Regional Office for Europe (2013). Status report on alcohol and health in 35 European countries. WHO Regional Office for Europe: Copenhagen
Wittchen HU, Jacobi F, Rehm J, Gustavsson A, Svensson M, Jönsson B, Olesen J, Allgulander C et al (2011) The size and burden of mental disorders and other disorders of the brain in Europe 2010. Eur Neuropsychopharmacol 21(9):655–679

Integrated Treatment: The Model and European Experiences

3

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Abstract

Integrated treatment of dual disorder patients was introduced in response to the failures of both sequential and parallel treatment approaches. Integrated treatment aims at treating both disorders concurrently, by one provider or a team of providers who are trained and knowledgeable in both fields (psychiatry and addiction). Care is delivered in a consistent manner, using the same philosophy and approach. There are several integrated care models, but the most elaborate one is the model for Integrated Dual Disorder Treatment (IDDT). The IDDT

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model consists of more than 20 treatment and organisational components, which makes it comprehensive but difficult to implement. Outreach, motivation-based treatment group treatment and specific pharmacological treatment are some of these components. Over the last decades, integrated treatment has, in many European countries, become the preferred treatment model for dual disorder patients and National expertise centres and consortiums have been established to facilitate and help organisations with the implementation of integrated treatment.

3.1 Introduction

The treatment of dual disorder patients has been associated with non-compliance, frequent relapses, and organisational difficulties Dijkhuizen et al. 2013. Important causes are the chronic nature and complexity of the combined disorders. But of no less importance has been the inadequate organisation of care around these patients. While consensus grew that in dual disorders patients psychiatric disorders and problems with substance use are interlinked and intertwined, the care for both disorders has been separately organised and executed for a long time. The most common models for dual disorder treatment have been, and in some places still are, the parallel and sequential treatment models.

Sequential treatment is based on the so-called secondary model of comorbidity (Mueser et al. 2003). This model explains the high rates of comorbidity based on the assumption that psychopathology is the consequence of substance use disorders or vice versa. There is some evidence that substance abuse can trigger mental illness in some individuals who are biologically vulnerable and who would maybe otherwise not have developed the disorder. This seems to be the case for a few specific combinations, especially extensive cannabis abuse and the onset of psychosis. This evidence does not explain the high comorbidity of so many other mental disorders with substance abuse.

The sequential treatment approach starts with treatment of what is considered the primary disorder and patient will not be eligible for treatment in another part of the system until that problem is resolved or stabilised (Mueser et al. 2003).

There are several drawbacks to this approach. More often than not there is no consensus between organizations on what the primary disorder actually is, since patients present themselves with a complex tangle of problems. It is unclear when one disorder has been treated successfully, and treatment of the other disorder can start. But most importantly, the untreated disorder will continue to influence the treated disorder and the treatment itself, thus making it very difficult to achieve stabilisation of any kind.

The parallel approach aims at treating both the mental disorder and the substance use disorder at the same time but in separate systems and, generally, in separate organisations; mental illness in mental health care and the substance abuse in

addiction services. In theory parallel treatment could, when properly coordinated, be effective for certain patients. The reality, however, is that coordination between professionals is hindered by organisational and administrative problems (Mueser et al. 2003). Organisations struggle with inadequate communication, uncertainty about responsibilities and finance, and, not the least, differences in philosophy, lack of a common approach, and lack of a common language and framework.

3.2 What Are Integrated Treatment and Its Components?

In the late1980s, the body of research on dual disorders and dual disorder treatment steadily grew, led by American researchers. One of the first findings was that the parallel but separate mental health and substance abuse treatment systems delivered fragmented and in-effective care (Torrey et al. 2001). The organisation of care often resulted in the exclusion of dual disorder patients instead of treatment.

For those reasons, clinicians, administrators, researchers, family organisations, and patients themselves had been asking for the integration of mental health and substance abuse services (Ridgely et al. 1987; Drake and Wallach 2000). Since then, integrated treatment programmes and services have started to develop worldwide.

Integrated treatment is designed to increase effectiveness by reducing the burden on the consumer in navigating through a fragmented and complex system (Chow et al. 2012). Integrated treatment aims at treating both disorders concurrently, by one provider or a team of providers who are trained and knowledgeable in both fields (psychiatry and addiction). Care is delivered in a consistent manner, using the same philosophy and approach.

Integrated treatment is based on the following principles:

3.2.1 Integration

Integration entails interventions that are aimed at both the substance abuse and the psychiatric disorder. Care is delivered by one professional or a team of professionals. Many of the disadvantages of working with parallel or sequential treatment will be lessened when both mental health and substance abuse services are delivered by the same team or professional. The difference in philosophical perspectives on how to treat substance abusing mental health patients is minimized when the professionals work side-by-side, and preferably, from the same organisation (Graham 2004).

This includes treatment components such as assessment and crisis interventions. If possible, interventions are aimed at both disorders. There is no primary or secondary disorder, both disorders are considered primary and should be addressed. A patient, for example, will be prescribed anti-psychotic medication while still using cocaine and at the same time taking part in a group to address substance abuse. These are not considered opposing interventions; on the contrary, these

interventions can reinforce each other when properly matched with the needs of the patient.

3.2.2 Comprehensive Services

People with dual disorders often cope with problems in several areas in their life. A major part of integrated treatment is aimed at reducing and stabilising both the substance abuse and the psychiatric symptoms. But working with patients on issues such as housing, debts and finance, social relations, and finding meaningful activities, is just as important. The problems people experience in these areas are almost always linked to their substance abuse and often to their psychiatric symptoms as well. Therefore, addressing these needs is necessary when treating the disorders. Interventions targeting these other problems will often precede interventions aimed at substance abuse and psychiatry. Patients, who have not come to terms with their illness or with the need to change their lifestyle, can thus start to achieve improvement. They will gain trust and hope that positive change is possible.

3.2.3 Assertive Outreach

Unfortunately, dual disorders patients are not characterised by their motivation to seek help or stay in treatment. They often drop out of treatment for several reasons. Patients may feel pressured by the chaos and tangle of problems in their "outside" life, may not actually believe that change is possible or are simply not able to commit, on account of—undetected—cognitive impairment.

Assertive outreach recognises that a professional cannot wait in his office for the patient to show up for his appointment or expect that the patients will seek help for substance abuse or mental health problems on their own. A professional will need to actively approach and seek patients in their own environment. Connecting with patients by offering assistance with practical problems has proven to be a successful strategy to build trust and a working relationship.

Assertive outreach is mainly associated with ambulatory services but should also be an integral part of clinical treatment approaches. Admitted patients should be actively involved in their treatment. Patients who withdraw to their rooms must be adressed and persuaded to engage in contact and participate in group activities.

3.2.4 Long-Term Perspective

Recovery from two chronic and interrelated disorders is complex and needs time. Serious dual disorders that are not treated or are treated in parallel or sequential systems tend to have a negative course and are characterised by relapses of both disorders. Studies (Drake et al. 2008) have shown that short-term treatment

programmes may be effective on reducing substance abuse and related negative outcomes, but will not change patients' lives significantly. Recovery is achieved over time and involves working on change in several areas. Patients need to regain old skills or, in many cases, learn skills that other people have developed in adolescence and early adulthood. It is therefore important that integrated programmes are able to offer long-term help without time limits.

3.2.5 Motivation-Based Treatment

Integrated treatment intends to offer the best suited interventions to treat mental illness and substance abuse. To do this, the interventions need to be matched to the motivation for change of the patient. Many integrated services use the stages of treatment (Osher and Kofoed 1989) and the transtheoretical model of change (Prochaska and DiClemente 1983; Prochaska et al. 1992) as a conceptual framework for this.

The Transtheoretical Model is an integrative, biopsychosocial model to conceptualise the process of intentional behavioural change. The model has integrated and included elements from other theories. One of the main elements of the Transtheoretical Model is the stages of change. The model argues that behavioural change happens with people moving through a series of small stages. These stages of change are: precontemplation, contemplation, preparation, action, and maintenance.

- Precontemplation: people in this stage are not thinking about changing problem behaviour in the near future or may not even be willing to consider change.
- Contemplation: in this stage people are starting to consider change and may think about the pros and cons of this change. Ambivalence is a common feature, since most people in this stage are still holding on to their (unhealthy) behaviour.
- Preparation: when people enter the preparation stage, the pros have been favoured over the cons. Action is seriously considered. It is common for people in this stage to be still slightly reluctant about the change that is considered.
- Action: the action stage marks the beginning of actual change in the behaviour. Unfortunately, this is also often the moment when relapse occurs.
- Maintenance: people reach the maintenance stage when they have successfully attained and maintained behaviour change for at least 6 months. Although relapse is still around the corner, maintaining the new behaviour is less of an effort.

As patients move through different stages of change, treatment (strategies and interventions) must move with them. This is necessary since interventions that work well early in treatment may be ineffective, and even harmful, if applied in the same way later in treatment (Flores 2001). The stages of treatment are based on observation of dual disorders patients in their recovery process. The motivation for treatment guides the choice of interventions (Osher and Kofoed 1989). The model

distinguishes four stages of treatment: engagement, persuasion, active treatment, and relapse prevention.

- Engagement: is defined by a lack of working alliance between worker and patient. There is sporadic/chaotic use of services and a lack of trust (from both patient and professional). The patient is resistant of and non-adherent to treatment proposals.
- Persuasion (often divided in an "early" and a "late" persuasion stage): a working relationship is established, although the patient does not always acknowledge problems with substance use. Although he may talk about changing behaviour no actual actions are taken.
- Active treatment (often divided in an "early" and a "late" action stage): the patient is engaged in treatment and has reduced substance use for more than the past month, but still meets criteria for substance abuse of dependence during this period of reduction.
- Relapse prevention: patients reach this stage when they have been persistent in the new and healthier behaviour for 6 months or more.

It is important to note that stage-wise treatment is not a failure if a person relapses. Relapses are a natural part of behaviour change and are to be expected. Therefore patients (and professionals) should be prepared for relapse and able to deal with it in a sensible and constructive way.

3.2.6 Harm Reduction

At the start of the treatment a large number of dual disorder patients will not agree that changing their substance use is necessary. In the absence of motivation to address either or both disorders, trust and the start of a working relationship can be built on working to reduce the negative consequences of alcohol and drug use. The consequences of having two serious disorders can indeed be very serious. Patients often face financial problems and are more often homeless. Poor nutrition and risky lifestyle choices will result in a range of health problems and increase the risk of infectious diseases. Harm reduction interventions are aimed to decrease the negative effects of problematic alcohol and drug use. Interventions include providing day- and night-time shelter, handing out meals, offering needle exchange facilities, and making condoms and other materials available.

3.2.7 Integrated Dual Disorder Treatment

The principles described above and the comprehensive care system based on them has been described and developed into detail by Mueser et al. (2003), in the model for *Integrated Dual Disorder Treatment* (*IDDT*). Although there are other integrated care models, this is the most elaborate one. Integrated treatment follows

Integrated Dual Disorder Treatment (IDDT)

The main principles of integrated treatment are:

- Integrated means:
  - one team
  - situated at one location
  - treating both disorders simultaneously
- Treatment is consistent with motivation for change in the patient
- Developed for severe mental illnesses

The basic components of integrated treatment

Knowledge about alcohol and drug use, as well as mental illnesses

Clinicians know the effects of alcohol and drugs and their interactions with mental illness;

- Clinicians provide services for *both mental illness and substance use* at the same time (instead of addiction first and mental health later or vice versa);
- *Stage-wise treatment*. All interventions are consistent with and determined by the patient's stage of treatment or recovery. The concept of stages of treatment (or stages of change) include:
  - *Engagement*: Forming a trusting working alliance/relationship.
  - *Motivation*: Helping the engaged patient develop the motivation to participate in recovery-oriented interventions.
  - *Action*: Helping the motivated patient acquire skills and support for managing illnesses and pursuing goals.
  - *Relapse Prevention*: Helping patients in stable remission develop and use strategies for maintaining recovery.
- Patients with DD are treated on a *long-term basis* with intensity modified according to need and degree of recovery and have access to *comprehensive services*
- For IDDT patients the program provides assertive *outreach*, characterized by some combination of meetings and practical assistance (e.g., housing assistance, medical care, crisis management, legal aid, etc.)
- All interactions with DD patients are based on *motivational interviewing* that includes: expressing empathy, developing discrepancy between goals and continued use, avoiding argumentation, rolling with resistance, instilling self-efficacy and hope
- *Substance abuse counselling* aimed at how to manage cues to use and consequences of use, relapse prevention strategies, drug and alcohol refusal skills, problem-solving skills training to avoid high-risk situations, challenging patients' beliefs about substance use; and coping skills and social skills training;
- *Group treatment* specifically designed to address both mental health and substance abuse problems

Fig. 1 (continued)

- *Family involvement* aimed at giving psycho-education about DD and coping skills to reduce stress in the family, and to promote collaboration with the treatment team;
- *Self-help:* clinicians connect patients with substance abuse or dual recovery in self-help programs
- Psychiatrists or others prescribing *medication* are trained in DD treatment and work with the patient and the IDDT team to increase medication adherence, to decrease the use of potentially addictive medication such as benzodiazepines, and to offer medication such as clozapine, disulfiram, or naltrexone that may help to reduce addictive behaviour
- *Interventions to promote health:* efforts are made to promote health through encouraging patients to practice a proper diet and exercise, find safe housing, and avoid high-risk behavior and situations. The intent is to directly reduce the negative consequences of substance abuse using methods other than substance use reduction itself;
- *Secondary interventions* are more intensive (and expensive) interventions that are reserved for people who do not respond to basic outpatient IDDT.

Fig. 3.1 Principles and components of Integrated Dual Disorder Treatment

the wishes and motivation of the patient. Treatment is multidisciplinary and combines pharmacological, psychological, educational, and social interventions to meet the needs of patients and the people around them. Integrated treatment seeks to actively involve the patient and his family in treatment. Working towards stable housing and meaningful daily activities are seen as essential for the road to recovery.

Integrated treatment is not an intervention aimed at one specific need such as, for instance, social skills training. It aims to redesign care systems, organizations as well as the care on an individual level to achieve positive change and recovery for dual disorder patients.

To accomplish this, the IDDT model is made up of a considerable number of components (Fig. 3.1).

The complexity of the IDDT model is both its strength and its weakness. Many organisations may not be prepared or even not be able to undertake such a far-reaching change. An organisation may decide to start with integrated treatment by making choices about setting, team or interventions. The guiding principles, however, must always be kept in mind to prevent a repetition of the negative consequences of the parallel and sequential treatment approaches.

3.3 Guidelines and Initiatives on Integrated Treatment

Integrated Dual Disorder Treatment (IDDT) was developed and studied by researchers at the Dartmouth Psychiatric Research Center (PRC) of the Dartmouth Medical School. The national implementation of the model was led by the Dartmouth PRC as well, via the Substance Abuse and Mental Health Services Administration. Technical support centres (such as the Ohio Substance Abuse and Mental Illness Coordinating Center of Excellence (CCOE)) participate in these national initiatives. The original IDDT programme was supported by a comprehensive set of materials, the implementation toolkit. This toolkit includes information for all stakeholders, educational materials (workbook), and fidelity scales. The IDDT fidelity scale is an important implementation tool and is designed to guide service organisations in their implementation of IDDT, the evidence-based practice, by focusing on the processes of organisational change and clinical change. The Fidelity Scales measures adherence to the Evidence-Based Practice as described in the toolkit. This is important since high fidelity is associated with better treatment outcome (Drake et al. 2004).

When the model was brought to Europe, however, it soon became clear that the model had to be "fitted" to match specific national situations. The position of addiction care services, for instance, is much more prominent in many European countries than the USA. This results in other dynamics. On the other hand, in America group treatment and self help are much more common than in most European countries. Despite these obstacles, the basic model of integrated treatment has been adopted all over Europe.

3.3.1 National Programmes

In the USA (and Australia) the implementation of integrated dual disorder treatment is largely organised on a national or state level. This seems to be more of a challenge for the European countries. Only the United Kingdom has a National Dual Diagnosis Programme.

In the United Kingdom the *National Dual Diagnosis Programme* (NDDP) was established in 2004/2005. Originally within the National Institute of Mental Health in England (NIMHE), then as a programme within Care Service Improvement Partnership (CSIP) and since April 2008 part of the Improving Mental Health Care Pathways programme within the National Mental Health Development Unit (NMHDU). The main aim of the programme has been to "actively promote and support the development of improvement in commissioning and service provision for people with a dual disorder and their families and carers, and to promote and embed the philosophy of 'mainstreaming' across mental health services to ensure that dual disorder is seen as everyone's business across health, social care and the criminal justice system" (Gorry and Dodd 2010).

The NDDP has commissioned the development of a range of products aimed at improving practices. Gap studies like the Dual Diagnosis Themed Review Report

(DH/NIMHE 2008) made it clear that the key to many of the difficulties experienced in the care for dual disorder patients, was improving the confidence and capabilities of the mental health and drug/alcohol workforce. Attention was therefore concentrated towards training and education. A capability framework was commissioned and produced which established a structured approach to identifying core skills, values, knowledge, and attitudes needed to work with dual disorder across all care settings (Hughes 2006).

3.3.2 Expertise Centres and Consortiums

In several European countries professionals and researchers in the field of dual disorders have formed consortia, societies, or expertise centres. These differ in scope, form, and size, but all are aimed at improving the quality of care and disseminating knowledge. Although there are contacts between some of these initiatives, so far no European wide initiatives have been organised. Described below are various types of national initiatives.

PROGRESS is a UK consortium of consultant nurses in dual diagnosis and substance, and works in partnership with the above mentioned National Dual Diagnosis Programme. Its aim is to improve the support and integrated treatment for individuals who have co-existing mental health and alcohol and drug difficulties.

In 2009, the web-based national resource was launched (www.dualdiagnosis.co.uk). This website wants to provide good quality information for individuals who have a dual disorder, their families and carers, and health and social care workers providing support and treatment.

In 2010, The National Dual Diagnosis Programme commissioned PROGRESS and Coventry University to develop an innovative online awareness raising resource relating to dual disorder. This Internet-based programme is free to access and aimed at clinical staff, people who use services and their carers, and other interested parties.

In the Netherlands, the *National Expertise Centre on Dual Disorders* (Landelijk Expertise-centrum Dubbele Diagnose, LEDD) started its activities in 2009. LEDD is a collaboration of the Trimbos Institute (Netherlands National institute of Mental Health and Addiction) and four mental health institutions: Mentrum (part of Arkin), GGzE and the Kempen, Palier (Parnassia Bavo Group), and Delta Psychiatric Centre. LEDD is established to help addiction care, mental health institutions, and other services with the process of implementing integrated treatment, through sharing knowledge and developing methodologies. LEDD also offers technical support and guidance. The website of LEDD (www.ledd.nl) offers a platform to all those working with dual disorder. In the last years a modular training programme has been developed and closer cooperation with the coordinating addiction organisations has taken place.

In Spain, the *Spanish Society of Dual Disorders* (Sociedad Española de Patología, SEPD) was founded in 2005. The society has over 1,600 members: multidisciplinary professionals, clinicians, and researchers. EDPS is scientifically

and medically orientated and aims to promote the study and development of dual disorder treatment and areas that are related, to offer scientific and technical assistance, teaching, and research. Among the activities of SEPD are training of professionals in the field of dual disorder; disseminate and raise awareness of the problem of dual disorder among professionals, government, and society in general and taking action to reduce the double stigma in dual disorder.

The *Swedish Network on Dual Diagnosis* (Svenska nätverket Dubbeldiagnoser, SN-DD) is a initiative that began in 2004. The main purpose of the network is to promote the development of care that meets the needs of dual disorder patients and the thought to improve their quality of life. Other activities are the monitoring of research and development of methodology and cooperating with other networks (including user organisations), to create a consensus based on research and experience. Unlike the above mentioned initiatives, the Swedish network includes representatives from municipalities, counties, correctional and private actors operating in the health-care sector.

3.3.3 Guidelines

Several European guidelines on dual disorders have been published in the last decade, though often aimed at a specific combination of a mental health disorder and substance use. The Spanish Society of Dual Disorders (SEPD) has, for instance, published a set of seven protocols for the clinical treatment of dual disorder patients (depression, anxiety, personality disorder, ADHD, schizophrenia, bipolar disorder, and treatment of adolescents). A training programme is linked to these protocols.

In the Netherlands, in 2003 the guideline "Dubbele diagnose Dubbele hulp, Richtlijnen voor diagnostiek en behandeling" (dual diagnosis, dual help, guidelines for diagnostics and treatment) was published Ontwikkelcentrum Kwaliteit en Innovatie van Zorg 2003. This in the same year that Mueser and his colleagues published their book on integrated treatment and there are many references in the Dutch guideline to their earlier publications and studies.

The report contains instruments and guidelines for screening en diagnostics.

As far as treatment is concerned there are no actual guidelines but it offers an overview of state-of-the-art scientific insights. The guideline has not been updated since. In national multidisciplinary psychiatric guidelines, however, more and more attention is given to co-occuring alcohol- and substance abuse.

In 2002, a framework for practice around dual disorder "Dual Diagnosis Good Practice Guide" had been produced by the English Department of Health. Then in 2011, the well-known English organisation National Institute for Health and Care Excellence (NICE), published the guideline "Psychosis with coexisting substance misuse. The NICE guideline on assessment and management in adults and young people". This is the first guideline in which NICE specifically addresses a co-occuring disorder. This guideline is relevant for adults and young people (aged 14 years and older) with psychosis and coexisting substance misuse and covers the care provided by primary, community, secondary, tertiary, and other health-care professionals.

The guideline opens with personal accounts of dual disorder patients and continues with chapters on assessment and care pathways, service delivery models, psychological and psychosocial interventions, pharmacological, and physical interventions. It concludes with a specific chapter on young people with psychosis and coexisting substance misuse.

3.4 Other Related Models

Although the most comprehensive and best researched, the IDDT model is not the only model for integrated treatment.

The Kingston Community Drug and Alcohol Team Dual Diagnosis Service (CDAT) (Lowe and Abou-Saleh 2004). This model combines interventions aimed at substance abuse with interventions based on mental health. CDAT is a multidisciplinary team of health and social care workers that provides assessment, detoxification, care planning, residential referrals, and day programmes. It also provides information, advice, counselling support, and acupuncture for people with drug and/or alcohol problems; home visits; liaison with statutory and voluntary agencies; prescriptions (in some cases); and specialist care for children and families and those with a dual disorder.

CDAT delivers integrated treatment by providing proactive outreach and positioning a CDAT link clinician in different settings. This professional supports assessment of dual disorders attends relevant meetings; identifies cases which should be dually assessed and gives feedback on cases to relevant organisations.

Behavioural Treatment for Substance Abuse in Serious and Persistent Mental Illness (BTSAS). BTSAS (Tenhula et al. 2009) is designed to reduce drug abuse in people with severe and persistent mental illnesses (SPMI) by incorporating strategies effective for treating substance use in primary substance abusers but modifying these strategies to make them more useful for people with SPMI. BTSAS is a highly structured group intervention with groups meeting twice per week for 6 months. It is a social learning treatment that is comprised of several interrelated components:

- Individual motivational interviews to discuss consequences of drug use, explore reasons for reducing use, and select a goal drug to focus on in BTSAS.
- Contingency management (CM) using urinalysis to reward reductions in use or abstinence.
- Collaborative goal-setting to identify specific and realistic short-term goals related to reducing drug use.
- Social skills training to teach drug refusal skills, enhance non-drug social contacts, and provide success experiences that increase self-efficacy for change.
- Psycho-education about the impact of drug use on individuals with SPMI, including reasons for use as well as particular dangers of use for persons with SPMI.
- Relapse prevention training to help participants manage urges to use drugs and other high-risk situations, as well as lapses in use.

The *Comorbidity Programme Audit and Self-Survey for Behavioural Health Services* (*COMPASS)* provides a service for people who experience severe and enduring or complex mental health difficulties (such as schizophrenia, psychosis, bipolar disorder, depression, and personality disorder) and who also use drugs and/or alcohol problematically. The programme began in 1998 and represents an "integrated shared care" approach and services people within the Northern Birmingham Mental Health NHS Trust. The service model aims to achieve integration of treatment both at the clinical and service level. Like the IDDT model, COMPASS is aimed at training and supporting staff within mental health settings, particularly assertive outreach teams, to deliver integrated treatment. If more specialised input is needed the addiction care is brought in. Cooperation is based on shared care agreements and protocols. Patients with mental health problems remain engaged with and case managed by mental health services, and if necessary care is shared with substance misuse services. In this respect, the COMPASS-model is still partly based on the parallel care model.

Compass staff provides the following within their service:

- Care coordination
- Screening and assessment
- Clinical assessment of drugs/alcohol
- Case formulation
- Treatment planning
- Engagement and building motivation to change
- Negotiating behaviour change
- Early relapse prevention
- Relapse prevention and relapse management
- Skills building and coping with different moods

Cognitive–Behavioural Integrated Treatment (C-BIT) In 2004, Graham et al. published a manual for cognitive–behavioural integrated treatment for substance misuse in people with severe mental health problems. They did this in cooperation with the developers of the IDDT model and followed the same principles. The overall principle of C-BIT is to help patients negotiate and maintain behaviour change related to their alcohol/drug use.

The aims of C-Bit are threefold:

(1) to identify, challenge, and undermine unrealistic beliefs about drugs or alcohol that maintain problematic use and to replace them with beliefs that will strengthen behavioural change, (2) to facilitate an understanding of the relationship between the substance abuse and the mental health problems, and (3) to teach specific skills to control and manage substance use and early symptoms and to develop social support for an alternative lifestyle.

The C-Bit programme consists of:

- An assessment phase: screening and assessment.
- Four treatment phases: engagement and building motivation to change; negotiating some behaviour change; early relapse prevention; relapse prevention; and relapse management.
- Two additional treatment components that are optional and designed to be used parallel with the treatment phases: skills building and social network members.

There are several other integrated psychotherapeutic approaches for dual disorder patients. These include Dual Recovery Therapy (DRT) (Ziedonis et al. 2005), Modified Cognitive Behavioural Therapy (Bellack et al. 2006), Modified Motivational Enhancement Therapy (MET) (Carey et al. 2007), and The Substance Abuse Management Module (SAMM) (Roberts et al. 1999). The main focus of these approaches is relapse prevention. They are more similar than different and all include elements of motivational enhancement, relapse prevention and social skills training, as does C-BIT. What sets them apart is their stronger focus on recovery and use of modified 12-step meetings (such as Dual Recovery Anonymous) (Ziedonis et al. (2007). None of the mentioned programmes offers the wide scope of the IDDT model which is aimed at organisation as well as treatment.

3.5 Dual Disorder Service Provision in Europe

The European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) included a section on co-morbidity with psychiatric disorders in their annual report of 2004. They named several obstacles to the treatment of co-morbidity in Europe. Firstly, psychiatric staff generally lacks knowledge on drugs and drugabuse-treatment and drug-treatment staff lacks knowledge about psychiatry. Secondly, the two specialties are built on different paradigms: psychiatry is medically and science based and tends to protect persons and the public. Addiction care is largely based on psychosocial methods and theories (though more and more on medical science as well) and expects patients to be motivated, to some degree, and to attend and comply with treatment. These different points of departure often prevent a global, integrated perception.

A quick scan among European countries led to the following, rather discouraging picture: A survey among Austrian psychotherapists revealed that only some are willing to admit drug-addicted patients as patients (Springer 2003). From Italy it is reported that there are no clear rules for the referral of patients from drug treatment services to mental health services and that there is resistance in mental health services because of lack of expertise. In Norway, referral from low-threshold drug services to psychiatric treatment is reported to be difficult. In Greece, 54 % of the drug-treatment programmes do not admit drug users with psychiatric disorders. In drug-free residential treatment in Slovenia, and also in other countries, treatment programmes require patients to be drug-free as a

condition for admission. In the case of dual disorder patients, this presents a serious obstacle, as complete abstinence would require the termination of other treatments, which is not always possible (EMCDDA 2004).

More recent, in 2011, a comparative European study was published that looked at the nature, level and type of networking for dual disorders patients (Baldacchino et al. 2011). The *Integrated Services Aimed at Dual Diagnosis and Optimal Recovery from Addiction* (ISADORA) project is a pan-European project carried out from November 2002 to October 2005. Seven sites across Europe collaborated on the project: Maison Blanche Hospital, Paris, France; University Hospital of Tampere, Finland; University of Dundee, Scotland; Institute of Psychiatry and Neurology, Warsaw, Poland; Middlesex University, London, England; Cambridge University and Peterborough Psychiatric Services, England and Aarhus County Psychiatric Services, Aarhus, Denmark. One of the first aims was to map service options and care coordination for people with dual disorder at the different European centres.

Although 50–90 % of the centres at the different ISADORA sites report some level of networking, only 32 % share patient records and have a joint care agreement in place with at least one other centre.

The reasons that were named for this low level are a lack of clear policy and network organisation that would allow coherent care pathways for patients and inadequate knowledge and skills about co-morbidity. There are no structures for cooperation. Collaboration is often restricted to informing and advising patients about other centres. The study concludes by stating that there is a need for formal and long-term treatment systems, to adequately respond to the complexities and varieties of problems that dual disorders patients present.

It is obvious that the implementation of integrated treatment is quite a challenge. It is not a single training programme or technique such as motivational interviewing. Starting integrated treatment involves a complex process of change that requires time and attention, not unlike the recovery process of dual disorder patients themselves.

The last decade of experience with implementing integrated treatment (in the USA specifically) has resulted in insight which factors are crucial for a successful implementation. Brunette et al. (2008) looked at the process in eleven American community mental health centres that participated in a large study of practice implementation. They identified the following facilitators and barriers that are supported by for instance the Dutch experience (van Wamel et al. 2009, van Giffen et al. 2012):

1. *Leadership*. Positive results are largely dependent on the presence of not only an enthusiastic, but able project leader, (top-down) guidance and motivated workers. The leader must be able to challenge and motivate workers, to prioritise the workload and to make logistic, strategic, and financial choices to enable change. A dually organised management structure, with two administrators, one with administrative skills and one with advanced clinical expertise, seems favourable for successful implementation.

2. *Consultation and training*. Consultation is aimed at initial and ongoing implementation plans, including the type and timing of implementation activities. Training enables staff and leaders in the information and skills necessary to deliver the service. Both are of great importance. It is recommended that organisations seek advice from experts on how to shape both process and content of integrated treatment.
3. *Supervision*. Supervision and coaching are essential to work in accordance with the principles of integrated dual disorder treatment. Workers need to be kept alert in the initial implementation phases. Brunette et al. (2008) recommend both individual and team coaching to facilitate the development of a shared vision from with to offer integrated care.
4. *Staff turnover*. High staff turnover is a negative factor in the continuity of care and the implementation process. Unfortunately, many health-care organisations experience significant staff turnover. Reasons may be that staff is unwilling to address dual disorders in which case hiring new staff may actually facilitate the implementation. Chronic staff turnover, however, appeared to be a much more difficult barrier, creating training and supervisory challenges. Even more difficult are periods of recession when teams are short-staffed for long periods, resulting in high work pressure. Prioritising and focussing on implementing one or a few key components may be all that is feasible in such a period.
5. *Finances*. Organisations who struggle with the implementation of integrated treatment often expressed concern about the financial implications of making organisational changes and providing training and supervision.

Conclusion and Recommendations

In the past decades, the awareness has grown that the treatment of patients with co-occuring psychiatric and substance/alcohol abuse disorders is complex and deserves special attention. Not only does it involve a large group of patients, but the problems these patients are confronted with have an impact on different areas of their lives and often interact with each other in a negative way.

Experience and research shows that caring for both problems separately, in most cases, does not lead to the desired results. This realisation has led to the development of integrated treatment methods. Although research generally shows positive results, the proven effectiveness of the approach is still insufficient. Nevertheless, experts and current guidelines advise integrated treatment as the current state of the art for the treatment of people with addiction and mental illness.

Dual disorder patients typically lead chaotic lives in which things seem to "happen" to them. They experience problems in different areas. They are not helped by treatment that is based on different approaches, visions, and expertise. Split care is time consuming and frustrating for care givers, let alone for people who have already—to a large extent—lost the grip on their lives.

The premise is integrated treatment, that takes the different disorders and problems in other areas into account, which should really be the case in all good care. In this approach, professionals start with evaluating, with the client, what would help this person, at this moment, the most.

There may be certain combinations of disorders, such as depression or an anxiety disorder and addiction that can be treated through a sequential model. In these examples treatment should start by addressing addiction first, since in many cases the psychiatric symptoms have been to shown to diminish.

But more often the psychiatric problem and the addiction problem are intertwined and so many other problems are thrown into the mix that an integrated vision and a consequent treatment are unavoidable. The prevalence of co-occuring psychiatric substance abuse disorders is higher than can be expected on the basis of the prevalence in the general population. This points towards an underlying common, possible neurobiological, factor for the development of both disorders. Therefore, treatment should be provided from an integrated system.

Patients themselves have questions about the relationship between their psychological problems and drug or alcohol use. The reasons they give for their use are the need to belong to a group, but more importantly, dealing with unpleasant, negative feelings. Not wanting to feel anxiety, sadness, or remembering traumatic experiences are important reasons for drug and alcohol use.

Experiences with integrated treatment have shown that dual disorder patients are no longer referred from one service to another without receiving the care they need. Treatment is patient-oriented and based on their motivation, wishes, and goals.

Integrated treatment also leads to more overall quality improvement. Up to date, integrated treatment plans, thorough screening, assessment and diagnostics, continuity of care, and varied treatment provision. Professionals develop a more patient-oriented attitude, learn to understand the mechanisms of addiction and accompanying problems and learn to use motivational skills.

They understand the connection between addiction and psychiatry and learn to regard dual disorder treatment as a long-term process. A process based on small, feasible goals that takes the limitations and incapacities of the patient into account, and especially relapses.

Experience has also shown that the implementation of integrated treatment is no small feat. The IDDT model may be the most comprehensive, but it has its drawbacks. The model focuses strongly on organisational change, as it should, since so many implementation barriers are organisational. But teams that are implementing integrated dual disorder treatment report that the treatment content should be expended with more recently developed interventions as for instance Seeking Safety (trauma and addiction) and the Community Reinforcement Approach.

The European studies have shown that there are still a lot of patients who do not receive integrated treatment. However, in recent years more and more integrated teams, departments and organisations have been established that offer dual disorder treatment programmes, suited to the variety of problems and based on available evidence. We applaud this development and expect that the distinction between care for substance abuse and mental health will, in time, be dissolved.

References

Baldacchino A, Greacen T, Hodges CL, Charzynska K, Sorsa M, Saias T, Clancy C, Lack C, Hyldager E, Merinder LB, Meder J, Henderson Z, Laijarvi H, Baeck-Moller K (2011) Nature, level and type of networking for individuals with dual diagnosis: a European perspective. Drugs Educ Prevent Pol 18(5):393–401

Bellack AS, Bennett ME, Gearon JS, Brown CH, Yang Y (2006) A randomized clinical trial of a new behavioral treatment for drug abuse in people with severe and persistent mental illness. Arch Gen Psychiatry 63:426–432

Brunette M, Asher D, Whitley R, Lutz W, Wieder B, Jones A et al (2008) Implementation of integrated dual disorders treatment: a qualitative analysis of facilitators and barriers. Psychiatr Serv 59:989–995

Carey KB, Leontieva L, Dimmock J, Maisto SA, Batki SL (2007) Adapting motivational interventions for comorbid schizophrenia and alcohol use disorders. Clin Psychol 14(1):39–57

Chow MC, Wieman D, Cichocki B, Qvicklund H, Hiersteiner D (2012) Mission impossible: treating serious mental illness and substance use co-occurring disorder with integrated treatment: a meta-analysis. Ment Health Subst Use 6(2):150–168

Departement of Health United Kingdom (2002) Dual diagnosis—good practice guidance. Mental Health Policy Implementation Guide

Dijkhuizen A, van Wamel A, Kikkert M (2013) Geïntegreerd behandelen. In: Dom G, Dijkhuizen A, van der Hoorn A et al (eds) Handboek Dubbele Diagnose. De Tijdstroom, Utrecht, pp 13–28

Drake RE, Wallach MA (2000) Dual diagnosis: 15 years of progress. Psychiatr Serv 51(9):1126–1129

Drake RE, Mueser KT, Brunette MF, McHugo GJ (2004) A review of treatments for people with severe mental illnesses and co-occurring substance use disorders. J Psychiatr Rehabil 27 (4):360–74

Drake RE, O'Neil EL, Wallach MA (2008) A systematic review of psychosocial research on psychosocial interventions for people with co-occuring severe mental and substance use disorders. J Subst Abuse Treat 34:123–138

European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) (2004) Selected issue. In: EMCDDA 2004 Annual report on the state of the drugs problem in the European Union and Norway

Flores P (2001) Addiction as an attachment disorder: Implications for group therapy. Int J Group Psychother 51(1):63–81

Gorry A, Dodd T (2010) Dual Diagnosis National Programme Legacy Report. National Dual Diagnosis Programme

Graham HL (2004) Cognitive-behavioural integrated treatment (C-BIT). A treatment manual for substance misuse in people with severe mental health problems. Wiley, Chichester

Hughes L (2006) Closing the gap: a capability framework for working effectively with people with combined mental health and substance use problems (dual diagnosis). Centre for Clinical and Academic Workforce Innovation (CCAWI), Mansfield

Lowe AL, Abou-Saleh MT (2004) The British experience of dual diagnosis in the national health service. Acta Neuropsychiatrica 16(1):41–46

Mueser KT, Noordsy DL, Drake RE, Fox L (2003) Integrated treatment for dual disorders: a guide to effective practice. Guilford, New York

National Institute for Health and Clinical Excellence NICE (2011) Psychosis with coexisting substance misuse (CG120), Clinical guidelines. NICE, London

Osher FC, Kofoed L (1989) Treatment of patients with psychiatric and psychoactive substance abuse disorders. Hosp Community Psychiatry 40:1025–1030

Prochaska JO, DiClemente CC (1983) Stages and processes of self-change in smoking: toward an integrative model of change. J Consult Clin Psychol 5:390–395

Prochaska JO, DiClemente CC, Norcross JC (1992) In search of how people change. Am Psychol 47:1102–1114

Ridgely MS, Osher FC, Goldman HH, Talbott JA (1987) Executive summary: chronic mentally ill young adults with substance abuse problems: a review of research, treatment, and training issues. Mental Health Services Research Center, University of Maryland School of Medicine, Baltimore

Roberts LJ, Shaner A, Eckman TA (1999) Overcoming addictions. Skills training for people with schizophrenia. W.W. Norton and Co., New York

Tenhula WN, Bennett ME, Strong Kinnaman JE (2009) Behavioral treatment of substance abuse in schizophrenia. J Clin Psychol 65(8):831–841

Torrey WC, Drake RE, Dixon L et al (2001) Implementing evidence-based practices for persons with severe mental illnesses. Psychiatr Serv 52:45–50

van Giffen M, Stolker JJ, van Rooijen S (2012) Implementatie van geïntegreerde behandeling volgens motivationele principes. In: Dom G, Dijkhuizen A, van der Hoorn A et al (eds) Handboek Dubbele Diagnose. De Tijdstroom, Utrecht, pp 95–109

van Wamel A, Kroon H, van Rooijen S (2009) Systematic implementation of integrated dual disorder treatment in the Netherlands. Ment Health Subst Use 2:101–110

Ontwikkelcentrum Kwaliteit en Innovatie van Zorg (2003) Dubbele diagnose, dubbele hulp. Richtlijnen voor diagnostiek en behandeling. Rapport project Dubbele Diagnose door Verslavingszorg Parnassia, psycho-medisch centrum Den Haag

Ziedonis DM, Smelson D, Rosenthal RN, Batki SL, Green AI, Henry RJ et al (2005) Improving the care of individuals with schizophrenia and substance use disorders: consensus recommendations. J Psychiatr Pract 11:315–339

Ziedonis D, Yanos PT, Silverstein M (2007) Relapse prevention for schizophrenia. In: Witkiewitz KA, Marlatt GA (eds) Therapist's guide to evidence-based relapse prevention. Academic, London

4 Care for Patients with Addiction and Concurrent Disorders in Europe, The United States of America, and Canada: Similarities and Differences

Michael Krausz, Marc Vogel, and Markus Ploesser

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Abstract

Dual disorders represent a major burden of disease in both North America and Europe. However, there are important differences concerning health systems and their financing as well as vulnerable subpopulations. Due to financial barriers or

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structural deficits, emergency rooms often provide the only available care for patients in the USA and Canada, while stepped care approaches are more common in Europe. Differing attitudes and policies impact on treatment paradigms, such as harm reduction, abstinence, or opioid maintenance treatment. These differences can be observed not only on a transatlantic but also on an intra-European level. Structural components and clinical pathways lead to dissimilarities in access to care, particularly detoxification, rehabilitation, and community services. The role of primary care as an important treatment interface is much more recognized in Europe. While innovation is on-going and great scientific progress has been made in the treatment of dual disorders in recent years, the implementation of these findings into "real-world practice" has been insufficient so far.

4.1 Introduction

There has been an increase of scientific attention in North America on the coincidence of addiction and other mental illness since the 1980s (Alterman 1985; Drake et al. 2008). One reason of this was the observation that substance use among psychotic clients was highly related to treatment drop-out, low retention, and worse outcomes. Classification systems at that time (ICD-9 and DSM-III) did not allow a more descriptive diagnostic approach. They summarized so-called secondary symptoms under the main categories, which supported significant neglect towards more differentiated treatment needs. The neglect of harmful substance use among patients with severe mental illness was typical internationally, having been well documented as clinical evidence as early as the beginning of the twentieth century for schizophrenic patients in hospital care (e.g. by Bleuler 1911).

The paradigm shift towards the descriptive psychopathology in ICD 10 (World Health Organization 1992) and DSM III-R (American Psychiatric Association 1987) addressed that trend and accommodated the fact that dual disorders are more a rule than an exception (Wang et al. 2005).

In response to the obvious clinical problems and special needs of these clients, particularly discussed and acknowledged for the coincidence of psychosis and addiction (Drake et al. 2008), specialized programmes were set up in the USA and very soon in Europe, too. These developments and their outcomes provide an opportunity to study and understand health-care system change in mental health based on research and paradigm shift in substantially different frameworks.

Importantly, despite more attention and some regional initiatives, the care for patients with dual disorders remains one of the biggest problem areas in the system of care (Committee on Crossing the Quality Chasm 2006).

Only every 10th client in the USA is seeing a specialist and 1/3 get professional care mainly through family medicine, while 2/3 receive no help from the system. The coverage in most of Western Europe is slightly better but with the same delay

in interventions and little support for those with addiction and concurrent mental disorders (Wienberg 2001). It takes on average 10 years from first symptoms to first professional interventions.

The United States represent one extreme version of a health-care system based on private insurance models, while many European countries function in the framework of public health care, with general insurance for everybody and sometimes optional additional private insurance. As one of President Obama's most important reform bills, his health-care initiative aims to provide health insurance for everybody.

Canada has a "single payer system", going farther than most European concepts. Due to the "Canada Health Act" (Madore 2005), health care is freely available to everybody and directly funded by the government. These different approaches allow for a very interesting "quasi-natural experiment" comparison and the discussion of a client and needs centred service delivery model.

4.2 Same Burden of Disease, Same Stigma, Different Cultures of Care

4.2.1 Epidemiology in the System

Substance use disorders and concurrent mental illness represent a comparable burden of disease on both continents (Wienberg 2001; Kessler and Merikangas 2004). However, between the USA, Canada, and Europe, but also between poor and rich countries in Europe itself, substantial differences exist in the proportions of subpopulations of complex patients and the barriers to support and health care.

The prevalence of individuals with addiction and mental illness is increasing when moving from the outside to the inside of the system of care. In emergency rooms (ERs) and acute care, patients with substance use disorders and additional mental as well as physical health concerns are more the rule than the exception (see Fig. 4.1). In North America it is a reflection of the existing system of care with little or no capacity for tertiary care services or comorbidity experts in the community. So the populations with high needs are not served and access the system only as emergency cases.

So if you move from milder symptoms not in need of acute or emergency care (level in front) towards a crisis and the need for acute care (level in the back) the complexity of symptoms increases, concurrent disorders become the rule and not the exception.

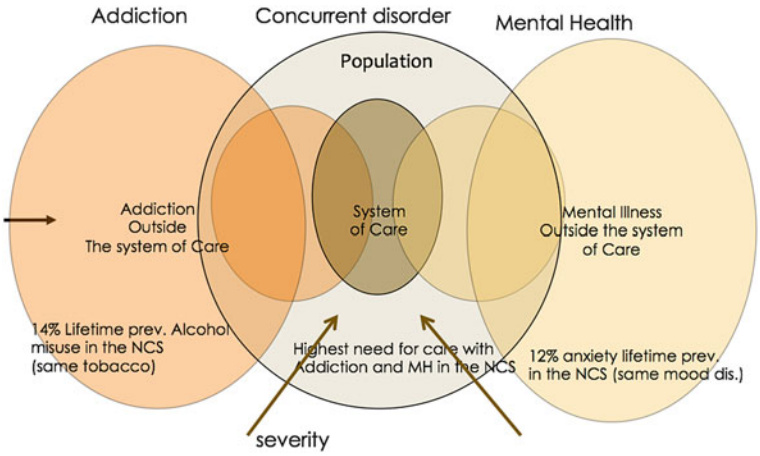

Fig. 4.1 Severe addiction and mental illness (SAMI) based on population and in the system of care; *NCS* National Comorbidity Survey (Kessler and Merikangas 2004)

4.2.2 Special High Need Populations

Patients with addiction and concurrent mental disorders form part of very different populations with all levels of social functioning. This is resulting in varying additional support needs, access to care and treatment options. Due to different social and health-care systems it is important to acknowledge these subpopulations with specific challenges for the system of care and society as a whole in both North America and Europe.

The ongoing *First Nations* and Native American health-care crisis (Krausz 2008; Spittal et al. 2007) is specific to North America. The indigenous population is in an especially critical state due to bad living conditions on reserve, social marginalization, and extreme levels of trauma, substance use, and lifestyle-related physical illness such as metabolic syndrome and obesity, with little or no health care available in their communities. They are also overrepresented in all particularly marginalized groups as homeless, in foster care, or early imprisonment. The prevalence of complex concurrent disorders is much higher than elsewhere in the society (Spittal et al. 2007).

Vulnerable urban populations (Krausz et al. 2013; Linden et al. 2013), including those living in substandard housing or homeless, are typical for large metropolitan areas. In large cities, poor neighbourhoods, like Vancouver's *Downtown Eastside,* are of special concern. They are known for extreme levels of harmful substance use, trauma, and mental illness (Krausz et al. 2013), and difficulties in provision of appropriate care due to the housing situation. That was the reason for a National research demonstration project in Canada, the *At-Home—Chez Soi* project (Goering et al. 2011), exploring housing and support for mentally ill homeless in five Canadian centres. It demonstrated that "housing first" with appropriate community

support enables recovery even of severely affected dual disorder patients (Schutz et al. 2013).

Migrants arriving in a new country are often amongst those listed as a vulnerable group. Language barriers, traumatic experiences, and insecure legal status can further complicate access to any support. In Canada and the USA, migrants in this category form a subpopulation nearly excluded from formal health care (Kluge et al. 2012). Even those able to access the systems have difficulties finding culturally appropriate programmes. In Vancouver, nearly 50 % of the people are of Asian origin, and in California Spanish has become the dominant language.

In Europe, other regionally differing cultures are suffering from exclusion, foremost those of African origin or individuals from the former Soviet Union member states and their political satellites. Even though there are specific programmes for migrants, they often suffer from the separation of treatment systems for substance use and mental health. This can lead to exclusion of patients with substance use in the case of psychiatric centres, or exclusive psychosocial support lacking medical assistance where services are provided by social workers in specific multicultural drug-counselling units.

4.2.3 Stigma and Marginalization in the System of Care

Addiction and mental illness are arguably the most stigmatized and structurally discriminated conditions in health care worldwide. The burden of disease particularly among young people is among the highest of all medical conditions and still growing, and the mortality is huge. Despite these stark facts, compared to other areas of health care, mental health and addiction remain the most underfunded area of medicine (Livingston et al. 2012).

4.2.4 Culture of Care

Stigma, poverty, homelessness and social marginalization, and substance use, mental and physical comorbidities form a vicious circle. Combined with the lack of specialized services these patients are frequently not in any regular mental health-care programmes. Consequently, these people often tumble from crisis to crisis and use ERs as their only access to care.

ERs in North America are often overcrowded and have little to offer in terms of treatment. Moreover, ER's are not funded or equipped to replace community services, especially for high need patients with complex concurrent disorders.

If families in North America can afford private treatment programmes, either residential or community based, a range of specialized providers are available. Particularly university-affiliated clinics offer standardized programmes (Savage et al. 2007; Torchalla et al. 2012) with proven effectiveness. But overall, these are neither accessible nor affordable for the average patient and relevant only for a small minority.

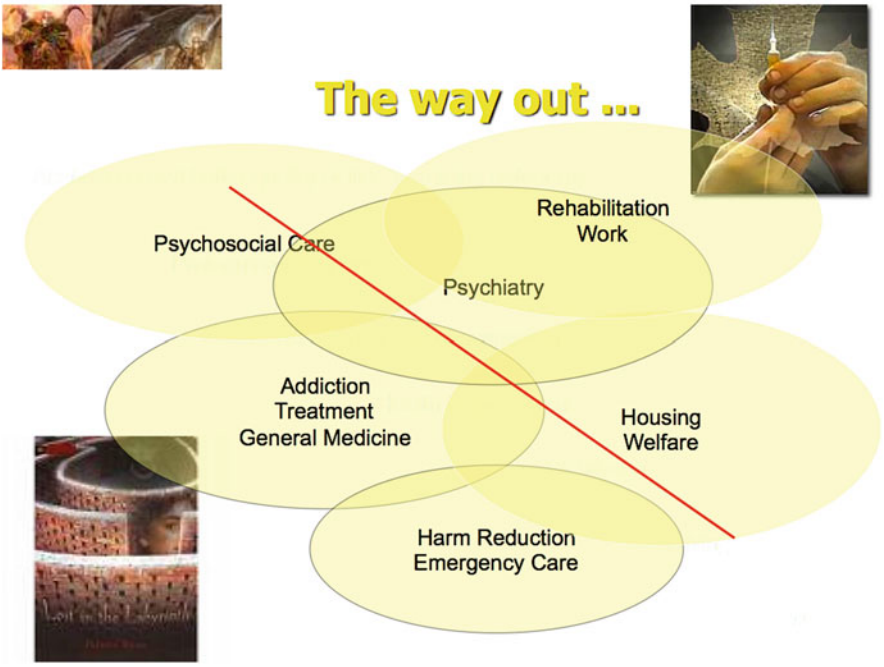

Fig. 4.2 Levels of care

With structural and funding problems in European countries similar trends can develop. Nevertheless clinical pathways and a coherent approach to care are far more common in Europe. Particularly effective are established pathways in the Netherlands with stepped care approaches (Schippers et al. 2002) or Switzerland and Germany (Wienberg 2001).

The Canadian culture of care is similar to the European system. However, while everybody has a right to be treated, the services needed for stepped care such as are mostly missing, so the ERs become the inefficient hub of triage and care.

So as shown in Fig. 4.2, ideally different levels and models should and could connect in clinical pathways (represented through the line), which unfortunately is often not the case. Even if the capacities are available, which is an exception, they are not integrated and connected.

4.3 Treatment Paradigms and Goals

The last two decades have been dynamic in terms of paradigm shifts in the area of mental health and addiction. Nearly every essential concept from harm reduction over methadone substitution, and controlled consumption to abstinence based care was questioned and subject to national and international reviews (e.g. European

Monitoring Centre for Drugs and Drug Addiction (EMCDDA) standards; Heroin assisted treatment (HAT); Harm reduction).

Substantial regional differences in best practice, especially in the treatment of addiction, significantly impact the treatment of dual disorders. The dominant paradigms changed in Europe as well as in the USA and Canada as a result of drug policy under pressure, the response to the HIV epidemic, and the obvious failure of the abstinence focused system of care.

In psychiatry, the neglect of substance use of patients with severe persistent mental illness in treatment undermined psychosocial treatment programmes and lead to low retention and compliance in the hospitals as well as community care. Single programs such as those in Dartmouth, USA (Alterman 1985; Drake et al. 2008), Hamburg, Germany (Krausz and Müller-Thomsen 1994) or Bern, Switzerland (Moggi et al. 2002) or Antwerp, Belgium (Morrens et al. 2011) started to address treatment of comorbid disorders, in particular of psychosis and addiction.

One of the most important lessons of the last decades is that treatment capacity, funding, best practice, and health politics are not only influenced by evidence but also and sometimes foremost by economic considerations and political priorities. Even drastic mortality rates and high public health risks are not per se a reason for most governments to respond. On the other hand, the implementation of harm reduction programmes as well as heroin-assisted treatment is demonstrate the major impact of clinical innovation. They saved thousands of lives, prevented life-threatening infections such as HIV and supported recovery on a large scale.

4.3.1 Harm Reduction

Why is the harm reduction paradigm of any relevance to the treatment of patients with mental illness and severe substance use? There are three reasons:

1. Due to their risk behaviours comorbid patients are very vulnerable to severe infections and physical harm (Dausey and Desai 2003) and need protection and support.
2. For those with dual disorders, access to the system is more complicated due to system thresholds, social marginalization, and homelessness but also due to some clinical disabilities like cognitive impairments. In the BC Homelessness survey we showed, that the sicker patients were, the more difficult it was for them to get appropriate support (Krausz et al. 2013). Harm reduction programmes are an important entry point to connect to mental health or addiction care.
3. Harm reduction is one of the oldest medical principles and the common ground for treatment approaches beyond. Without survival, prevention of physical harm and trauma, any recovery may be impossible. When the "harm" in harm reduction is defined a little wider than just AIDS, e.g. by including social deterioration, deprivation or criminalization, then it becomes obvious that this is a prerequisite for any further step. The identification of dual disorder patients

along with provision of psychiatric services in harm reduction facilities would be "low threshold" indeed. An example of such an intervention is the provision of opioid maintenance treatment (OMT) in safe injection facilities established in some Swiss cities today.

The US government and its funding agencies have only recently opened up to "harm reduction" strategies and approaches. Until the Obama presidency "harm reduction" was more of a "non-word", which might well have influenced the decision of the National Institute of Drug Addiction (NIDA) to withhold funding or any other support from programmes pursuing such harm reduction approach.

Canadian provincial governments, which are in charge of health-care legislation and organization, took a different route, sometimes in conflict with the Federal government in Ottawa. The only official "safe injection site" in North America today, opened in Vancouver backed by the provincial government in British Columbia (BC). *Insite* in Vancouver is still questioned and legally battled by the conservative Canadian federal government (Wells 2011), despite needle exchange and similar low threshold programmes being widely accepted since the HIV epidemic.

In Europe, harm reduction strategies were implemented first in Switzerland, Germany, and the Netherlands in the 1980s with a lag of about 10 years in the southern European states as Spain, Italy, and Greece. This led to up to tenfold differences in the HIV prevalence rate between states. For example in Hamburg, the prevalence rate is about 3 % but in Barcelona about 30 % (EMCDDA 1999). The joint EU guidelines on harm reduction are the result of that experience. Even fierce opponents of harm reduction changed their approach based on an unfortunate "natural public health experience" with hundreds of thousands infected and dying of HIV despite knowledge of what could help to prevent it.

4.3.2 Abstinence and Controlled/Moderate Use

Internationally, most mental health programmes for the treatment of comorbid patients are based on abstinence as treatment prerequisite and certainly as a treatment goal. This is based on the conceptual understanding that substance use including alcohol and cannabis can trigger psychotic symptoms or mood swings. In most Canadian and US health-care institutions, supported housing and other social services, even moderate substance use is unacceptable. Noncompliant patients are either forced to abstain through certification or seclusion, or are denied access to care (e.g., in residential care settings). With this approach the most vulnerable urban populations with complex concurrent disorders and long histories of severe substance use are again excluded from care and social support.

It is only recently that in Germany OMT patients are allowed to participate in residential rehabilitation programmes, which play a major role in the German addiction treatment system. Similarly, there was a trend in Switzerland over the past 15 years in favour of acceptance of OMT in these institutions.

Specialized programmes working with the full range of addiction treatments in medicine are rare. Psychiatry is thus accepting a situation where we are not able to help complex concurrent disorder clients.

In response to the lack of alternatives some treatment providers in Canada have started pilot projects with severely alcohol dependent patients to prevent them from drinking very harmful "non-beverage alcohol" such as hand sanitizer with up to 80 % alcohol, easy to find in any emergency department. These programmes distribute hard liquor to severe alcohol dependent patients in a controlled way, sometimes along with case management.

Despite the scepticism among the AA community, the discussion on "controlled use" initiated a new approach in places such as in Germany (Koerkel 2002). The idea behind this is that for some it is possible to control and limit their use to a non-harmful level. This is much better to try in a structured and supported environment.

The Burnaby-based treatment centre for mental health and addiction is a Canadian example of a service focusing especially on patients (Schutz et al. 2013) with a long history of trauma, severe substance use, and physical as well as mental illness. The goal still is abstinence but with the approach, that relapse is part of the disorder necessitating constructive attention and not exclusion.

4.3.3 Maintenance

Treatment goals and legal regulations of OMT differ not only between North America and Europe. While abstinence is still the mandatory goal in Germany, and treatment providers are sometimes forced to terminate OMT in case of on-going substance use, which is not the case in Switzerland. Furthermore the experience in substitution in the USA showed that the exclusion from methadone maintenance programmes based on additional use led to higher mortality rates and not to improvement (McLellan et al. 1996).

There is a substantial difference in substitution treatment, e.g., in Germany or Switzerland and in the USA. In the former, psychosocial counselling is always available for all clients, who want to have it. In most programmes in the USA and Canada systematic counselling is an exception.

Mental health care is even more complicated to get. Only a tiny fraction of all substitution treatment programmes is provided by psychiatrists. Substance users are still excluded from psychotherapy and marginalized in the system. Likewise in Europe, OMT providers are often not prepared to address comorbid mental illness although it is known how critical and how prevalent trauma, depression, or attachment disorders are for sustainable recovery. For example, the larger part of maintenance treatments in Switzerland, Germany, Austria, etc., is still provided by family physicians (Bundesamt für Arzneimittel und Medizinprodukte 2013; Hošek 2006).

4.3.4 Integrated Versus Sequential Treatment of Dual Disorders

Abstinence based programmes normally focus first on detoxification and start with psychosocial programmes later. Detoxification in North America is also extremely short, less than a week. Thus, many patients leave after just basic stabilization and before detoxification is finished.

That is slightly different in Germany, Switzerland, or the Netherlands where the integration of counselling and cognitive behavioural therapy into the early stages of treatment including detoxification is established and called "qualified detoxification".

Why is that relevant for the treatment of concurrent disorders? There are three reasons:

1. For a substantial group of patients emergency care or detoxification is a short window of opportunity, because they are only in a pre-contemplative phase (DiClemente et al. 2008) and are not sure about additional treatments. The functional component of their substance use (Khantzian et al. 1974) that is, dealing with their "emotional pain," motivates them not to give away this (at least partially) effective tool although they may be conscious of the risks.
2. Acute crisis and the experiences around it play an important role in the perception of one's own mental challenges. A reduction of treatment to the basic minimum of physical management wastes an opportunity and is insufficient.
3. During acute situations all mental symptoms are experienced more intensely. Anxiety, mood swings, psychotic symptoms as well as flash backs intensify the suffering and require a response. When care is insufficient, these experiences are often a reason that patients leave prematurely addiction treatment "against medical advice".

4.4 Structural Components and Clinical Pathways

Treatment settings in the USA, Canada, and the European countries work distinctly and carry different burdens in the system. Primary care is as important in the treatment of comorbid clients as for the treatment of substance use and mental illness "alone" (Wienberg 2001). This fact was acknowledged in Europe decades ago and is a hot topic in the system reform in Canada right now. Family medicine is the main interface to the community but often not equipped and trained to deal with patients who need special care.

The role of emergency departments is a more central one in North America due to the insurance system and a limited availability especially of mental health services (long waiting times, no psychiatrists, no detoxification capacity). As a result, ERs play a key role in several regards. They are no longer just a last resort, to be used if nothing else is available. They are used also because of a lack of access to alternatives and if the person in need is not insured. In these situations emergency rooms can provide emergency triage and support often together with police.

However, despite this important role, acute care has a relatively small capacity. For example, in comparison with Germany, Canada has less than 50 % of the available beds in mental health. Unfortunately community services are also less equipped. Canada is investing about the same amount of funding per capita into health care but psychiatry is the most underfunded area of all.

Although most of the addiction programmes besides OMT in the USA and Canada are based on abstinence, detoxification and residential capacity are only accessible as an exception or for private payers.

These basic features of care are far more accessible in Europe and in better quality. For example, in Germany, a separate system of "rehabilitation clinics" is providing psychotherapy and "psychosomatic" care including addiction treatment, something that does not exist in North America.

4.5 Innovation in Europe and North America

New treatment settings for high need populations are being established in both inpatient and outpatient settings. Psychiatric hospitals mainly in Europe increasingly offer dual disorder units, where, ideally, substance use and comorbidities are being addressed simultaneously (not always, however, do treatment concepts of these units reflect this goal adequately). The Burnaby centre in Vancouver, offering outpatient treatment for dual disorder patients, also reflects this approach. Gradually, in light of the aging population of OMT patients in Switzerland, service providers are integrating somatic health specialists (Krausz 2009). Best practice guidelines are also upgraded and increasingly reflect the common occurrence of dual disorders (see, e.g. Swiss Society of Addiction Medicine (SSAM) 2012).

Progressively, standardized interventions targeting comorbid disorders in substance users are invented, evaluated and established. These include specific training programmes, e.g. *seeking safety*, which targets trauma-related symptoms (Najavits 2002).

Conclusions

Despite very small treatment capacities in both regions of the two continents Europe and North America for the most vulnerable, the last 30 years contributed substantially to the development of more effective and specific treatment approaches.

Differences between the USA, Canada, and Europe are still significant especially in the readiness to build treatment approaches based on health outcomes instead of prohibition and the abstinence paradigm.

Clinical research could demonstrate effective treatment strategies and settings, which, if available, would improve care substantially. If the mental health system were organized more based on evidence and proven effectiveness many more vulnerable individuals would have a chance to survive and recover. Patients with complex concurrent conditions could be treated successfully. That would decrease mortality and save resources from all kinds of ineffective system use.

References

Alterman AI (1985) Substance abuse and psychopathology. Plenum, New York, London
American Psychiatric Association (1987) Diagnostic and statistical manual of mental disorders: DSM-III-R, 3rd ed rev edn, 3rd edn. American Psychiatric Association, Washington, DC
Bleuler E (1911) Dementia praecox oder Gruppe der Schizophrenien. Handbuch der Psychiatrie. Spezieller Teil. Franz Deuticke, Leipzig
Bundesamt für Arzneimittel und Medizinprodukte (2013) Report on the Substitution Register [Bericht zum Substitutionsregister]. Federal Institute for Drugs and Medical Devices [Bundesamt für Arzneimittel und Medizinprodukte], Bonn
Committee on Crossing the Quality Chasm (2006) Improving the quality of health care for mental and substance-use conditions. National Academy Press, Washington, DC
Dausey DJ, Desai RA (2003) Psychiatric comorbidity and the prevalence of HIV infection in a sample of patients in treatment for substance abuse. J Nerv Ment Dis 191(1):10–17. doi:10.1097/01.NMD.0000044704.49418.E2
DiClemente CC, Nidecker M, Bellack AS (2008) Motivation and the stages of change among individuals with severe mental illness and substance abuse disorders. J Subst Abuse Treat 34(1):25–35. doi:10.1016/j.jsat.2006.12.034
Drake RE, O'Neal EL, Wallach MA (2008) A systematic review of psychosocial research on psychosocial interventions for people with co-occurring severe mental and substance use disorders. J Subst Abuse Treat 34(1):123–138. doi:10.1016/j.jsat.2007.01.011
EMCDDA (1999) Annual report on the state of the drugs problem in the European Union. European Monitoring Centre for Drugs and Drug Addiction, Lisbon
Goering PN, Streiner DL, Adair C, Aubry T, Barker J, Distasio J, Hwang SW, Komaroff J, Latimer E, Somers J, Zabkiewicz DM (2011) The At Home/Chez Soi trial protocol: a pragmatic, multi-site, randomised controlled trial of a Housing First intervention for homeless individuals with mental illness in five Canadian cities. BMJ 1(2):e000323. doi:10.1136/bmjopen-2011-000323
Hošek M (2006) Substitutionsbehandlungen in der Schweiz: Fortsetzung einer Erfolgsgeschichte. SuchtMagazin 06(1):3–9
Kessler RC, Merikangas KR (2004) The National Comorbidity Survey Replication (NCS-R): background and aims. Int J Methods Psychiatr Res 13(2):60–68
Khantzian EJ, Mack JE, Schatzberg AF (1974) Heroin use as an attempt to cope: clinical observations. Am J Psychiatry 131(2):160–164
Kluge U, Bogic M, Deville W, Greacen T, Dauvrin M, Dias S, Gaddini A, Koitzsch Jensen N, Ioannidi-Kapolou E, Mertaniemi R, Puipcinos IRR, Sandhu S, Sarvary A, Soares JJ, Stankunas M, Strassmayr C, Welbel M, Heinz A, Priebe S (2012) Health services and the treatment of immigrants: data on service use, interpreting services and immigrant staff members in services across Europe. Eur Psychiatry 27(Suppl 2):S56–62. doi:10.1016/S0924-9338(12)75709-7
Koerkel J (2002) Controlled drinking as a treatment goal in Germany. J Drug Iss 32(2):667–688
Krausz M (2008) Verwundete Seelen—Von transgenerationaler Traumatisierung zur individuellen Reviktimisierung. Die Situation der Aboriginals in Australien, Neuseeland und Nordamerika. Trauma und Gewalt 2:88–95
Krausz M (2009) Blick über die Grenzen—Von den globalen Lehren in der Suchttherapie. Suchttherapie 10(02):52–53. doi:10.1055/s-0029-1224806
Krausz M, Müller-Thomsen T (1994) Komorbidität: Therapie von psychiatrischen Störungen und Sucht: Konzepte für Diagnostik, Behandlung und Rehabilitation. Freiburg im Breisgau, Lambertus
Krausz RM, Clarkson AF, Strehlau V, Torchalla I, Li K, Schuetz CG (2013) Mental disorder, service use, and barriers to care among 500 homeless people in 3 different urban settings. Soc Psychiatry Psychiatr Epidemiol 48(8):1235–1243. doi:10.1007/s00127-012-0649-8

Linden IA, Mar MY, Werker GR, Jang K, Krausz M (2013) Research on a vulnerable neighborhood-the vancouver downtown eastside from 2001 to 2011. J Urban Health 90 (3):559–573. doi:10.1007/s11524-012-9771-x

Livingston JD, Milne T, Fang ML, Amari E (2012) The effectiveness of interventions for reducing stigma related to substance use disorders: a systematic review. Addiction 107(1):39–50. doi:10.1111/j.1360-0443.2011.03601.x

Madore O (2005) The Canada Health Act: overview and options. Current issue review. Parliament of Canada, Ottawa

McLellan AT, Woody GE, Metzger D, McKay J, Durrell J, Alterman AI, O'Brien CP (1996) Evaluating the effectiveness of addiction treatments: reasonable expectations, appropriate comparisons. Milbank Q 74(1):51–85

Moggi F, Brodbeck J, Költzsch K, Bachmann KM (2002) One-year follow-up of dual diagnosis patients attending a 4-months integrative inpatient treatment. Eur Addict Res 8:30–37

Morrens M, Dewilde B, Sabbe B, Dom G, De Cuyper R, Moggi F (2011) Treatment outcomes of an integrated residential programme for patients with schizophrenia and substance use disorder. Eur Addict Res 17(3):154–163. doi:10.1159/000324480

Najavits LM (2002) Seeking safety: a treatment manual for PTSD and substance abuse. Guilford, New York, NY

Savage A, Quiros L, Dodd S-J, Bonavota D (2007) Building trauma informed practice: appreciating the impact of trauma in the lives of women with substance abuse and mental health problems. J Soc Work Pract Addict 7(1–2):91–116. doi:10.1300/J160v07n01_06

Schippers GM, Schramade M, Walburg JA (2002) Reforming Dutch substance abuse treatment services. Addict Behav 27(6):995–1007

Schutz C, Linden IA, Torchalla I, Li K, Al-Desouki M, Krausz M (2013) The Burnaby Treatment Center for Mental Health and Addiction, a novel integrated treatment program for patients with addiction and concurrent disorders: results from a program evaluation. BMC Health Serv Res 13:288. doi:10.1186/1472-6963-13-288

Spittal PM, Craib KJ, Teegee M, Baylis C, Christian WM, Moniruzzaman AK, Schechter MT, Cedar Project P (2007) The Cedar project: prevalence and correlates of HIV infection among young Aboriginal people who use drugs in two Canadian cities. Int J Circumpolar Health 66 (3):226–240

Swiss Society of Addiction Medicine (SSAM) (2012) Clinical recommendations for substitution-assisted treatment in opioid Dependence 2012. SSAM. http://www.ssam.ch/SSAM/sites/default/files/Empfehlungen%20SGB_2012_FINAL_05%2003%202013.pdf. Accessed January 24th 2014

Torchalla I, Nosen L, Rostam H, Allen P (2012) Integrated treatment programs for individuals with concurrent substance use disorders and trauma experiences: a systematic review and meta-analysis. J Subst Abuse Treat 42(1):65–77. doi:10.1016/j.jsat.2011.09.001

Wang PS, Berglund P, Olfson M, Pincus HA, Wells KB, Kessler RC (2005) Failure and delay in initial treatment contact after first onset of mental disorders in the National Comorbidity Survey Replication. Arch Gen Psychiatry 62(6):603–613. doi:10.1001/archpsyc.62.6.603

Wells P (2011) Harper swings and misses on Insite. Maclean's

Wienberg G (2001) Auf dem Weg zur vergessenen Mehrheit: innovative Konzepte für die Versorgung von Menschen mit Alkoholproblemen. Psychiatrie, Bonn

World Health Organization (1992) International statistical classification of diseases and related health problems, 10th edn. World Health Organization, Geneva

The Pathogenesis of Dual Disorders: Neurobiological Perspectives

5

Geert Dom and Marcin Wojnar

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Abstract

Dual disorder patients are characterized by a highly variable and phenotypically complex presentation. Recent research suggests that impairments within a limited number of functional neurobiological dimensions may play a central role in the vulnerability for development of dual disorders. Specifically impairments in the central regulatory role of the hippocampus and brain circuitries underlying behavioural control and stress regulation may be proposed as "trans-disease", i.e. processes that occur across a range of disorders, making findings from one

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disorder relevant to the other disorders. This line of thinking may open up new ways of exploring not only the pathogenesis of dual disorders, but most importantly, may provide new targets for both treatment and prevention interventions for these patients.

5.1 Introduction

Addictive behaviours, defined as compulsive drug seeking and drug use despite of negative consequences, are highly prevalent disorders in the general population worldwide. Of importance, their clinical manifestation ("phenotype") is highly variable depending on multiple, genetic, and environmental factors (e.g. availability and local culture concerning use of psychoactive substances). In contrast with their phenotypical heterogeneity, a common hallmark among many patients suffering from severe addictions is the very high rate of psychiatric comorbidity (Reissner et al. 2012). Indeed, rates of comorbidity are far higher than can be expected, by pure chance, based upon the relative risks and prevalence of different individual psychiatric disorders.

Different hypotheses on causal pathways have been put forward to explain this excess in comorbidity (Moggi 2005). Many of these are explored in depth in the subsequent, disorder-oriented chapters within this book. However, although all these different causal models are of importance, they basically come down to two separate theories. On the one-hand models, having some form of a self-medication hypothesis at their basis. On the other-hand models that suggest that common neurobiological vulnerabilities underlie both psychiatric disorders and addictions. Evidence in support of the self-medication hypothesis has remained up to now limited and inconsistently supported by the data. In contrast, evidence is accumulating that impairments in (common) neurobiological processes might be underlying the susceptibility of individuals to develop (comorbid) substance use and psychiatric disorders.

5.2 Neurobiological Pathways Involved in Addictive Disorders

Although it is beyond the scope of this textbook to provide a comprehensive overview on the neurobiology of addiction [see for review (Volkow and Baler 2014)], some essential elements need to be noted. A wealth of evidence indicates substantial commonalities among the different substance use disorders categories, including non-chemical addictive behaviours. These findings weaken the hypothesis that different addictions represent discrete disorders. Non drug-specific mechanisms (e.g. the neurobiological processes underlying drug-related reinforcement) represent a commonality of many drug effects. These mechanisms involve dopaminergic and other major neurobiological systems, despite differences in routes

of administration, biotransformation pathways and primary neurochemical targets of the different psychoactive substances (Vanyukov et al. 2012). This commonality is clinically reflected by the high prevalence of comorbidity between types of addictions (e.g. alcohol and nicotine) and the highly frequent switching from one substance to another in the course of addictive disorders (e.g. heroine to alcohol).

Depending on the focus and the neurobiological level studied, addiction has been characterized as a disorder of the brain, learning, memory, neuronal maturation and neuroplasticity, homeostatic regulation, and compulsion. In addition, genetic association studies have shown that the genes that are associated to variations in risks of developing addictive behavioural are not unique for a specific drug or drug categories of abuse (Vanyukov et al. 2012). In addition, neurobiological characteristics associated with risk for addiction are found not only in the "disease" affected individuals, but are also, often in a lesser degree, in unaffected family members.

Of importance, within the context of dual disorders, is that evidence is accumulating that the same neurobiological factors that carry risk of addictive disorders, may also be involved in the pathogenesis of other psychiatric disorders, thus representing a common underlying vulnerability to develop both addictive (chemical and behavioural) and other mental disorders.

5.3 Vulnerabilities in Neurobiological Pathways: A Common Underground for Comorbidity?

From a neurobiological perspective, vulnerabilities underlying both major forms of mental illnesses and addictions are intimately inter-related and in some aspects inseparable pathogenic disease processes (Chambers 2007, 2013). This is paralleled by their clinical presentations where mental disorders and addictions often unfold as intertwined chronic conditions punctuated by episodes of relapse and recovery in psychiatric and/or addiction symptoms. Symptomatic exacerbations of these dual disorders, "relapses", are associated with novel or destabilizing environmental contexts, psychological stress, and exposure to addictive drugs and/or associated cues.

Although the research field is as yet in full development and the complexities of neural circuitries are far from being fully understood, some neurobiological hypotheses are taking shape.

5.3.1 Hippocampal Neurogenesis

Within the context of pathogenesis of dual disorders, the hippocampus might take up a central position. Animal and human studies reveal abnormal or maladaptive hippocampal neurogenic activity in the pathogenesis of a range of psychiatric disorders. These disorders, including schizophrenia, post-traumatic stress disorder (PTSD), mood disorders, and some personality disorders (cluster B) are all highly comorbid with substance use disorders (Kessler 2004). Although these disorders

involve many different symptom domains and etiologic and developmental aspects, they do share three hippocampus-related attributes: (1) disturbance in Hypothalamic–pituitary–adrenocortical (HPA) axis regulation and stress-reactivity, (2) hippocampal atrophy, and (3) disturbances in hippocampal learning and memory (Chambers 2007, 2013). Loss of hippocampal network vitality (due to deficits in neurogenesis) impairs not only learning and memory but also the hippocampal feedback regulation of the HPA axis activity affecting negatively stress resilience. Alternatively, (chronic) repeated surges of corticosteroids can further impair hippocampal neurogenesis and functionality, a mechanism that overall induces a vicious circle of further impairment. In addition, and highly relevant in the context of dual disorders, all addictive drugs when used chronically, share a capacity to reduce hippocampal neurogenic activity (Chambers 2013; Noonan et al. 2010).

Importantly, whatever its initial cause, animal studies show that the suppression of hippocampal neurogenesis has important addiction enhancing effects both to the initiation (increase of self-administration) as to the continuation (diminished extinction of drug seeking). Moreover, suppression of hippocampal neurogenic proliferation has been shown to enhance substance-primed reinstatement of drug seeking in animals that have previously been extinguished from drug-seeking behaviour (Chambers 2013).

Taken together, there is growing evidence, admittedly largely based upon animal studies, supporting a central role for hippocampal dysfunction in the pathogenesis of psychiatric disorders, addictions, and their comorbidity. This model allows explaining how low states of hippocampal neurogenesis, whether generated by underlying mental illness, prior addictive drug exposure or by their combination, evokes changes in corticostriatal circuitry function. These changes enhance learning associated with drug reinforcement, at the expense of learning and maintaining more adaptive natural-reward focused behaviours (Chambers 2013). Moreover other aspects of hippocampus-dependent learning, i.e. memory are impaired in the process. In addition, given the deleterious effects of chronic substance use on the hippocampal functionality and its associated deregulation of stress mechanisms, pathogenesis of dual disorders might have the character of a vicious circle aggravating the pathogenic factors during the course of the disorders. These mechanisms may explain how addictive drug use typically worsens rather than improves psychiatric symptoms. This finding provides further support to the hypothesis that dual disorders represent disease synergy rather than reflect self-medication process.

5.3.2 Externalizing and Internalizing Dimensions of Psychiatric Disorders

In addition to a proposed central role of the “hippocampus” hypothesis, other related neurobiological factors can be identified underlying the vulnerability to dual disorders. Based upon epidemiological data, Kessler and colleagues (Kessler

et al. 2011) suggest categorizing psychiatric disorders in two broad categories—internalizing and externalizing disorders. Specific phobia and obsessive compulsive disorder are considered the most characteristic internalizing disorders while hyperactivity disorder and oppositional-defiant disorder are typical examples of externalizing disorders (Kessler et al. 2011). Of importance, both broad categories of disorders are characterized by a high comorbidity with other disorders within the same categories. Interestingly, although substance use disorders are positioned within the externalizing spectrum, comorbidity with SUD is found in disorders from both internalizing and externalizing categories. Thus, these two pathways, associating SUD with internalizing and externalizing disorders respectively may reflect common underlying neurobiological vulnerabilities.

5.3.2.1 Impulse Regulation and the Externalizing Spectrum

Impairments in self-regulation and inhibitory control have been proposed as central to various stages of substance abuse such as increasing susceptibility to initial use, transition to dependence, maintenance, and relapse (Goldstein and Volkow 2011). Converging evidence (structural and functional neuroimaging, electrophysiological) points to the involvement (hypo-functionality) of the pre-supplementary motor area (pre-SME) in dorsomedial prefrontal cortex (dmPFC) and the right ventrolateral PFC encompassing the anterior insula and inferior frontal gyrus in response inhibition (Morein-Zamir et al. 2013). Although these findings may reflect a consequence of the neurotoxicity associated with chronic substance abuse, pre-existing genetic and environmental vulnerabilities likely interact with short- and long-term effects of substance use on behaviour and brain to produce these deficits. Evidence suggests that impaired response regulation and control are present in individuals with a family history of drug and alcohol dependence. Moreover, these characteristics when found in childhood predict an early age of onset of addictive disorders (Tarter et al. 2003). Of importance, these impairments of regulatory control, as reflected by abnormalities in both structural and functional brain circuitries, are also a hallmark of other psychiatric often, developmental disorders (e.g. ADHD, ODD, conduct disorder).

In addition to response inhibition, efficient executive control requires monitoring for errors or conflicting response plans. These functions are particularly impaired in addictive behaviours. Key region suggested here is the anterior cingulate cortex (ACC). ACC hypo activity has been reported in users of different substances of abuse (Morein-Zamir et al. 2013). Deficient error and conflict monitoring associated with ACC hypo activation could play a role in drug abuse development, maintenance, and relapse (Connolly et al. 2012). Again, impairments in error/conflict monitoring are not typical for SUD, but a hallmark of many other "externalizing" disorders such as borderline and antisocial personality disorder, ADHD (Brazil et al. 2009; de Bruijn et al. 2006; Shiels and Hawk 2010).

Taken together, clinical features of behavioural under-control and their neurobiological correlates may represent a common underlying vulnerability to develop a wide range of externalizing comorbid disorders, e.g. CD, ADHD, and SUD. This hypothesis is supported by longitudinal studies relating these features in children

with an increased risk on a broad area of disinhibited behavioural disorders (e.g. sexual risk behaviour, SUD) (Vanyukov et al. 2012). Of importance, this opens up a window of opportunity for potential treatments and prevention. Indeed, behavioural and pharmacological treatment, improving behavioural control might help to regain control over substance use in established SUD patients and if applied early in life, diminishes the risk in impulsive children to develop behavioural and substance use disorders later in life.

5.3.2.2 Internalizing Disorders

Brain-Stress Systems

The concept of stress refers to processes aimed at the perception, appraisal and response to (potentially) harmful or threatening stimuli. Brain regions such as the amygdala, hippocampus, insula, orbitofrontal cortex, and anterior cingulate ("limbic circuitry") are all involved in the appraisal of stressful stimuli. Other regions, such as the locus coeruleus, hypothalamus, thalamus, and striatum are involved in the physiological and emotional responses. Although developed as highly important adaptive mechanisms, abnormalities with stress processing are at the base of many psychiatric disorders and symptoms. Specifically, chronic stress and early childhood adversities can have profound effects on many ("trans-disease") psychiatric disorders and their potential co-occurrence.

Early Childhood Adversity

Epidemiological studies have shown that people who experience chronic, early childhood adversity (ECA) have a greater likelihood of developing and phenotypically shaping addictive and other psychiatric disorders (Benjet et al. 2013). In analysing the data of the adolescent participants in the National Comorbidity Survey (NCS-A), McLaughlin and colleagues showed that ECA is associated with a substantial proportion of child–adolescent onset of psychiatric disorders, including more than 40 % of onsets of behaviour disorders and one-third of onset of substance use disorders. A finding reflected in animal research where ECA consistently has been associated with both an increase in self-administration of substances and a higher likelihood of developing addictive and other behavioural and mood-regulation disorders. Multiple hypotheses have been suggested to explain this association. The two most substantiated are on the one hand the so-called self-medication hypothesis and on the other hand changes in neurobiological pathways induced by early, chronic or repetitive stress. As indicated earlier, self-medication refers to the process of alleviating the pain of trauma, negative experiences both within the context of trauma and possible associated psychiatric disorders (e.g. Post Traumatic Stress Disorder, PTSD, Mood Disorders, MD). On the other hand, ECA can induce changes in neurobiological and neurohormonal pathways ultimately altering learning, reward, craving, and self-regulation (impulsivity) mechanisms through stress allostasis (Benjet et al. 2013). The concept of allostatic load proposes that the process of achieving stability through alteration of neural, neuroendocrinal,

and immune mechanisms, while adaptive in the short run, becomes overloaded and ultimately maladaptive with chronic stress (McEwen 2000).

Adverse life events are associated with a wide range of psychopathology, including an increased risk for substance abuse. The interaction of exposure during a sensitive period and neuronal maturational events produces a cascade that leads to the initiation of substance use at younger ages, and increases the likelihood of addiction by adolescence or early adulthood. Three main factors contribute to this age-based progression of increased drug use: (1) a sensitized stress response system; (2) sensitive periods of vulnerability; and (3) neuronal maturational processes during adolescence. Together, these factors may explain why exposure to early adversity increases risk to abuse substances during adolescence (Andersen and Teicher 2009). Overall, ECA is an important factor underlying the pathogenesis of many types of dual disorders.

5.4 Interaction Between Internalizing and Externalizing Dimensions

Within both healthy persons and individuals with psychiatric disorders, different systems interact and influence each other. One example is the interaction between childhood adversity and impulsivity. As found in epidemiological prevalence studies, the frequent association between ECA with both substance use disorders and behavioural disorders, may reflect the effect of ECA on the development of brain areas linked with impulsivity (McLaughlin et al. 2012). Lovallo recently showed that early life adversity reduces stress reactivity and enhances impulsive behaviour with negative health implications as a consequence (Lovallo 2013). This has also been documented in alcohol dependent patients, where ECA was associated with an increased impulsivity (Jakubczyk et al. 2013). Of importance within the context of comorbidity, impulsivity in alcohol dependent patients was associated with the severity of the comorbid depressive symptoms (Jakubczyk et al. 2012). The complex role of impulsivity in addictive processes has been recently demonstrated in another study showing that the risk of relapse in nicotine dependent patients was mediated specifically by the interaction between stress and impulsivity (Ansell et al. 2012a). In the context of comorbidity, these results provide some rationale for other findings, e.g. that patients with schizophrenia and comorbid SUD show both higher prevalence's of PTSD and early life adversity, together with higher indices of impulsivity, compared with patients without SUD (Jurado-Barba et al. 2011; Scheller-Gilkey et al. 2004).

Overall, findings as exemplified above suggest that the pathogenic processes leading to the development of comorbid phenotypes (dual disorders) are highly complex and variable. This implies that developing treatment approaches need to take into account the specific, individual characteristics of a patient. This is in contrast with some current treatment approach, developing, for example programs for patients with schizophrenia and SUD. Indeed, although phenotypically

resembling each other, the underlying pathways may differ fundamentally between patients with the same diagnoses.

5.5 Relapse

Addictive disorders are chronic relapsing disorders. Recent estimates suggest that more than two-thirds of individuals relapse within weeks to months after initiating treatment (Sinha 2011). The chronic relapsing nature of addictive disorders is a key factor contributing to the high disease burden associated with these disorders.

Of importance, patients with dual disorders tend to have even higher relapse rates compared with individuals without psychiatric disorders. So, exploring the (neurobiological) factors mitigating the risk for relapse is of high importance within the context of treatment of addictive disorders and dual disorder patients.

The search for factors that allow predicting risk of relapse for an individual patient is the "Holy Grale" in addiction research. Current research has focused on different types of eligible variables; clinical, biological, neuroimaging, and cognitive factors are among the most frequently explored candidates.

On the clinical ("phenotypical") level, features such as depressive symptoms, history of trauma, high stress, and high levels of subjective drug craving in patients entering treatment have all been associated with a higher risk of early relapse to substance use. Importantly, many of these clinical features are frequently co-occurring in patients with dual disorders. The relative accumulation of these risk factors for relapse within an individual (dual disorder) patient may explain the higher risk on relapse in this challenging group of patients.

On a biological level, vulnerabilities in stress regulation systems have been identified as important risk factors for relapse. High levels of serum Brain-Derived Neurotrophic Factor (BDNF) and high levels of adrenal sensitivity (cortisol/Adrenocorticotropic Hormone ratio) at entry to treatment were found to be predictive of relapse in patients using different substances (e.g. alcohol, cocaine) (Sinha, 2011). Although it might be hypothesized that these stress regulation vulnerabilities can be caused by long-lasting substance use and subsequent withdrawal, as has been confirmed by many data, similar abnormalities in stress biology systems can be found in many psychiatric disorders (e.g. in consequences of ECA, PTSD, and borderline personality disorder). Dual disorder patients with these disorders might be particularly prone to relapse when confronted with stressful life events.

Using neuroimaging techniques, brain (grey matter) volume reductions in the prefrontal cortex were found to be predictive of relapse in alcohol use. Again, these deficits may be both the consequence of long-lasting substance abuse but also be an abnormality related with other psychiatric disorders (e.g. ADHD, schizophrenia). Illustrative are the findings of Ansell and colleagues showing that cumulative exposure to adverse life events (ECA) is associated with smaller grey matter volumes in key prefrontal and limbic regions involved in stress, emotion, reward, and self-control regulation (Ansell et al. 2012b). Dual disorder patients may accumulate these types of risk factors resulting in an increased risk for relapse.

Finally, an accumulating number of studies have identified impairments in neurocognitive functions (i.e. those related with self-control mechanisms) as potential predictors of relapse (Stevens et al. 2014). Specifically impaired decision-making has been found to be an important factor, predicting relapse in different types of SUD patients (e.g. amphetamine, alcohol, nicotine) (De Wilde et al. 2013; Paulus et al. 2005). Of importance, impaired decision-making is also a hallmark of different psychiatric disorders such as CD, ADHD, borderline and antisocial personality disorder, and in some patients with schizophrenia. Patients with these dual disorders are characterized by more severe abnormalities in decision-making compared with patients that suffer only one of these disorders (Dom et al. 2006). Thus, specifically these dual disorder patients might be highly susceptible for relapse.

Taken together, many of the currently known, neurobiological, risk factors for relapse in addictive disorders seem to accumulate in dual disorder patients. This might account for higher risk of relapse that has been found in clinical population of these patients.

Conclusions

Dual disorder patients are characterized by a highly variable and phenotypically complex presentation. Both environmental and neurobiological processes and their interactions play a pivotal role in their pathogenesis. In the following chapters of this book, these processes will be highlighted for every specific disorder. However, although there remain disorder specific aspects, recent research suggests a broader context proposing that impairments within a limited number of functional neurobiological dimensions play a central role in the vulnerability for development of dual disorders. Specifically impairments in the central regulatory role of the hippocampus and brain circuitries underlying behaviour control and stress regulation may be proposed as "trans-disease" processes (i.e. processes that occur across a range of disorders, making findings from one disorder relevant to the other disorders) (Bickel and Mueller 2009). Although preliminary, this view is in line with the RDoC (Research Domain Criteria)—initiative that provides a framework for conducting research in terms of fundamental circuit-based behavioural dimensions that cut across traditional diagnostic categories (Cuthbert 2014). This line of thinking may open up new ways of exploring not only the pathogenesis of dual disorders, but most importantly, may provide new targets for treatment and prevention interventions for these, often highly disease burdened, patients.

References

Andersen SL, Teicher MH (2009) Desperately driven and no brakes: developmental stress exposure and subsequent risk for substance abuse. Neurosci Biobehav Rev 33(4):516–524. doi:10.1016/j.neubiorev.2008.09.009

Ansell EB, Gu P, Tuit K, Sinha R (2012a) Effects of cumulative stress and impulsivity on smoking status. Hum Psychopharmacol 27(2):200–208. doi:10.1002/hup.1269

Ansell EB, Rando K, Tuit K, Guarnaccia J, Sinha R (2012b) Cumulative adversity and smaller gray matter volume in medial prefrontal, anterior cingulate, and insula regions. Biol Psychiatry 72(1):57–64. doi:10.1016/j.biopsych.2011.11.022

Benjet C, Borges G, Medina-Mora ME, Mendez E (2013) Chronic childhood adversity and stages of substance use involvement in adolescents. Drug Alcohol Depend 131(1–2):85–91. doi:10.1016/j.drugalcdep.2012.12.002

Bickel WK, Mueller ET (2009) Toward the Study of Trans-Disease Processes: a novel approach with special reference to the study of co-morbidity. J Dual Diagn 5(2):131–138. doi:10.1080/15504260902869147

Brazil IA, de Bruijn ER, Bulten BH, von Borries AK, van Lankveld JJ, Buitelaar JK, Verkes RJ (2009) Early and late components of error monitoring in violent offenders with psychopathy. Biol Psychiatry 65(2):137–143. doi:10.1016/j.biopsych.2008.08.011

Chambers RA (2007) Animal modeling and neurocircuitry of dual diagnosis. J Dual Diagn 3 (2):19–29. doi:10.1300/J374v03n02_04

Chambers RA (2013) Adult hippocampal neurogenesis in the pathogenesis of addiction and dual diagnosis disorders. Drug Alcohol Depend 130(1–3):1–12. doi:10.1016/j.drugalcdep.2012.12.005

Connolly CG, Foxe JJ, Nierenberg J, Shpaner M, Garavan H (2012) The neurobiology of cognitive control in successful cocaine abstinence. Drug Alcohol Depend 121(1–2):45–53. doi:10.1016/j.drugalcdep.2011.08.007

Cuthbert BN (2014) The RDoC framework: facilitating transition from ICD/DSM to dimensional approaches that integrate neuroscience and psychopathology. World Psychiatry 13(1):28–35. doi:10.1002/wps.20087

de Bruijn ER, Grootens KP, Verkes RJ, Buchholz V, Hummelen JW, Hulstijn W (2006) Neural correlates of impulsive responding in borderline personality disorder: ERP evidence for reduced action monitoring. J Psychiatr Res 40(5):428–437. doi:10.1016/j.jpsychires.2005.09.004

De Wilde B, Verdejo-Garcia A, Sabbe B, Hulstijn W, Dom G (2013) Affective decision-making is predictive of three-month relapse in polysubstance-dependent alcoholics. Eur Addict Res 19 (1):21–28. doi:10.1159/000339290

Dom G, De Wilde B, Hulstijn W, van den Brink W, Sabbe B (2006) Decision-making deficits in alcohol-dependent patients with and without comorbid personality disorder. Alcohol Clin Exp Res 30(10):1670–1677. doi:10.1111/j.1530-0277.2006.00202.x

Goldstein RZ, Volkow ND (2011) Dysfunction of the prefrontal cortex in addiction: neuroimaging findings and clinical implications. Nat Rev Neurosci 12(11):652–669. doi:10.1038/nrn3119

Jakubczyk A, Klimkiewicz A, Mika K, Bugaj M, Konopa A, Podgorska A, Wojnar M (2013) Psychosocial predictors of impulsivity in alcohol-dependent patients. J Nerv Ment Dis 201 (1):43–47. doi:10.1097/NMD.0b013e31827aaf9d

Jakubczyk A, Klimkiewicz A, Topolewska-Wochowska A, Serafin P, Sadowska-Mazuryk J, Pupek-Pyziol J, Wojnar M (2012) Relationships of impulsiveness and depressive symptoms in alcohol dependence. J Affect Disord 136(3):841–847. doi:10.1016/j.jad.2011.09.028

Jurado-Barba R, Morales-Munoz I, Del Manzano BA, Fernandez-Guinea S, Caballero M, Martinez-Gras I, Rubio-Valladolid G (2011) Relationship between measures of inhibitory processes in patients with schizophrenia: role of substance abuse disorders. Psychiatry Res 190(2–3):187–192. doi:10.1016/j.psychres.2011.06.002

Kessler RC (2004) The epidemiology of dual diagnosis. Biol Psychiatry 56(10):730–737. doi:10.1016/j.biopsych.2004.06.034

Kessler RC, Petukhova M, Zaslavsky AM (2011) The role of latent internalizing and externalizing predispositions in accounting for the development of comorbidity among common mental disorders. Curr Opin Psychiatry 24(4):307–312. doi:10.1097/YCO.0b013e3283477b22

Lovallo WR (2013) Early life adversity reduces stress reactivity and enhances impulsive behavior: implications for health behaviors. Int J Psychophysiol 90(1):8–16. doi:10.1016/j.ijpsycho.2012.10.006

McEwen BS (2000) The neurobiology of stress: from serendipity to clinical relevance. Brain Res 886(1–2):172–189

McLaughlin KA, Greif Green J, Gruber MJ, Sampson NA, Zaslavsky AM, Kessler RC (2012) Childhood adversities and first onset of psychiatric disorders in a national sample of US adolescents. Arch Gen Psychiatry 69(11):1151–1160. doi:10.1001/archgenpsychiatry.2011.2277

Moggi F (2005) Etiological theories on the relationship of mental disorders and substance use disorders. In: Stohler R, Rossler W (eds) Dual Diagnosis. The evolving conceptual framework, vol 172, Bilblotheca Psychiatrica. Karger, Basel, pp 1–14

Morein-Zamir S, Simon Jones P, Bullmore ET, Robbins TW, Ersche KD (2013) Prefrontal hypoactivity associated with impaired inhibition in stimulant-dependent individuals but evidence for hyperactivation in their unaffected siblings. Neuropsychopharmacology 38(10):1945–1953. doi:10.1038/npp.2013.90

Noonan MA, Bulin SE, Fuller DC, Eisch AJ (2010) Reduction of adult hippocampal neurogenesis confers vulnerability in an animal model of cocaine addiction. J Neurosci 30(1):304–315. doi:10.1523/JNEUROSCI.4256-09.2010

Paulus MP, Tapert SF, Schuckit MA (2005) Neural activation patterns of methamphetamine-dependent subjects during decision making predict relapse. Arch Gen Psychiatry 62(7):761–768. doi:10.1001/archpsyc.62.7.761

Reissner V, Kokkevi A, Schifano F, Room R, Storbjork J, Stohler R, Scherbaum N (2012) Differences in drug consumption, comorbidity and health service use of opioid addicts across six European urban regions (TREAT-project). Eur Psychiatry 27(6):455–462. doi:10.1016/j.eurpsy.2010.10.001

Scheller-Gilkey G, Moynes K, Cooper I, Kant C, Miller AH (2004) Early life stress and PTSD symptoms in patients with comorbid schizophrenia and substance abuse. Schizophr Res 69(2–3):167–174

Shiels K, Hawk LW Jr (2010) Self-regulation in ADHD: the role of error processing. Clin Psychol Rev 30(8):951–961. doi:10.1016/j.cpr.2010.06.010

Sinha R (2011) New findings on biological factors predicting addiction relapse vulnerability. Curr Psychiatry Rep 13(5):398–405. doi:10.1007/s11920-011-0224-0

Stevens L, Verdejo-Garcia A, Goudriaan AE, Roeyers H, Dom G, Vanderplasschen W (2014) Impulsivity as a vulnerability factor for poor addiction treatment outcomes: a review of neurocognitive findings among individuals with substance use disorders. J Subst Abuse Treat 47(1):58–72. doi:10.1016/j.jsat.2014.01.008

Tarter RE, Kirisci L, Mezzich A, Cornelius JR, Pajer K, Vanyukov M, Clark D (2003) Neurobehavioral disinhibition in childhood predicts early age at onset of substance use disorder. Am J Psychiatry 160(6):1078–1085

Vanyukov MM, Tarter RE, Kirillova GP, Kirisci L, Reynolds MD, Kreek MJ, Ridenour TA (2012) Common liability to addiction and "gateway hypothesis": theoretical, empirical and evolutionary perspective. Drug Alcohol Depend 123(Suppl 1):S3–S17. doi:10.1016/j.drugalcdep.2011.12.018

Volkow ND, Baler RD (2014) Addiction science: uncovering neurobiological complexity. Neuropharmacology 76(Pt B):235–249. doi:10.1016/j.neuropharm.2013.05.007

Part II

Specific Disorders

Schizophrenia and Addiction

6

Euphrosyne Gouzoulis-Mayfrank and Marc Walter

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Abstract

Substance use disorders are highly prevalent among people with schizophrenia. Dually diagnosed patients present with unfavorable course and poor long-term outcomes. Integrated, motivation-based treatment for both disorders in the same setting is considered the treatment of choice for this challenging population. Treatment programs include state-of-the-art pharmacotherapy and psychosocial interventions such as motivational interviewing, psychoeducation, and cognitive–behavioral approaches.

6.1 Introduction

Schizophrenia is a major mental illness characterized by psychotic and negative symptoms as well as cognitive impairment. Psychotic symptoms involve the loss of contact with reality, including false beliefs (delusions), perceptual experiences not shared by others (hallucinations) and bizarre behaviors. The most frequently confirmed neurobiological finding is the enlargement of the ventricular system compared to healthy controls. Regions such as the frontal lobes, amygdala, hippocampus, parahippocampus, thalamus, medial temporal lobes, cingulate gyrus, and superior temporal gyrus are smaller in schizophrenic patients compared to healthy controls (Wright et al. 2000). Interestingly, these reductions in brain volume are already found in individuals at high risk for schizophrenia (Borgwardt et al. 2007).

Addiction is a chronic relapsing brain disorder characterized by an overwhelming compulsion to seek and use drugs or alcohol, despite their negative consequences. This compulsion is frequently driven by craving which is triggered by stress and drug-related stimuli (Sinha et al. 2006, Walter et al. 2013). The mesolimbic dopamine pathway—dopamine cells in the ventral tegmental area projecting into the nucleus accumbens—is considered essential for drug reward and drug-seeking behavior (Volkow et al. 2011).

6.2 Epidemiology

Substance use disorders (SUD) are the most common concurrent disorder in schizophrenia. The Epidemiological Catchment Area study (ECA) of the National Institute of Mental Health reported a lifetime prevalence of 47 % for SUD in psychotic patients (Regier et al. 1990). Patients with schizophrenia were three times more likely to have an alcohol use disorder and six times more likely to have a drug use disorder compared to the average population (Regier et al. 1990). In schizophrenia, lifetime prevalence rates for cocaine use disorders range from 15 to 50 %, for amphetamine use disorders from 2 to 25 %, for alcohol use disorders from 20 to 60 %, and for cannabis use disorders from 12 to 42 % (Chambers et al. 2001).

Male gender, young age, low educational levels, high impulsivity, and sensation seeking are risk factors for the development of SUD in psychotic patients (Drake and Mueser 2000; Gouzoulis-Mayfrank 2007).

6.3 Models of Comorbidity

6.3.1 Models of Schizophrenia and Secondary Development of SUD

The *self-medication hypothesis* proposed that certain substances are used by psychotic patients because of their psychotropic effects against certain psychiatric symptoms and/or side effects of antipsychotic drugs (e.g., use of amphetamines because of/against lack of energy, or use of sedating substances such as benzodiazepines or alcohol because of/against anxiety and agitation). However, recent studies have found only limited empirical evidence for this hypothesis (Chambers et al. 2001; Gouzoulis-Mayfrank 2007).

According to the *affect regulation model*, substance abuse is a dysfunctional coping strategy against unspecific negative affective states related to schizophrenia. A tendency toward negative affect, neuroticism, impulsivity, and disinhibition are known to interact with psychosocial stress, maladaptive coping strategies, and problem-solving deficits in patients with schizophrenia promoting the development of SUD in this population (Blanchard et al. 2000). This model is compatible with the fact that substance abuse often manifests itself before the onset of psychotic positive symptoms and it is often maintained over long periods of time, despite fluctuations in schizophrenic symptoms.

The s*upersensitivity model* (Mueser et al. 1998) is based on reports that patients with schizophrenia develop complications from substance use such as substance-induced psychosis at relatively low levels of substance consumption. The *supersensitivity model* takes an intermediate position between the two models of secondary SUD and secondary psychosis (see below), since it requires an increased vulnerability to psychosis, but it also recognizes the role of substance use in the manifestation of psychosis.

Finally, the socioeconomic decline of patients with schizophrenia may also play a role in the development of SUD in this population (*social drift hypothesis*) (Mueser et al. 1998).

6.3.2 Models of SUD and Secondary Development of Schizophrenia

The second model of psychosis induced by the consumption of psychotropic substances refers mainly to the effects of cannabis and stimulants. These substances can produce psychotic-like states during acute intoxication (International Classification of Diseases ICD-10: F1x.03, F1x.04) and they can induce time-limited

psychoses which may persist up to several weeks following drug use (ICD-10 F1x.5). However, the model of SUD and secondary development of schizophrenia goes beyond these time-limited complications. It is based on the observation that consumption of cannabis (and stimulants) often precedes the onset of psychoses, but these psychoses do not differ from other schizophrenic disorders in terms of their long-term course and outcome.

In recent years, cumulative evidence has supported the validity of this model of secondary development of schizophrenia following drug use, especially following the use of cannabis. Prospective epidemiological studies have shown that cannabis use is a significant risk factor for the development of schizophrenia. Early onset of cannabis use and heavy patterns of consumption were found to be associated with increased risk for later development of schizophrenia (Moore et al. 2007). In fact, it is assumed that use of cannabis interacts with the individual neurobiological vulnerability for psychosis. This is supported by the finding that comorbid patients are on average younger at the onset of schizophrenia compared to patients without comorbidity with SUD.

In this context there is merit in examining whether a possible change of the incidence of psychosis mirrors the increase in cannabis use in the general population. In fact, the worldwide average incidence of psychosis has remained approximately constant or has even slightly decreased over the last decades. However, recent studies demonstrated surprisingly strong regional differences with a sharp increase in the incidence of psychosis in South London and Zurich over the last 30 years. Assuming that cannabis use has increased more in these urban areas compared to other regions, there is speculation that cannabis may be partially responsible for the high regional incidence of schizophrenia in certain European cities (Gouzoulis-Mayfrank 2007; Moore et al. 2007).

6.3.3 Other Models of Comorbidity

Alternative models of comorbidity include the existence of common predisposing factors for schizophrenia and SUD. One of these models refers to a primary neurobiological dysfunction in the mesolimbic dopaminergic system (Chambers et al. 2001). Abnormalities in hippocampal formation and frontal brain regions in patients with schizophrenia may facilitate the positive reinforcing effects of drugs and reduce inhibitory control over drug-seeking behavior. Hence, according to the *primary addiction hypothesis,* psychotic patients may also be more vulnerable to develop a substance use disorder after been exposed to various psychoactive substances, irrespective of their specific short- and long-term effects (Walter et al. 2012). The *primary addiction hypothesis* is supported both by clinical arguments and the results of basic research and animal models. It implies that specific interventions for SUD such as psychoeducation should be integrated early in the treatment of young patients with psychosis even before the manifestation of SUD (Chambers et al. 2001).

Another model of common predisposition refers to the presence of antisocial personality traits or antisocial personality disorder in a subgroup of patients with particularly poor prognosis (Mueser et al. 2000).

Finally, bidirectional interrelations between psychosis and SUD are also possible or even plausible: Substance use may precipitate psychosis in vulnerable individuals, who may then continue using the drug in order to cope with dysphoric states related to the disorder (Gouzoulis-Mayfrank 2007).

In conclusion, every single model has its strengths and weaknesses, and no model can explain the full range of comorbidity of schizophrenia and addiction. It is possible that different models are valid for distinct subgroups of dually diagnosed patients. Moreover, it is even possible that different models are valid for single patients in different phases or episodes of their disorders.

6.4 Diagnostics/Assessment

SUD tends to be overlooked in people with schizophrenia; therefore, it is recommended to screen patients by means of standardized short instruments such as the Alcohol Use Disorders Identification Test AUDIT (Cassidy et al. 2008). When a cannabis or stimulant user presents for the first time with psychosis, then an initial diagnosis of drug-induced psychosis should be given (ICD-10 Code F1x.5x), unless there are clear indications for prodromal signs of psychosis preceding the onset of drug use. According to ICD-10, a drug-induced psychosis will manifest itself directly after, or at the latest within 2 weeks from the last use, it will mostly take days or weeks to remit, and sometimes some weak symptoms may persist for as long as 6 months. Hence, the initial diagnosis will have to be discarded in the course of the disorder and changed to schizophrenia (ICD-10 Code F2x), if psychotic symptoms persist for longer than 6 months despite drug abstinence, or if the patient recovers initially, but later relapses with psychosis, without having resumed drug consumption. Needless to say, if a patient continues using drugs, it will be extremely difficult to give a definite diagnosis. Toxicological screening procedures may help verify abstinence and support diagnostics; however, clinicians have to be aware of their limitations (e.g., screens for stimulants positive only for a few days after use; screens for cannabis positive for up to several weeks after last use).

6.5 Clinical Characteristics

A number of studies confirm the clinical impression that the average course and long-term outcome of patients with schizophrenia and comorbid SUD are poorer compared to the course of patients with schizophrenia only (Table 6.1).

In general, SUD is associated with more positive symptoms, aggressive behavior, increased rates of suicide, and poorer sociorehabilitative outcomes in patients with schizophrenia (Duke et al. 2001). Moreover, weaker compliance, poorer therapy response, higher relapse frequency, and higher sensitivity to extrapyramidal

Table 6.1 Characteristics of patients with psychosis and comorbid substance use disorder compared to patients with psychosis only (see Mueser et al. 2000, Gouzoulis-Mayfrank 2007)

• High relapse rate, more frequent emergency hospital admissions
• Poorer compliance, more changes in medication and intermittent high doses of antipsychotic medication
• More extrapyramidal side effects including tardive dyskinesia
• Poorer sociorehabilitative outcome, more financial and family problems, poorer family conditions, homelessness
• Aggressive and violent behavior, more frequent conflicts with law
• More frequent suicide attempts and suicides

side effects have been reported in schizophrenic patients with concurrent cannabis use disorder (Lazary 2012). The high relapse rate may be due to the direct pro-psychotic effects of drugs such as cannabis and stimulants, but it may also be due to the poorer compliance of comorbid patients with their antipsychotic medication. A higher incidence of extrapyramidal side effects including tardive dyskinesia in dually diagnosed patients may be linked to the intermittent administration of high doses of typical neuroleptic drugs during psychotic exacerbations. The association of comorbidity with aggressive and violent behavior is consistent with the results of the epidemiological ECA study, which reported 90 % comorbidity rates among prisoners (Regier et al. 1990). In summary, it is clear that SUD adversely affects the long-term course of comorbid schizophrenia.

6.6 Treatment

6.6.1 General Guidelines/Setting

It is common clinical experience that outcomes for people suffering from schizophrenia and SUD are unfavorable, particularly when patients are treated sequentially or in parallel, but in separate settings for the two disorders. This is probably related to fundamental differences in the philosophies of psychiatric and addiction care services, which often result in strict exclusions and low tolerance for symptoms from the "other" disorder in many traditional treatment settings. These problems contribute to the low compliance of patients who thus fall "between the cracks."

By now, the dominant view amongst experts favors *integrated treatment* approaches delivered by multidisciplinary teams of therapists who are experienced and competent in the treatment of both schizophrenia and SUD. The integrated treatment approach should adapt and balance supportive elements of psychiatric care with elements from addiction therapies which tend to rely on patients assuming responsibility for themselves. Beginning in the late 1990s integrated treatment programs were developed and implemented in the USA and in several European countries such as the UK (Lowe and Abou-Saleh 2004), Switzerland (Moggi et al. 2002), and Belgium (Morrens et al. 2011). Several reports from model

projects and over 50 controlled and quasiexperimental studies showed better long-term outcomes particularly for low-threshold, long-term outpatient therapeutic programs (Drake and Mueser 2000; Drake et al. 2004, 2008; De Witte et al. 2013). Such programs with out-reaching components do not require absolute abstinence; rather they aim at low patient attrition and strengthening of patient motivation to reduce substance use.

All programs with relatively favorable long-term outcomes combine pharmacotherapy, psychoeducation, and motivational approaches. In addition, some programs offer cognitive behavioral therapies and family interventions and some cooperate with self-help groups for dually diagnosed patients (*double trouble (DT) groups*).

6.6.2 Psychosocial Therapies

Motivational Interviewing (MI) is a core component of treatments for addictive disorders. For people with comorbid schizophrenia, interview techniques have to be modified and adapted in order to account for the common cognitive deficits of this population [MBDDT: Motivation-Based Dual Diagnosis Treatment (Drake and Mueser 2000)]. MI and psychoeducation are core interventions for the majority of patients who are in low motivational states. Even short motivational interventions consisting of four, three, or even a single session were shown to be effective in terms of higher utilization of further treatment offers (Gouzoulis-Mayfrank 2007; Bechdolf et al. 2012). However, motivational interventions alone are rarely sufficient to reduce substance use.

Psychoeducation is the second corner stone of psychosocial therapies for people with schizophrenia and SUD. Patients have to be informed about the interrelations between psychosis and substance use, about the interaction between drug effects and the individual vulnerability for psychosis and about the negative impact of drug use, particularly cannabis, on the course of psychosis. Effective psychoeducation may serve to build and enhance motivation to stop or at least reduce substance use. To date, there are two published German language manuals for group psychoeducation for dual disorder patients (*Komorbidität Psychose und Abhängigkeit,* KomPAkt, Gouzoulis-Mayfrank 2007; *Gesund und Ohne Abhängigkeit Leben*, GOAL, D'Amelio and Behrendt 2007).

Cognitive behavioral therapies are indicated for patients in higher motivational states. Nevertheless, it is important to take into account the limited cognitive resources of patients with schizophrenia in terms of concentration and abstraction abilities. In *Dual Diagnosis Relapse Prevention Therapy* (DDRP, Ziedonis and D'Avanzo 1998) specific abstinence-related skills such as recognition and avoidance of risk situations and resistance skills are combined with general social skills such as communication skills and assertiveness. In *Behavioral Treatment of Substance Abuse in Schizophrenia* (BTSAS, Bennett et al. 2001) patients are trained in general social skills ahead of abstinence related skills and problem solving. The German language program *Komorbidität Psychose und Abhängigkeit Skills*

Training (KomPASs, Gouzoulis-Mayfrank 2007) adds cognitive techniques to the training range focusing on cognitions, behaviors, and risk situations relevant for both psychosis and SUD.

Finally, *family interventions* use cognitive behavioral techniques and psychoeducation. Key focus areas are the interrelations between psychosis and substance use and a broadening of the biological concept of psychosis so as to include SUD. Communication training aims to blunt emotional dynamics in the family and reduce *high expressed emotion*, which presents risks for relapse and long-term outcomes of patients. *Family Intervention for Dual Disorders* (FIDD, Mueser and Fox 2002) includes both psychoeducation and communication training. The German language program *Gesund und Ohne Abhängigkeit Leben* (GOAL, D'Amelio and Behrendt 2007) concentrates on psychoeducation.

6.6.3 Effectiveness of Integrated Treatment

The treatment of patients with schizophrenia and SUD is difficult. Subject to realistic targets and a long-term treatment plan, positive outcomes are nevertheless possible. By now, there is a plethora of controlled experimental or quasiexperimental studies in different settings.

Drake and coworkers published the first qualitative reviews of the literature in 1998, followed by subsequent reviews in 2004 and 2008. The more recent review analyzed 45 randomized and nonrandomized controlled studies with samples between 25 and several hundred patients (Drake et al. 2008). Control groups received standard, non-integrated treatment (TAU) with follow-up up to several months after termination of treatment. In summary, intensive residential programs with strict abstinence requirements and lasting up to 6 months resulted in high drop-out rates of 45–85 % and high relapse rates of up to 95 % within a few months of termination of treatment. In contrast, low threshold, long-term, motivation-based out-patient programs delivered the best results in cost–benefit terms; drop-out rates were below 25 % and roughly half the patients achieved a gradual reduction of substance use accompanied by stabilization of their psychosis and reduction in the frequency of emergency admissions. Studies on the most severely affected homeless patients showed over the 1–3 years course of their treatment a reduction in medical complications related to substance use and improvements in their general medical condition and their social adjustment. However, despite these encouraging results, about half the dually diagnosed patients made only limited progress and about a quarter did not benefit at all from integrated out-patient treatment ("Nonresponder") (Drake et al. 2008).

Similarly, a recent review of 14 RCTs on integrated treatment programs for dually diagnosed outpatients reported some advantages of the integrated treatment approach; however, effect sizes were mostly modest (De Witte et al. 2013). The authors claimed that more homogeneous and qualitative sound studies are needed. In addition, a Cochrane analysis of 25 RCTs carried out in different settings, failed to demonstrate an overall superiority of integrated programs compared to other

treatments, although some studies did show advantages over the control conditions (Cleary et al. 2010). Cleary et al. (2010) also claimed that studies were too heterogeneous. Drake et al. (2008) suggested that some nonresponders may benefit from more intensive residential treatments incorporating elements of the anglosaxon *therapeutic communities* ("stepped care"). In their most recent literature review, they found that in those cases better results were achieved through longer treatments of at least a year compared to shorter treatments of 6 months or less (Drake et al. 2008).

In our view, the impact of even moderate therapeutic improvements on the lives of dually diagnosed patients should not be underestimated. On the other hand, it is important to set realistic therapeutic goals, to avoid overstretching both patients and therapists and to prevent drop-outs.

6.6.4 Pharmacotherapy

A reliable **antipsychotic medication** with a favorable side effect profile is the basis for the treatment of patients with schizophrenia and SUD. Typical neuroleptics may enhance addiction mechanisms through the selective blockade of mesolimbic dopamine D2 receptors. In addition, they may cause anhedonia, dysphoric mood, and extrapyramidal side effects (EPMS), which, in turn, may strengthen the tendency to (mis)use alcohol or drugs for self-medication. Most atypical antipsychotics have broader receptor profiles, they are more effective against negative symptoms and their side effect profile in terms of EPMS, dysphoria, anhedonia, and agitation is more favorable compared to typical neuroleptics. Hence, atypical antipsychotics may have advantages for the treatment of patients with schizophrenia and SUD over typical neuroleptics. Indeed, several case reports and naturalistic studies reported that dually diagnosed patients who were switched from typical to atypical antipsychotics suffered less from craving thereafter (Gouzoulis-Mayfrank 2007; Green et al. 2008).

Up to now, the evidence is best for clozapine, for which there are open, retrospective, and prospective studies showing reduction in the use of alcohol or drugs following switch to this drug. Newer atypical antipsychotics may also be considered, but they are thought be less effective than clozapine (Green et al. 2008). However, a recent, small pilot RCT failed to demonstrate superiority of clozapine over the newer atypical antipsychotic ziprasidone in dually diagnosed patients (Schnell et al. 2014). Given the fragile compliance of dual disorder patients, injectable *depot medications* offer a clear advantage and should be considered whenever patients consent. The best evidence is currently available for risperidone depot (Rubio et al. 2006).

In conclusion, the evidence for different antipsychotics for schizophrenia with comorbid SUD is limited. In general, atypical antipsychotics should be given preference over typical neuroleptics. Aspects such as side effect profiles and patient preferences have to be taken into account when making the choice of medication.

Apart from antipsychotics, there is a rationale for *concomitant medications with antidepressants and/or mood stabilizers* in cases of persistent depressive mood, apathy, or mood shifts and impaired impulse control in spite of otherwise effective antipsychotic medication. However, to date there are no controlled studies for combined antipsychotics and antidepressants and/or mood stabilizers treatment for dually diagnosed patients.

In contrast, there is some literature on the *combination of antipsychotics with pharmacotherapies for SUD* in patients with schizophrenia. An extensive retrospective analysis of patient records and two RCTs showed that the μ-opiate receptor antagonist *naltrexone* reduced craving and alcohol consumption in patients with schizophrenia and alcoholism (Petrakis et al. 2005). Similarly, several case reports, an open-pilot study, a retrospective analysis of patient records and a large RCT showed that dually diagnosed patients consumed less alcohol when they were on *disulfiram* (Petrakis et al. 2005; Gouzoulis-Mayfrank 2007). In these studies, disulfiram was tolerated well with neither serious side effects nor deterioration of psychotic symptoms. Unlike naltrexon and disulfiram, a recent, small RCT showed no advantage of *acamprosate* over placebo in terms of alcohol consumption in dually diagnosed patients (Ralevski et al. 2011).

6.7 Summary and Perspectives

The common comorbidity of schizophrenia and SUD is associated with poor long-term outcomes. The integrated treatment approach focuses on long-term, motivation based, out-patient programs and offers some advantages over standard care. Unfortunately, integrated treatment programs are not readily available. Moreover, about a quarter of dually diagnosed patients will not benefit from integrated out-patient treatment and may need more intensive residential programs. Subgroups of dually diagnosed patients are likely to respond to different treatments. Hence, the identification of distinct subgroups may be an important aspect for future research. In any case, implementation of integrated treatment programs has to be taken further and the programs have to be evaluated and modified according to different settings and local conditions.

References

Bechdolf A, Pohlmann B, Güttgemanns J et al (2012) State-dependent motivational interviewing for people with schizophrenia and substance use: results of a randomised controlled trial. Nervenarzt 83:888–896

Bennett ME, Bellack AS, Gearon JS (2001) Treating substance abuse in schizophrenia. An initial report. J Subst Abuse Treat 20:163–175

Blanchard JJ, Brown SA, Horan WP, Sherwood AR (2000) Substance use disorders in schizophrenia: review, integration, and a proposed model. Clin Psychol Rev 20:207–234

Borgwardt SJ, Riecher-Rossler A, Dazzan P (2007) Regional gray matter volume abnormalities in the at risk mental state. Biol Psychiatry 61:1148–1156

Cassidy CM, Schmitz N, Malla A (2008) Validation of the alcohol use disorders identification test and the drug abuse screening test in first episode psychosis. Can J Psychiatry 53:26–33
Chambers RA, Krystal JH, Self DW (2001) A neurobiological basis for substance abuse comorbidity in schizophrenia. Biol Psychiatry 50:71–83
Cleary M, Hunt GE, Matheson SL, Siegfried N, Walter G (2010) Psychosocial interventions for people with both severe mental illness and substance misuse. The Cochrane Collaboration. Editorial Group: Cochrane Schizophrenia Group. Wiley
D'Amelio R, Behrendt BWT (2007) Psychoedukation Schizophrenie und Sucht. Manual zur Leitung von Patienten-und Angehörigengruppen. Elsevier/Urban and Fischer, Munich
De Witte NA, Crunelle CL, Sabbe B, Moggi F, Dom G (2013) Treatment for outpatients with comorbid schizophrenia and substance use disorders: a review. Eur Addict Res 20:105–114
Drake RE, Mueser KT (2000) Psychosocial approaches to dual diagnosis. Schizophr Bull 26:105–118
Drake RE, Mueser KT, Brunette MF, McHugo GJ (2004) A review of treatments for people with severe mental illnesses and co-occurring substance use disorders. Psychiatr Rehabil J 27:360–374
Drake RE, O'Neal EL, Wallach MA (2008) A systematic review of psychosocial research on psychosocial interventions for people with co-occurring severe mental and substance use disorders. J Subst Abuse Treat 34:123–138
Duke PJ, Pantelis C, McPhillips MA, Barnes TRE (2001) Comorbid non-alcohol substance misuse among people with schizophrenia. Br J Psychiatry 179:509–513
Gouzoulis-Mayfrank E (2007) Komorbidität Psychose und Sucht—Grundlagen und Praxis—Mit Manualen für die Psychoedukation und Verhaltenstherapie, 2nd edn. Steinkopff, Darmstadt
Green AI, Noordsy DL, Brunette MF, O'Keefe C (2008) Substance abuse and schizophrenia: pharmacotherapeutic intervention. J Subst Abuse Treat 34:61–71
Lazary J (2012) Psychopharmacological boundaries of schizophrenia with comorbid cannabis use disorder: a critical review. Curr Pharm Des 18:4890–4896
Lowe AL, Abou-Saleh MT (2004) The British experience of dual diagnosis in the national health service. Acta Neuropsychiatrica 16:41–46
Moggi F, Brodbeck J, Költzsch K, Hirsbrunner H-P, Bachmann KM (2002) One-year follow-up of dual diagnosis patients attending a 4-month integrated inpatient treatment. Eur Addict Res 8:30–37
Moore TH, Zammit S, Lingford-Hughes A et al (2007) Cannabis use and risk of psychotic or affective mental health outcomes: a systematic review. Lancet 370:319–328
Morrens M, Dewilde B, Sabbe B, Dom G, De Cuyper R, Moggi F (2011) Treatment Outcomes of an Integrated Residential Programme for patients with schizophrenia and substance use disorder. Eur Addict Res 17:154–163
Mueser KT, Fox L (2002) A family intervention program for dual disorders. Community Ment Health J 38:253–270
Mueser KT, Drake RE, Wallach MA (1998) Dual diagnosis: a review of etiological theories. Addict Behav 23:717–734
Mueser KT, Yarnold PR, Rosenberg SD, Swett C Jr, Miles KM, Hill D (2000) Substance use disorder in hospitalized severely mentally ill psychiatric patients: prevalence, correlates, and subgroups. Schizophr Bull 26:179–192
Petrakis IL, Poling J, Levinson C, Nich C, Carroll K, Rounsaville B (2005) Naltrexone and disulfiram in patients with alcohol dependence and comorbid psychiatric disorders. Biol Psychiatry 57:1128–1137
Ralevski E, O'Brien E, Jane S, Dean E, Dwan R, Petrakis I (2011) Effects of acamprosate in a treatment study of patients with schizophrenia spectrum disorders and comorbid alcohol dependence. J Nerv Mental Dis 199:499–505
Regier DA, Farmer ME, Rae DS et al (1990) Comorbidity of mental disorders with alcohol and other drug abuse. Results from the Epidemiologic Catchment Area (ECA) Study. JAMA 264:2511–2518

Rubio G, Martínez I, Ponce G, Jiménez-Arriero MA, López-Muñoz F, Alamo C (2006) Long-acting injectable risperidone compared with zuclopenthixol in the treatment of schizophrenia with substance abuse comorbidity. Can J Psychiatry 51:531–539

Schnell T, Koethe D, Krasnianski A, Gairing S, Schnell K, Daumann J, Gouzoulis-Mayfrank E (2014) Ziprasidone versus clozapine in the treatment of dually diagnosed (DD) patients with schizophrenia and cannabis use disorders: a randomized study. Am J Addict 23:308–312

Sinha R, Garcia M, Paliwal P, Kreek MJ, Rounsaville BJ (2006) Stress-induced cocaine craving and hypothalamic-pituitary-adrenal responses are predictive of cocaine relapse outcome. Arch Gen Psychiatry 63:324–331

Volkow ND, Wang GJ, Fowler JS, Tomasi D, Telang F (2011) Addiction: beyond dopamine reward circuitry. Proc Natl Acad Sci U S A 108:15037–15042

Walter M, Denier N, Vogel M, Lang UE (2012) Effects of psychoactive substances in schizophrenia. Curr Top Med Chem 12:2426–2433

Walter M, Gerber H, Kuhl HC et al (2013) Acute effects of intravenous diacetylmorphine on the hypothalamic-pituitary-adrenal axis response. J Clin Psychopharmacol 33:193–198

Wright IC, Rabe-Hesketh S, Woodruff PW, David AS, Murray RM, Bullmore ET (2000) Meta-analysis of regional brain volumes in schizophrenia. Am J Psychiatry 157:16–25

Ziedonis DM, D'Avanzo K (1998) Schizophrenia and substance abuse. In: Kranzler HR, Rounsaville BJ (eds) Dual diagnosis and treatment. Marcel Dekker, New York, pp 427–465

Substance-Induced Psychotic Symptoms

7

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Abstract

Psychosis can be brought on by a number of different substances such as alcohol, cannabis, sedatives, cocaine, stimulants, and hallucinogens. For some substances the psychosis is predominant in the acute phase (cannabis, cocaine, stimulants, and hallucinogens), but for others the withdrawal phase infers the heightened risk (alcohol and sedatives). Some drugs may also increase the risk of

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longer lasting psychotic disorders (cannabis and central stimulants), but it remains an area of dispute whether these drugs cause the primary psychosis or whether they precipitate psychosis in individuals who are already vulnerable. This chapter reviews the literature on this topic and gives advice on the treatment of acute and prolonged psychotic illness in relationship to drug use, including delirium tremens caused by withdrawal from alcohol or sedatives.

7.1 Introduction

Psychotic disorders are characterized by a set of severe mental symptoms including delusions and hallucinations that disrupt a person's perceptions, thoughts, emotions, and behaviour. Disorders that feature psychotic symptoms include schizophrenia, schizoaffective disorder, schizophreniform disorder, and delusional disorder but also bipolar disorder and other affective psychoses, and substance-induced psychotic disorders. In the International Classification of Diseases (WHO), *substance-induced psychoses* are defined in connection with alcohol (F10.5), cannabis (F12.5), sedatives (F13.5), cocaine (F14.5), stimulants (F15.5), and hallucinogens (F16.5). Although different drugs may produce symptoms via distinct pathophysiological mechanisms, the clinical pictures often present similarities. However, it is still difficult to distinguish when psychotic symptoms in individuals with current or recent heavy substance use are due to an intoxication that mimics a functional psychosis; represent a drug-induced relapse into or symptomatic influence on a pre-existing psychotic disorder (e.g. schizophrenia); or are a "true" substance-induced psychosis, which refers to psychotic symptoms which arise in the context of drug intoxication but persist beyond elimination of the drug (Núñez and Gurpegui 2002). Irrespective of these possible mechanisms, the treatment is symptomatic and includes providing a calm and safe environment, discontinuing the drug intake, and sometimes the use of sedative and antipsychotic medications. This chapter aims to provide a brief overview of substance-induced psychotic symptoms caused by different classes of substances either in the acute phase or the long term, be it due to intoxication or withdrawal. We will discuss the etiology, to the extent that this is known, and the clinical management of these conditions.

7.2 Acute Psychotic Symptoms Following Substance Intake

7.2.1 Cannabis-Induced Psychotic Symptoms

After the intake of cannabis the user will experience a "high" from 10 to 15 min up to 4–8 h after intake depending on the dose and route of administration. Cannabis is reported to produce subjective effects such as greater enjoyment of food taste and

aroma, enhanced appreciation of music, and marked distortions in perception of time and space. Higher doses may produce altered body image, auditory and/or visual illusions, and hallucinations with a varying degree of delusion. With even higher doses, perceptional distortion becomes more pronounced and psychotic symptoms, including depersonalization, derealization, and paranoia, may occur. Panic attacks may be seen in unaccustomed users. Usually, these symptoms subside when the psychoactive components of cannabis are eliminated from the body, but the effects can last for more or less time than would be explained by the pharmacology of the active compounds. This may be related to the tendency for cannabis to cause psychosis in vulnerable individuals (see later).

Cannabis is a drug of abuse that includes more than 100 different chemical compounds, more than 40 of which are psychoactive. The most prominent active ingredient, delta-9-tetrahydrocannabinol (THC), is the one most likely to cause psychosis. Other psychoactive substances, like cannabidiol (CBD) are thought to have an opposite effect and may protect against psychotic symptoms (Zuardi et al. 2012). Today, cannabis products are often grown with the intention of giving products with a higher THC/CBD ratio, thereby possibly increasing the risk for triggering psychosis. Likewise, newer synthetic cannabinoids will lack the potentially more balanced effects of naturally occurring cannabis products so they may also be associated with an increased risk of drug-induced psychotic disorders, although there is little data available yet.

7.2.2 Stimulant-Induced Psychotic Symptoms

The symptoms of psychosis induced by stimulants (amphetamine, methamphetamine, cocaine, and others) are often similar to those of acute schizophrenia spectrum psychosis and include difficulties concentrating, delusions of persecution, increased motor activity, akathisia (inner restlessness), disorganization of thoughts, lack of insight, anxiety, suspicion, and auditory hallucinations (Srisurapanont et al. 2011). Some studies have suggested differences between stimulant-induced psychosis and schizophrenia spectrum psychosis where the former is associated with more pronounced grandiosity and visual hallucinations, for example (Leamon et al. 2010). However, distinguishing between the two types of psychosis on the basis of acute symptoms is problematic (Medhus et al. 2013). The similarities in symptoms between acute schizophrenia and stimulant psychosis are so pronounced that stimulant-induced psychosis has been suggested as an experimental model for primary psychotic disorders (Bell 1965). Acute psychosis induced by amphetamines seems to have a faster recovery (Yeh et al. 2001), and typically appears to resolve with abstinence in most cases, although the recovery may be incomplete (Ujike and Sato 2004).

Both amphetamines and cocaine are often taken several times over the course of a number of days in "runs" or "binges". Users will often end these binges by using sedating drugs such as alcohol, benzodiazepines, opiates, or cannabis. This could be seen as a form of self-medication and may be one reason why users often develop

problems with several drugs. The ICD-10 distinguishes between cocaine psychosis (F14.5) and psychosis from other stimulants (F15.5). These are very similar (Curran et al. 2004), and psychotic states have also been described as a consequence of using other types of stimulant, including caffeine (Hedges et al. 2009).

7.2.3 Hallucinogen-Induced Psychotic Symptoms

A hallucinogenic drug is, by definition, a compound that may induce psychotic symptoms. They include ecstasy (MDMA; with central stimulant properties; see above), ketamine (an anaesthetic), psilocybin (psychedelic tryptamine from mushrooms), mescaline (from the peyote cactus), LSD (lysergic acid diethylamide, a powerful synthetic), and phencyclidine (PCP; "angel dust"). These drugs stimulate different glutamate and serotonin receptors. They may acutely cause a series of psychotic symptoms, including distortion of vision, sense of space, hearing, and touch, disorientation in time, and paranoia.

Flashbacks after the drug has been cleared from the body have been reported. Flashbacks are a poorly understood phenomenon, described as sudden but transient psychotic episodes thought to be related to the use of a drug, but dissociated in time from the intake, sometimes appearing days or weeks after the last drug use.

7.2.4 Paradoxical "Psychotic" Reactions to Alcohol and/or Benzodiazepines

The expected reaction to the use of alcohol and benzodiazepines is to become sedated or relaxed. Some patients may react differently, with agitation, disinhibition, aggression, and exaltation. Such reactions are referred to as *paradoxical*. Their aetiology is not clear, but certain pathologies increase the risk of a paradoxical reaction. Having a psychiatric illness including bipolar disorder, schizophrenia, or severe personality disorder (antisocial, histrionic or borderline) increases the risk of paradoxical reaction (Cole and Kando 1993). Younger children also have an increased risk of paradoxical reactions, presumably because their central nervous system is not fully developed. Paradoxical reactions need not be treated pharmacologically, but adequate symptomatic or psychosocial support must be offered to prevent damage to the individual or the environment.

It is sometimes claimed that taking a low dose of benzodiazepines leads to sedation whereas a higher dose may cause agitation. This is a popular myth with little empirical evidence to support it. It may reflect expectations, or it could be that individuals willing to ingest large doses of benzodiazepines have a higher prevalence of the risk factors associated with paradoxical reactions.

A common consequence of benzodiazepine use is *anterograde amnesia*, which may also occur following intake of large amounts of alcohol (black-out). In the case of benzodiazepines (and other GABAergic drugs such as GHB), anterograde amnesia is not always linked to sedation. A person may appear awake and oriented,

but have no recollection of what has passed after "waking up". Benzodiazepines, GHB, and related compounds are sometimes used as "date-rape drugs", leaving the victim apparently awake but with no recollection of what has passed. This phenomenon is most likely due to the expected and imminent amnesia following the intake of benzodiazepines and should not be considered a paradoxical reaction.

Paradoxical reactions should not be mistaken for delirious or confusional states that may occur in elderly patients after using benzodiazepines. Such reactions are rather considered to reflect a general deterioration in cognitive functioning due to aging of the nervous system, atherosclerosis, dementia, or a combination of those factors. Lastly, a paradoxical reaction is related to, but not the same as, *pathological intoxication*, a term sometimes used in forensic psychiatry. This relates to the fact that some people become very agitated, amnesic and even psychotic after drinking a very small amount of alcohol. In some countries this is considered a mediating circumstance in the judicial system on first offence. The empirical evidence for this phenomenon is meagre.

7.2.5 Assessment and Treatment of Acute Psychotic Symptoms Induced by the Intake of Drugs

Patients who present with newly developed psychotic symptoms should always be thoroughly investigated and symptoms assessed, preferably in a hospital setting. An immediate and primary goal of treatment is to prevent the patient from self-harm and/or violent behaviour that may injure other people.

In the acute phase it may be impossible to differentiate between a drug-induced psychosis and acute schizophreniform psychosis on the basis of symptoms. A thorough medical history with the emphasis on drug intake should be obtained. It is also preferable, if possible, to obtain a supervised urine sample to screen for illicit drugs since drug use is a common etiological factor and cannot be dismissed unless objective assays are performed. However, a positive or negative urine drug screen can, in itself, neither confirm nor refute the etiology of the psychosis.

An immediate goal of treatment is to calm down the situation and help the psychotic individual to feel as safe and secure as possible. In addition to environmental measures (see Box 7.1) initial pharmacological treatment with a benzodiazepine sedative should be considered. The choice of benzodiazepine varies between guidelines and may be guided by side-effect profiles. Antipsychotic medication should be used if the situation is not resolved with benzodiazepines.

Box 7.1. Caring for Patients with Acute Psychotic Symptoms

- Reduce stimuli in the environment (e.g. not allowing TV or contact with other patients in the ward)
- A kind and non-confrontational approach, while allowing the patient to speak
- Communicate calmness and security when approaching the patient
- Offer company in the room
- Make sure that the patient does not become dehydrated
- Regularly check pulse, blood pressure, body temperature, and psychiatric status

Even though many episodes of drug-induced psychosis resolve within a short time, it must be kept in mind that some patients may eventually develop a primary psychosis, possibly because of pre-morbid vulnerability factors. Individuals with a drug-induced psychosis should therefore be considered as high risk patients who need to be followed over time.

In addition to the symptoms mentioned above, an acute stimulant-induced psychosis is often characterized by disorganized behaviour, psychomotor agitation, and aggression and may require mandatory care to protect the patient from self-harm. Mandatory care that includes physical restraint may potentially lead to an increased risk of sudden death (due to cardiac arrest) although the research literature on this topic is not consistent.

Sedating drugs such as benzodiazepines are often beneficial in the acute phase if non-medication interventions are not enough. Extreme aggression with violent behaviour may necessitate a combination of measures. The evidence for specific pharmacological treatments for drug-induced psychosis is sparse. Amphetamine-induced psychotic symptoms are commonly treated using either antipsychotic medications (dopamine antagonists) and/or benzodiazepines. Only one randomized controlled trial of antipsychotic medication (olanzapine and haloperidol) has shown that medication significantly reduces psychotic symptoms and that olanzapine was associated with fewer side effects (mostly extrapyramidal symptoms) than haloperidol (Leelahanaj et al. 2005). Antipsychotics are most often used in situations where the patient displays disorganized behaviour and aggression. A drug-induced psychotic episode is a condition that normally has a dramatic but transient course, with the majority of patients recovering rapidly with reduced agitation and anxiety and improved perception of reality within a day or two. The goal of the pharmacological treatment is to sedate the patient until they sleep. If this is achieved the prognosis is usually good. Most psychotic experiences induced by hallucinogens do not require treatment, but more prolonged states may be calmed by the use of benzodiazepines, and possibly, in severe cases, small doses of antipsychotics.

Some guidelines for treating acute psychosis induced by central stimulants suggest that antipsychotic medication should be used with particular caution because of the risk of sudden hypotension or, in a worst case, a circulatory collapse, presumably related to antagonism at alpha$_1$-receptors (Allen et al. 2005). Although

the American Food and Drug Administration (FDA) has issued a black box warning against the use of antipsychotics (specifically the use of droperidol) such adverse effects have not been described in the scientific literature, nor have they been registered in the Norwegian or Swedish national databases on medication side effects. Amphetamines have sympathomimetic effects (i.e. mimic the effects of activation of the sympathetic nervous system), which to a certain degree may be blunted by dopamine antagonists, thereby increasing the risk of a fall in blood pressure. Theoretically, central stimulants may give rise to changes in the heart rhythm which can also be precipitated by dopamine antagonists (e.g. prolonged QT-time in the heart's conduction system which can be detected by electrocardiography). It is unknown whether there is any specific interaction between central stimulant drugs and dopamine antagonists that may lead to an increased risk for arrhythmias. Nor has it been established whether the risk of cardiac effects from antipsychotic medication might be greater in amphetamine-induced psychosis compared to psychotic states due to other causes.

Different international guidelines recommend that benzodiazepines should be the first line treatment of drug-induced psychosis and that antipsychotics should only be used when benzodiazepines fail to reach the target. The very definite warnings against the use of antipsychotics in the acute phase found in the US guidelines are not mirrored in guidelines from other countries. For example, the Australian guidelines recommend the use of oral lorazepam 2–4 mg and repeated once, alternatively 5 mg midazolam as an intramuscular injection (McIver et al. 2006). If this does not calm the patient, 10 mg of olanzapine is recommended. No European guidelines for the acute treatment of drug-induced psychosis have been identified. The reluctance to use antipsychotics must be weighed against the possible beneficial effects of these drugs. It has been suggested that antipsychotics may protect against some of the neurotoxic effects of stimulant drugs (Curran et al. 2004). Furthermore, the emergence of a drug-induced psychosis may be the first sign of a primary psychotic disorder (see later). The use of antipsychotics in the acute phase might thus be seen as early treatment of vulnerable patients.

7.3 Psychotic Symptoms Due to Substance Withdrawal

7.3.1 Withdrawal

Withdrawal symptoms can occur even after smaller doses of drugs or alcohol. Most such withdrawal reactions are mild and will not need medical interventions as they improve after rest and sleep in a tranquil environment. When higher doses of alcohol have been used, especially over an extended period, withdrawal symptoms on reducing or stopping use may become more severe. Such withdrawal symptoms are often the opposite to the effects of the drugs themselves. Users experience anxiety, sleeplessness, sedation, nausea, vomiting, headaches, and tremor of different degrees of seriousness. A list of these symptoms is given in Box 7.2. The symptoms typically appear 6–12 h after the withdrawal from alcohol, but may appear much later (even days later) if caused by withdrawal from benzodiazepines,

for example. If the withdrawal reaction becomes severe it may necessitate medical intervention. The withdrawal severity can be assessed using the Clinical Institute Withdrawal Assessment of Alcohol Scale, Revised (CIWA-Ar) (Sullivan et al. 1989). Severe withdrawal states are often associated with anxiety and sleep disorder. This may need professional attention including support, rest, and adequate nutrition.

Withdrawal from alcohol and benzodiazepines (and related compounds) is associated with a risk of seizures (generalized tonic–clonic epileptiform seizures with temporary unconsciousness). To prevent this, prophylactic treatment with drugs that show some cross-tolerance with the abused drug may be started. For the prevention of alcohol withdrawal seizures, benzodiazepines have the best evidence base (Amato et al. 2011). Monotherapy with benzodiazepines should always be preferred as it is easier to monitor. Short-acting benzodiazepines (e.g. lorazepam) may be associated with a slightly greater risk of seizures than long-acting compounds, presumably because of rapid variations in plasma concentrations and the need for more frequent administration. However, long-acting benzodiazepines (e.g. diazepam) have a longer elimination time which can be a problem if the patient is released from hospital shortly after intake. Carbamazepine is an alternative, but it has several side effects which need to be considered and has less evidence in the literature. The combination of benzodiazepines and carbamazepine should always be avoided.

Box 7.2. Signs and Symptoms of Alcohol and Benzodiazepine Withdrawal, Including Delirium Tremens

Signs and symptoms range from the small and insignificant, needing no medical treatment, to the very severe requiring hospitalization and sedation

- Anxiety
- Confusion/disorientation
- Trouble sleeping
- Bad dreams
- Severe agitation
- Fever
- Hallucinations (perceptions of a thing, voice, or person that is not present. Can be visual, auditory, and/or tactical)
- Delusions (a false belief that is strongly held)
- Tremors of the hands, head, or body
- Severe sweating
- Rapid heartbeat
- Nausea
- Increased rate of breathing
- Increased blood pressure
- Increased body temperature
- Epileptiform seizures

7.3.2 Delirium Tremens

Delirium tremens is a psychotic disorder that develops after particularly long and heavy drinking periods when alcohol intake is rapidly reduced, or stopped. Delirium tremens is a potentially lethal condition and should always be treated in hospital. Lack of sleep, physical illness, and poor nutrition increases the risk of delirium (Box 7.3). Although the condition typically develops after alcohol intake has stopped, it sometimes becomes manifest only after one or more abstinent days, with few or no symptoms of alcohol withdrawal. This delay sometimes makes the diagnosis difficult as signs and symptoms of alcohol withdrawal may have abated by the time the hallucinations and confusion become apparent.

Delirium tremens is an entirely clinical diagnosis, as there are no specific laboratory tests or other biomarkers. This makes it important to consider and exclude alternative diagnoses (e.g. other psychotic disorders; dementia; organic brain damage, including traumatic brain injury). As a prerequisite, there should be a long and heavy consumption of alcohol that often (but not always) involves signs and symptoms of alcohol withdrawal (increased pulse rate, sweating, nausea, tremor, hypertension, and sleep disorder) at some stage. On top of that, the patient gradually develops hallucinations, sometimes beginning with auditory (e.g. hearing music, or voices) but as the condition worsens the visual sensorium becomes clouded and the patient may experience illusions (mistaking staff for imagined figures) and ultimately visual and/or tactical hallucinations. This stage is commonly referred to as "pre-delirium". The third symptom level includes confusion, which is the final component of the diagnostic entity that constitutes delirium tremens.

Box 7.3. Risk Factors for Delirium Tremens

- Prolonged, heavy alcohol intake (rule of thumb: daily intake of >250 g pure ethanol/day continuously for at least 3 weeks. The amount corresponds to 70 cl hard liquor, *or* 4 bottles of wine, *or* 10 cans of beer)
- One or more previous episodes of delirium tremens
- Withdrawal signs occurring already during intoxication (i.e. at a blood alcohol concentration >0.1 %)
- Concurrent abuse of benzodiazepines, barbiturates or other GABAergic drugs
- Pulse rate >120 beats per minute
- Poor general condition (e.g. malnutrition)
- Chronic somatic disorder that may affect the patient's general condition (e.g. diabetes)
- Physical trauma (fractures, large soft tissue damage, organic brain damage)
- Infection (e.g. urinary, pulmonary)
- Fever

Although delirium tremens is characterized by anxiety, psychomotor restlessness, often vivid visual and tactile hallucinations, confusion and paranoia, the patients may present with fewer symptoms. Therefore, patients with hallucinations and a clouded sensorium should be rapidly and adequately assessed with regard to recent alcohol (or barbiturate or benzodiazepine) intake. There is often increased blood pressure and body temperature. Fluid and electrolyte status may often be disturbed.

The overreaching goal in the treatment of delirium tremens is to induce sleep by using sedatives with cross-tolerance to alcohol. Benzodiazepines should always be considered as the first choice of medication owing to their low toxicity and low risk for respiratory depression, but barbiturates or clomethiazole may also be considered although they generally require a more specialized setting with staff used to these drugs, more intense supervision of the patient and more careful dose titration. Diazepam may be considered the "golden standard" as its long half-life allows for variations in the dosing schedule. The drug is given by oral or parenteral administration until sleep is induced. The usual procedure is to start with 20 mg diazepam (10–20 mg if parenteral), then 10–20 mg (5–10 mg if parenteral) every hour until sleep. The risk of overdosing is small unless other sedating drugs are used concomitantly. The presence of a detectable blood alcohol concentration is not a contraindication for benzodiazepine therapy if the patients also show signs of alcohol withdrawal. If the patient develops seizures, 10–20 mg diazepam should immediately be given rectally (or intravenously if there is already an intravenous canula in place). If the seizure persists, the dose should be reiterated immediately, and the procedure for acute assessment and treatment of *status epilepticus* initiated. The aim of treatment for delirium tremens is to allow the patient to sleep for at least 24 h. The total dose during the first 12–24 h may dramatically exceed the levels used for treatment of other conditions, e.g. anxiety, and sometimes several hundred milligrams may be needed for a therapeutic response. The need for such doses is explained by the increased tolerance to GABAergic agonists produced by heavy and prolonged alcohol intake. Patients with delirium tremens should be carefully monitored with regard to respiration. If respiratory depression occurs, flumazenil (an antidote for benzodiazepines) should be administered. If the patient cannot be satisfactorily sedated by benzodiazepines alone, a barbiturate, clomethiazole, or even full anaesthesia may be needed. If barbiturates are used, the patient must be more closely monitored with regard to respiration, blood pressure, temperature, and fluid balance. An antipsychotic medication may be added to reduce psychomotor agitation.

Delirium tremens following the withdrawal from benzodiazepines should be treated according to the same principles as for withdrawal from alcohol.

One of the most important points when treating patients at risk of delirium tremens, or who have developed a delirious state, is prophylactic treatment with thiamin (vitamin B_1) to avoid Wernicke–Korsakoff's syndrome. Wernicke–Korsakoff's syndrome is caused by lack of thiamine and is most often caused by an alcohol-use disorder. The syndrome is also present in other conditions such as severe eating disorders (e.g. anorexia nervosa), prolonged vomiting, and obesity

surgery and involves small haemorrhages and necrosis in the central nervous system grey matter. To prevent Wernicke–Korsakoff, patients at risk should be given 100–200 mg thiamin intravenously, unless it is obviously unnecessary (e.g. if the patient has received large doses of thiamin during a previous, recent treatment episode only days before). The dose should be repeated 2–3 times during the following days. Historically, the syndrome was perceived as having two phases: Wernicke's encephalopathy is a triad of (1) vision disturbance with diplopia, (2) ataxia (unsteadiness), and (3) confusion, whereas Korsakoff's psychosis is an amnestic disorder that develops as a consequence of the encephalopathy. Korsakoff's psychosis is characterized by confusion and a severe deficiency of short term memory, often compensated for by vivid confabulation (filling in the blanks with more or less well-fitting information). The treatment is immediate (urgent) administration of high doses of thiamin. If a patient presents with the full clinical picture of Wernicke–Korsakoff, thiamin 400–500 mg should be given slowly intravenously for 3 days, followed by 200 mg/day i.v. or intramuscularly for 5 days, followed by oral medication for 2 weeks. Vitamin B complex should be given at the same time. The oral bioavailability of thiamin varies and may be reduced by chronic alcohol use. It is therefore of the utmost importance that patients who are in a poor physical condition are immediately treated with large doses of thiamin. However this may be equally important for patients who appear well-nourished but have consumed large quantities of alcohol over longer periods, in order to replenish the tissue concentration of this important vitamin. There is a lack of evidence about the duration of thiamin replacement therapy, and the doses required, but the connection between thiamin deficiency and Wernicke–Korsakoff is well established. Clinical experience suggests that high doses of thiamine are needed to prevent and treat this very serious and incapacitating condition. Oral administration of multi-vitamin B complex preparations is recommended for patients with poor nutritional status and chronic relapsing alcohol-use disorder but this cannot replace the initial parenteral administration.

7.4 Long-term Psychosis Following Substance Intake

7.4.1 Cannabis and the Risk of Schizophrenia

Repeated cannabis use is associated not only with an increased risk of acute psychotic symptoms and mania, but also with an increased risk of developing schizophrenia. The most comprehensive meta-analysis to date shows a 40 % increase in risk of psychosis in participants who had ever used cannabis and a clear dose–response effect with a 50–200 % increased risk in the most frequent users (Moore et al. 2007). In some cases high consumption of cannabis may produce symptoms that are indistinguishable from those of an acute schizophreniform psychosis. If the cannabis intake is stopped, symptoms usually subside within hours to days. In patients who present with a first onset psychotic episode, cannabis users who reduced or stopped their use had greater improvement

in psychotic symptoms at 1 year compared with continued users and non-users (Stone et al. 2013). Continued users remained more symptomatic than non-users at follow-up. Thus, by reducing cannabis use, patients with first-episode psychotic symptoms may achieve significant health benefits. In fact, the overwhelming majority of studies in this area have reported an improvement in functioning with reduction in cannabis use (Stone et al. 2013). Among patients with schizophrenia, cannabis use is more common among individuals with a first episode, younger people and males rather than females (Koskinen et al. 2010). It has been debated for a long time whether a specific form of acute and/or chronic psychosis exists that is associated directly with cannabis use. In fact, despite much research, there is little evidence for any specific psychopathology which is distinct from that of other types of psychosis (Baldacchino et al. 2012).

Regular consumption of cannabis may lead to an *amotivational syndrome*. The user spends a lot of time on use and has great difficulty getting started on other activities. The syndrome is very similar to the initial stages of schizophrenia with many negative symptoms, lack of initiative, social isolation, and passing the time without doing anything productive, or not reaching desired goals. In recent years it has been questioned whether such an amotivational syndrome really exists as an entity in its own right (Johns 2001), or whether it is an umbrella term for several phenomena. It might represent the rebellion of young individuals against the grown-up world's ambitions and conservative lifestyle, or the effects of cannabis on the brain, or even a prodromal phase of schizophrenia, or a combination of these.

The relationship between cannabis use and acute psychotic episodes (with hallucinations; see above), and the similarities between amotivational syndrome and the initial phases of schizophrenia, have led to the suggestion that cannabis use may be causal in the development of chronic psychoses, especially schizophrenia. Indeed, it has long been recognized that people who have used cannabis have an increased risk of having a diagnosis of schizophrenia. In a series of studies of Swedish conscripts (Andréasson et al. 1987; Zammit et al. 2002), cannabis use in individuals with no signs of schizophrenia significantly increased the risk of developing the disease later in life. A dose–response relationship has also been observed, with those smoking more cannabis having a greater risk. These findings have been replicated in other populations and in other contexts (Moore et al. 2007). Since the smoking of cannabis occurs many years before the onset of schizophrenia it has been argued that a reversed causality is unlikely, i.e. that schizophrenia leads to the early cannabis smoking although a common vulnerability cannot be ruled out.

However, there are arguments against such a causal relationship between cannabis use and schizophrenia. In the last 50 years there has been a large increase in cannabis use in the Western world. At the same time, the incidence of schizophrenia in the population has been remarkably stable. Thus, at the epidemiological level, there is no support for the hypothesis of a causal relationship (Degenhardt and Lynskey 2003). Also, individuals with schizophrenia generally have a higher use of addictive drugs. For example, between 80 and 90 % of all patients with schizophrenia smoke tobacco. Smoking often starts long before any sign or symptom of schizophrenia. Despite this strong relationship, smoking is rarely suggested as a

cause of schizophrenia. Finally, in the case of schizophrenia, it is difficult to point out the exact onset of the disorder, as both hereditary factors and conditions related to pregnancy may be involved. It may therefore be assumed that the pathophysiology of schizophrenia develops early in life, long before the initial signs. This means that although it precedes the onset of the disorder, cannabis use cannot at the moment be regarded as a causal factor in itself but rather as a disease modulator that increases the risk of developing schizophrenia in individuals with other vulnerability factors.

Thus, on the basis of the available evidence, those who are vulnerable to psychosis or schizophrenia should be strongly discouraged from using cannabis. There is no doubt that cannabis use can trigger psychosis and exacerbate psychotic episodes in the vulnerable. The evidence suggesting greater deterioration in the course of illness is overwhelming, even if most people who smoke cannabis will never experience a psychosis. The advice to avoid cannabis should be heeded by many because

- Presently it is not possible to identify every vulnerable individual.
- It has been estimated that over 10 % of cases of schizophrenia could be avoided if all cannabis smokers were to stop using it.
- In a group of 100 non-cannabis smokers, on average, one person will get a diagnosis of schizophrenia. In a group of 100 cannabis smokers, on average, two people will get a diagnosis of schizophrenia.

However, even if the relative increased risk of developing schizophrenia is doubled or even tripled in cannabis users, the absolute increase in the risk for schizophrenia is quite small, and as many as 2,4000 people would have to stop using cannabis to prevent one case of schizophrenia (Hickman et al. 2009).

7.4.2 Psychosis Following Long-term Stimulant Use

Many of the same arguments as for cannabis can be made for the relationship between stimulants and the development of psychosis. Cocaine, amphetamine, and methamphetamine have been connected with longer lasting, more chronic psychotic disorders (Grelotti et al. 2010). It is a topic under debate whether this should be viewed as a chronic form of a stimulant psychosis or as a primary psychosis (e.g. schizophrenia) triggered by the use of stimulants. It is already difficult to separate diagnostically between stimulant-induced psychosis and acute schizophrenia in the acute phase. In addition, individuals with psychotic disorders have increased use of stimulant drugs, as have those vulnerable to the development of psychosis. Patients who were originally diagnosed with a drug-induced psychosis may later be diagnosed with primary psychosis. Therefore, it is reasonable to assume that we may view stimulant psychosis as lying within the traditional stress-vulnerability paradigm (Fig. 7.1), with vulnerable individuals needing less stimulant exposure to precipitate a psychotic episode. In addition, stimulant use

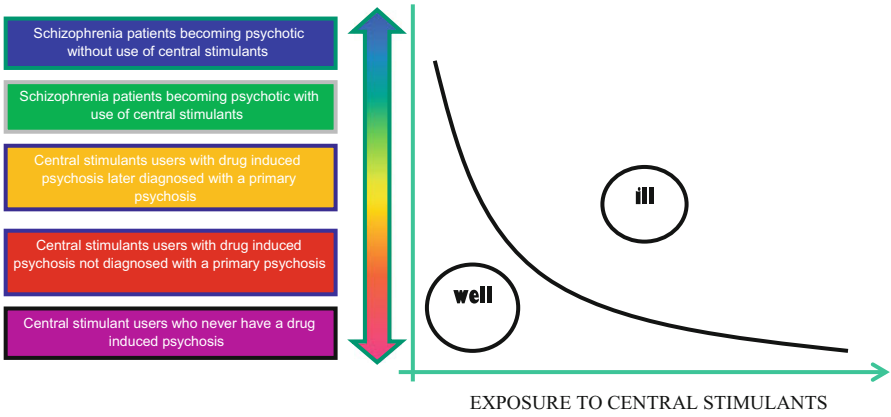

Fig. 7.1 A theoretical relationship between the use of central stimulants and primary psychosis. In some vulnerable individuals, a small intake of central stimulants may be sufficient to precipitate psychosis, whereas others do not develop psychotic symptoms even after intake of larger amounts (from Bramness et al. 2012)

may, in itself, increase vulnerability, at least at higher doses, through the neurotoxic effects of the drugs.

7.4.3 Consequences for Treatment

The frequent coexistence of drug use and psychotic symptoms has important implications for how to organize clinical treatment and care irrespective of whether a patient's drug use precipitated a primary psychotic disorder or a primary psychosis has led to a substance-use disorder. Patients with drug-induced psychosis are at high risk of developing primary psychotic disorder (Caton et al. 2005). Rather than seeing drug-induced psychosis as a phenomenon distinct from primary psychosis, we should consider those who develop psychosis following drug use to be at high risk of developing primary psychosis (Bramness et al. 2012). These patients need to be monitored for signs of primary psychosis to avoid unnecessary delays in treatment, which are associated with poorer outcomes. In the acute phase, pharmacological treatment using both benzodiazepines and antipsychotics should be considered. Antipsychotics may be useful for curbing the acute psychosis and have been found effective in a meta-analysis (Shoptaw et al. 2009), but may also have neuroprotective effects (Curran et al. 2004). The use of benzodiazepines might reduce the need for antipsychotics and may be used to induce sleep, a desired effect in the management of any acute psychotic episode irrespective of its etiology.

References

Allen MH, Currier GW, Carpenter D et al (2005) The expert consensus guideline series. Treatment of behavioral emergencies 2005. J Psychiatr Pract 1(11 Suppl):5–108

Amato L, Minozzi S, Davoli M (2011) Efficacy and safety of pharmacological interventions for the treatment of the alcohol withdrawal syndrome. Cochrane Database of Systematic reviews. doi: 10.1002/14651858.CD008537.

Andréasson S, Allebeck P, Engström A, Rydberg U (1987) Cannabis and schizophrenia. A longitudinal study of Swedish conscripts. Lancet 8574:1483–1486

Baldacchino A, Hughes Z, Kehoe M et al (2012) Cannabis psychosis: examining the evidence for a distinctive psychopathology in a systematic and narrative review. Am J Addict 21(Suppl 1): S88–S98

Bell DS (1965) Comparison of amphetamine psychosis and schizophrenia. Br J Psychiatry 111:701–707

Bramness JG, Gundersen ØH, Guterstam J et al (2012) Amphetamine-induced psychosis–a separate diagnostic entity or primary psychosis triggered in the vulnerable? BMC Psychiatry 12:221

Caton CL, Drake RE, Hasin DS et al (2005) Differences between early-phase primary psychotic disorders with concurrent substance use and substance-induced psychoses. Arch Gen Psychiatry 62(2):137–145

Cole J, Kando J (1993) Adverse behavioral events reported in patients taking alprazolam and other benzodiazepines. J Clin Psychiatry 54:49–61

Curran C, Byrappa N, McBride A (2004) Stimulant psychosis: systematic review. Br J Psychiatry 185:196–204

Degenhardt HW, Lynskey M (2003) Testing hypotheses about the relationship between cannabis use and psychosis. Drug Alcohol Depend 71:37–48

Grelotti DJ, Kanayama G, Pope HG Jr (2010) Remission of persistent methamphetamine-induced psychosis after electroconvulsive therapy: presentation of a case and review of the literature. Am J Psychiatry 167(1):17–23

Hedges DW, Woon FL, Hoopes SP (2009) Caffeine-induced psychosis. CNS Spectr 14:127–129

Hickman M, Vickerman P, Macleod J et al (2009) If cannabis caused schizophrenia–how many cannabis users may need to be prevented in order to prevent one case of schizophrenia? England and Wales calculations. Addiction 104:1856–1861

Johns A (2001) Psychiatric effects of cannabis. Br J Psychiatry 178:116–122

Koskinen J, Löhönen J, Koponen H et al (2010) Rate of cannabis use disorders in clinical samples of patients with schizophrenia: a meta-analysis. Schizophr Bull 36(6):1115–1130

Leamon MH, Flower K, Salo RE et al (2010) Methamphetamine and paranoia: the methamphetamine experience questionnaire. Am J Addict 19(2):155–168

Leelahanaj T, Kongsakon R, Netrakom P (2005) A 4-week, double-blind comparison of olanzapine with haloperidol in the treatment of amphetamine psychosis. J Med Assoc Thai 88(Suppl 3):S43–S52

McIver C, McGregor C, Baigant M et al (2006) Guidelines for the medical management of patients with methamphetamine psychosis. Drug and Alcohol Services, South Australia

Medhus S, Mordal J, Holm B et al (2013) A comparison of symptoms and drug use between patients with methamphetamine associated psychoses and patients diagnosed with schizophrenia in two acute psychiatric wards. Psychiatry Res 206:17–21

Moore TH, Zammit S, Lingford-Hughes A et al (2007) Cannabis use and risk of psychotic or affective mental health outcomes: a systematic review. Lancet 370:319–328

Núñez LA, Gurpegui M (2002) Cannabis-induced psychosis: a cross-sectional comparison with acute schizophrenia. Acta Psychiatr Scand 105(3):173–178

Shoptaw SJ, Kao U, Ling W (2009) Treatment for amphetamine psychosis. Cochrane Database Syst Rev (1):CD003026

Srisurapanont M, Arunpongpaisal S, Wada K et al (2011) Comparisons of methamphetamine psychotic and schizophrenic symptoms: a differential item functioning analysis. Prog Neuropsychopharmacol Biol Psychiatry 35(4):959–964

Stone JM, Fisher HL, Major B et al (2013) Cannabis use and first-episode psychosis: relationship with manic and psychotic symptoms, and with age at presentation. Psychol Med 24:1–8

Sullivan JT, Sykora K, Schneiderman J et al (1989) Assessment of Alcohol Withdrawal: the revised clinical institute withdrawal assessment for alcohol scale (CIWA-Ar). Br J Addict 84 (11):1353–1357

Ujike H, Sato M (2004) Clinical features of sensitization to methamphetamine observed in patients with methamphetamine dependence and psychosis. Ann N Y Acad Sci 1025:279–287

Yeh HS, Lee YC, Sun HJ, Wan SR (2001) Six months follow-up of patients with methamphetamine psychosis. Zhonghua Yi Xue Za Zhi (Taipei) 64:388–394

Zammit S, Allebeck P, Andreasson S et al (2002) Self reported cannabis use as a risk factor for schizophrenia in Swedish conscripts of 1969: historical cohort study. BMJ 325:1199

Zuardi AW, Crippa JA, Hallak JE et al (2012) A critical review of the antipsychotic effects of cannabidiol: 30 years of a translational investigation. Curr Pharm Des 18:5131–5140

Mood Disorders and Addiction

8

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Abstract

Comorbidity of mood and substance use disorders is the most common dual pathologies in the substance abuse field. High prevalence rates and challenging clinical management of patients diagnosed with this dual disorder imply a great burden for health care systems. Major Depression has been studied in comorbidity with the different drugs of abuse (e.g., alcohol, nicotine, cocaine, heroin, cannabis) with consistent findings throughout the world. Various neurobiological mechanisms are believed to play a role in the etiology of this comorbidity, often

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determining a severe clinical phenotype with poorer prognosis when compared to addiction and mood disorders only. Treatment of the co-occurrence of depression and substance use disorder involves an integrated approach, simultaneously addressing both the psychiatric and the addictive disorder. Current research into pharmacological—in particular antidepressant drugs—and psychosocial treatments has provided controversial results. More data are needed to develop stronger evidence for the treatment of comorbid major depression and substance use disorders.

8.1 Introduction

The coexistence of Mood and Substance Use Disorders (SUD) is a fairly common occurrence. It has aroused growing interest among the scientific community due to both its high prevalence rates and the challenging clinical management of its patients. Despite the burden that SUD and mood disorders represent for clinicians and health care providers, to date, there are relatively few evidence-based data concerning such a complex comorbidity. Prevalence rates and clinical characteristics are consistent throughout different countries and cultures, despite the heterogeneity of the environmental factors involved. This chapter will focus on one of the most common mood disorders, Major Depression (MD), comorbid with substance addiction disorders.

8.2 Epidemiology

Comorbidity of MD and SUD encompasses values from 12 % to 80 % (Compton et al. 2007; Conner et al. 2008a, b, 2009; Torrens et al. 2011a). This wide range depends on a number of factors, including the sample recruitment characteristics such as general population, patients in a primary care setting, patients being treated in a psychiatric or addiction facilities, substance users not seeking treatment (e.g., in the street or prison), and even the main drug of abuse considered (e.g., opioids, alcohol, and cocaine). All these cases provide different results for prevalence, incidence, and severity indices. Moreover, variations may be related to trends in the drug-using population, such as changes in the availability, accessibility, and price of the different substances (e.g., tobacco, alcohol, cocaine, cannabis, and heroin) and drug treatment policies (e.g., accessibility to drug abuse and mental health disorder treatment) or the presence of other concurrent conditions (e.g., HIV or HCV infections), which may also be related to psychiatric comorbidity. Finally, methodological differences such as the diagnostic criteria used (Diagnostic and Statistical Manual of Mental Disorders (DSM) or the International Classification of Diseases Diagnostic Criteria [ICD], in their different versions), the diagnostic instruments employed (e.g., the Structured Clinical Interview (SCID), the Schedule for Clinical Assessment in Neuropsychiatry (SCAN), and the Psychiatric Research

Interview for Substance and Mental Disorders (PRISM)), and the period of time assessed (e.g., last month, last year, lifetime) may modify the figures of prevalence and incidence.

The *PsycoBarcelona* study included a population of more than 600 illicit drug users both seeking treatment in drug abuse facilities or non-seeking treatment (assessed in epidemiological research units). They were evaluated over the same period of time and in the same city (exactly similar availability, accessibility, and price of the different substances and drug treatment policies) using identical diagnostic criteria and instruments. An almost 42 % lifetime prevalence of Axis I non-SUD diagnosis was reported. The most prevalent diagnosis was independent MD (17 %) while induced MD accounted for 10 %. The drug use assessment in the study indicated that more than half the sample (from 51 % to 96 % depending on the population studied) was actively consuming more than one substance, excluding nicotine (Torrens et al. 2011a).

Worldwide, alcohol and tobacco are the most commonly used drugs. The current prevalence of alcohol use disorders in the general population ranges from almost 2 % to more than 4 %, while lifetime prevalence of alcohol dependence and abuse reaches more than 13 %. Comorbidity of alcohol dependence and MD shows a lifetime prevalence as high as 21 % (Hasin et al. 2007). Concurring data were found in a Dutch cohort of patients where comorbidity of alcohol and depression rose to 20 % (Boschloo et al. 2011). Data suggest that the presence of either alcohol abuse or MD doubles the risk of developing the other disorder (Boden and Fergusson 2011) and increases severity. The comorbidity of MD and alcohol dependence is associated with a higher risk of suicide in depressed patients; in addition, alcohol addiction has been identified as one of the strongest predictors of a repeated suicide attempt (Beghi et al. 2013).

The impact of psychiatric comorbidity has also been investigated in heroin-dependent patients. Major depression was again the most prevalent Axis I diagnosis with a prevalence ranging from 18 % to 46 % in different samples (Rodriguez-Llera et al. 2006; Astals et al. 2008; Maremmani et al. 2011),

In cocaine users, Spanish studies have reported a prevalence rate of comorbid MD (both independent or induced) disorders from 16 % in sample of outpatients to 34 % in individuals admitted to a therapeutic community (Araos et al. 2013; Herrero et al. 2008; Vergara-Moragues et al. 2012).

Within samples of cannabis-dependent subjects, figures of MD comorbidity range from 13.5 % to 38 % (Cuenca-Royo et al. 2013; Guillem et al. 2009). In the study of Cuenca-Royo et al. (2013), 18 % of regular cannabis users, assessed in nonclinical settings, presented some Axis I diagnosis other than SUD, mood disorders being the most prevalent (13.5 %). Cannabis use associated with alcohol consumption at an early age correlates with the presence of a comorbid psychiatric disorder. In addition, more severe cannabis dependence measured as the number of joints per month is related to comorbidity with both SUD and non-SUD diagnosis. With other less commonly used drugs such as ecstasy or amphetamine, the more frequent psychiatric comorbid disorder is MD (Martin-Santos et al. 2010; Salo et al. 2011). Table 8.1 summarizes some of the studies performed within the European Union about the lifetime prevalence of MD among different substance abusers assessed in various contexts.

Table 8.1 Lifetime prevalence of MD among different substance abusers, assessed in various contexts in different studies in European countries

Study	Subjects	Main drug of abuse	Sample	Diagnosis criteria	Diagnostic instrument	Lifetime prevalence of MD		
						Any (%)	Primary (%)	Induced (%)
Boschloo et al. (2011)	2,329	Alcohol	Netherlands Study of Depression and Anxiety (NESDA) cohort	DSM IV	CIDI	16.5	–	–
Rodriguez-Llera et al. (2006)	149	Heroin	Non-treatment-seeking users	DSM IV	PRISM	26.8	17.4	9.4
Astals et al. (2008)	189	Heroin	Treatment-seeking users	DSM IV	PRISM	18	12.7	5.3
Maremmani et al. (2011)	1,090	Heroin	Treatment-seeking users	DSM IV	DAH-RS (substance use) Decision Trees for Differential Diagnosis + SID	55.8 (11.8 undetermined)	25.1	18.9
Herrero et al. (2008)	139	Cocaine	Non-treatment-seeking users	DSM IV	PRISM	30.2	19.4	10.8
Araos et al. (2013)	110	Cocaine	Treatment-seeking users	DSM IV	PRISM	40.9	16.4	24.5
Cuenca-Royo et al. (2013)	289	Cannabis	General population	DSM IV	PRISM	17	13.5	3.5
Martin-Santos et al. (2010)	37	Ecstasy	Non-treatment-seeking users	DSM IV	PRISM	40.5	13.5	27

DSM IV Diagnostic and Statistic Manual of Mental Disorder IV edition, *PRISM* Psychiatric Research Interview for Substance and Mental Disorders, *DAHRS* Drug Addiction History Rating Scale, *SID* Semi-structured Interview for Depression, *CIDI* Composite International Diagnostic Interview

Interest is growing with respect to the relationship between nicotine dependence and psychiatric comorbidity. Patients affected by a depressive disorder have been described as having twice the probability to be also nicotine dependent (Hughes and Hatsukami 1992; Mendelsohn 2012). As much as 30 % of those with at least one previous depressive episode are active smokers (Cappelleri et al. 2005; Mendelsohn 2012). Furthermore, people with nicotine dependence have a higher risk (from a two- to threefold increase) of developing a mood disorder as compared to nonsmokers (John et al. 2004).

Studies carried out in both general and clinical populations indicate that women with SUD present comorbid MD more frequently than men. Moreover, in women with SUD the prevalence of MD is twice as usually found in a general European female population which makes them an especially vulnerable collective and a particularly sensitive target for treatment policies (Torrens et al. 2011a).

8.3 Etiology

Different hypothesis have been proposed to explain such a high joint occurrence of SUD and MD. In brief: (1) SUD and comorbid MD share common risk factor disorders such as stressful events, psychological trauma, genetic vulnerability, and/or similar preexisting neurobiological alterations that lead to co-occurring expression, without one disorder causing the other; (2) continued use of substances induces neurobiological changes through neuro-adaptative mechanisms that mediate MD; (3) SUD is developed in order to soothe MD symptoms (self-medication hypothesis); and (4) there are common symptoms between addiction and mood disorders which can be mistakenly diagnosed as a co-occurring MD (Schuckit 2006).

For both MD and SUD genetic and environmental factors are crucial in the induction of the neurobiological mechanisms related to their pathogenesis (Brady and Sinha 2005; Schuckit 2006). The principal neuronal and molecular mechanisms involved in the neurobiology of depression include (1) monoaminergic neurotransmission systems; (2) hypothalamus–pituitary axis (HHA); (3) immunological system; (4) neurotrophic factors (e.g., BDNF, Brain-Derived Neurotrophic Factor); (5) endocannabinoid system; and (6) food intake, metabolism, and circadian rhythm control system (Belmaker and Agam 2008; Krishnan and Nestler 2008; Valverde et al. 2009; Valverde and Torrens 2012). Some of these mechanisms involved in MD also play a role in SUD (Brady and Sinha 2005). Moreover, reward circuits, one of the most important pathways in SUD (Wise 1989), have also been hypothesized as being implicated in the neurobiology of depressive disorders (Nestler and Carlezon 2006).

8.4 Clinical Characteristics

8.4.1 Diagnosis

As previously described, the clinical identification of MD in substance abusers constitutes a challenge for both medical care and research. Firstly, acute or chronic effects of substance use can mimic MD symptoms, making it difficult to differentiate the psychiatric symptoms that represent an independent (primary) MD from those related to an acute or chronic substance use or withdrawal. Furthermore, psychiatric diagnoses such as MD are syndromes rather than diseases with well-known pathophysiology and associated biological markers. The lack of biological markers has forced psychiatrists to develop operational diagnostic criteria, including the DSM and the ICD, and to design structured clinical diagnostic interviews in order to improve the validity and reliability of diagnoses. The use of standard criteria based on directly observable behavioral symptoms, and the incorporation of these into structured interviews, maximizes the extent to which identical information can be elicited and applied to the same criteria to achieve diagnosis. As mentioned before, methodological differences, particularly regarding the diagnostic criteria (e.g., DSM-III-R, DSM-IV, ICD-9, ICD-10) and assessment instruments used (e.g., the Structured Clinical Interview for DSM Disorders, SCID, the Psychiatric Research Interview for Substance and Mental Disorders, PRISM, and the Schedules for Clinical Assessment in Neuropsychiatry, SCAN), can also influence the prevalence rates of dual disorders (Torrens et al. 2006).

Among the assessment instruments available, the PRISM (Hasin et al. 2006) is a semi-structured interview that facilitates the distinction among independent (primary) disorder, substance-induced disorder, and the expected effects of the substance. The PRISM interview has demonstrated good psychometric properties in terms of test—retest reliability (Hasin et al. 2006), inter-rater reliability (Morgello et al. 2006), and validity (Torrens et al. 2004) to diagnose psychiatric disorders among substance users. That is to say, it is able to discern among *MD independent from substance* (when symptoms are substantially in excess of what would be expected given the type or the amount of the substance used or the duration of use; the onset of depressive symptoms precedes the onset of the substance use; or the symptoms persist for a period of time after the cessation of intoxication or acute withdrawal); *substance-induced MD* (when the episode occurs entirely during a period of heavy substance use or within the first 4 weeks after cessation of use, and the substance used is relevant to the disorder and the symptoms are greater than the expected effects of intoxication and/or withdrawal); and the *expected effects* (expected physiological effects of a substance, as a result of intoxication or withdrawal—e.g., insomnia—which may be identical to symptoms found in independent MD).

Distinguishing between independent and induced MD in a patient with a substance use disorder represents a challenge; nevertheless, we are able to highlight a few differential characteristics of the two forms that may be of help in clinical practice. On the one hand, a sudden change, either an increase or reduction in substance intake in the SUD, prior to the onset of depressive symptoms may indicate that the mood disorder was induced by the SUD. On the other hand,

Table 8.2 Clinical indicators for the diagnosis of a depressive episode concurrent with substance use disorder

Induced depression	Independent depression
• Emergence of depressive symptoms during an escalation of consumption • Emergence of depressive symptoms during a significant drop in consumption	• Emergence of depressive symptoms during a period of stable or occasional consumption • Persistence of depressive symptoms after one week of withdrawal • History of depression in the absence of substance use • Family history of depression. • History of good response to antidepressant treatments in the past

emergence of depressive symptoms during a period of stable consumption, or the persistence of depressive symptoms after clinically relevant withdrawal, probably suggests an independent MD disorder. Furthermore, in the absence of substance use, the presence of a previous history of depression or familial antecedents may indicate the existence of MD. In addition, patients with independent MD are more likely to have a history of good response to antidepressant treatments (Table 8.2). Some patients can present both independent and induced MD and undergo an increasing number of depressive symptoms throughout their lives. They are more frequently found with comorbid anxiety disorders, and are more likely to have attempted suicide (Torrens et al. 2011b).

8.4.2 Course and Prognosis

It is important to highlight that the studies that distinguish between independent and induced MD have found a clearly higher prevalence of independent MD (Torrens et al. 2011a). Furthermore, recent data from one of the most representative epidemiological study in the United States, the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), are shedding light on a new perspective with respect to substance dependence and comorbid MD (Blanco et al. 2012). The subgroup of patients diagnosed at an earlier stage with induced MD or dysthymia together with SUD, when reevaluated at a second time point 3 years later, were reclassified as being affected by independent MD. Also, in a follow-up study of a Spanish cohort of ecstasy users, most of the induced MD diagnosed at the baseline t of the study were diagnosed as independent MD at a 3-year follow-up (Martin-Santos et al. 2010). This may have been due to a number of factors including a higher probability of being diagnosed with an induced affective disorder when severe drug dependence symptoms are present, or that the diagnosis of induced disorders captures subjects with a preexisting higher risk for MD whose symptoms are precipitated by substance use. It may also indicate that SUD had precipitated an MD whose erroneous diagnosis had been masked by the substance consumption (Magidson et al. 2013).

Clinical data indicate that people affected by MD present a higher vulnerability to developing a SUD, and individuals with SUD have a higher risk of developing MD when compared to the general population. Furthermore, co-occurrence of SUD and MD is a predictor of clinical severity: patients show a more severe clinical course, less response to treatment, and a poorer prognosis for both disorders overall (Boschloo et al. 2013; Conner et al. 2012; Samet et al. 2013). These dually diagnosed patients additionally present a higher prevalence of attempted/completed suicide than those with only one disorder (Conner et al. 2012; Marmorstein 2011; Blanco et al. 2012).

Besides MD, patients with comorbid SUD often manifest or develop other medical, psychiatric, and substance use comorbidities, thus making treatment even more challenging. As expected from such a severe clinical picture, dual disorder patients have considerable psychosocial disability and require an increased utilization of health care resources, including emergency rooms and psychiatric hospitalization (Mueller et al. 1994; Martín-Santos et al. 2006; Pettinati et al. 2013; Samet et al. 2013).

8.5 Treatment

Given its psychopathological, medical, and social severity and relevance in prognosis, adequate treatment for comorbid MD and SUD is needed. However, in spite of the high association between substance use and MD, there is a surprising paucity of studies related to treatment and outcome. A few well-designed studies, mainly concerning MD comorbid with alcohol dependence, have been published, and more work of this nature is required in order to address the challenges of dual disorder treatment. A summary of the available evidence about current status of the clinical management of MD in patients with SUD is presented.

8.5.1 Pharmacological Treatment

The main results coming from the systematic reviews and meta-analyses of comorbid MD and SUD randomized clinical trials (Nunes and Levin 2004; Torrens et al. 2005; Pani et al. 2010) indicate that (1) antidepressant drugs improve comorbid depression with alcohol dependence but not the depression that concurrently occurs with cocaine or opiate dependence. Furthermore, the improvement of depression, together with alcohol dependence, takes place only with imipramine, desipramine, and nefazodone; while selective inhibitors of serotonin reuptake (SSRIs) are not effective, (2) treating depressed substance-dependent patients with antidepressants does not directly improve substance use. When the antidepressants improve depressive symptoms, there is also a quantitative reduction in the use of the substance of abuse, but no effect on the acquisition of abstinence or total remission of these substances use. Thus a specific and concomitant treatment for SUD is required. In a recent trial for comorbid MD and alcohol dependence, a combined treatment of a medication for depression (sertraline) and another for alcohol dependence (naltrexone) was found to simultaneously reduce depressive symptoms and excessive drinking (Pettinati et al. 2010).

An additional concern when treating these dual disorder patients is the safety of the treatment itself due to the frequency of comorbid physical illness (e.g., HIV and/or HVC infections, hepatic cirrhosis) and the risk of interactions with other drugs that the person may be taking (e.g., risk of QTc prolongation in HIV-infected patient receiving methadone maintenance treatment and SSRI) (Funk and Bostwick 2013; Vallecillo et al. 2013). The main interactions and general recommendations about the clinical management of patients with MD and SUD are summarized in Table 8.3. Besides aspects of efficacy, safety of antidepressant use, and possible interactions with the consumption of various substances or other drugs, the

Table 8.3 Principal interactions of antidepressants with drugs used treating addiction and substances of abuse

Drug	Antidepressant	Effect
Benzodiazepines	Tricyclic	Increase plasma concentrations of *desipramine* and *imipramine*
	SSRIs	With *fluoxetine* and *fluvoxamine* decrease metabolism and increase plasma concentrations of *alprazolam* and *diazepam*
Disulfiram	Tricyclic	Increase plasma concentrations of *desipramine* and *amitriptyline* due to decrease of metabolism, neurotoxicity of the combination
	MAOI	With *tranylcypromine*, confusional psychosis with the combination
Opioids	Tricyclic	TCA + methadone correlated with ↑ overdose risk Increase of bioavailability and analgesic effect with morphine *Amitriptyline*: ↑ overdose risk with methadone. Reports of respiratory depression with buprenorphine *Desipramine*: ↑ plasma concentrations with methadone
	SSRIs	With *fluvoxamine* ↑ plasma concentrations of methadone due to ↓ elimination
	MAOI/RIMA	Increase of fatal serotonin syndrome risk with *methadone* and *buprenorphine* *Moclobemide:* ↑ effect of morphine, fentanyl, and methadone plasma concentrations
Alcohol	Tricyclic	Increased toxicity of alcohol and decreased cognitive function *Maprotiline:* risk of convulsions
	SSRIs	Increase effect of alcohol
	MAOI	Hypertensive crisis, by increased release of catecholamines. Increased sedation
	Other antidepressant	*Trazodone* and *mirtazapine:* increased sedation
Cocaine	Tricyclics and SSRIs	Reduce craving and seizure threshold Increased heart rate, diastolic pressure, and risk of arrhythmia

SSRIs selective inhibitors of serotonin reuptake, *MAOI* monoamine oxidase inhibitors, *OWS* Opiate Withdrawal Syndrome, *RIMA* reversible inhibitor of MAO-A

potential for the abuse of the different drugs used for depression treatment should also be taken into account. A review conducted by Haddad suggested that antidepressants have no potential for dependence with the exception of tranylcypromine or amineptine for their dopaminergic effects and stimulant properties (Haddad 1999).

8.5.2 Psychosocial Interventions

Cognitive behavioral therapy (CBT) is a well-established tool for the treatment of both MD and substance disorders. The combined treatment of dual disorders is still not as commonly practiced, as it should be, despite the fact that most published data and clinical experience indicate that it could be of great importance to achieve a better outcome. Nevertheless, a growing number of combined treatments for comorbid MD and SUD are available, including psychotherapeutic treatments as an adjunct or alternative to pharmacological treatment. In a recently published meta-analysis, the impact of a number of psychotherapies, such as CBT, Twelve-Step facilitation (TSF), and motivational interviewing (MI) on MD or on SUD alone, has been evaluated with controversial results. The effectiveness of psychotherapy was also investigated in dual disorders with encouraging results (Riper et al. 2014). Data about MI alone, or associated with CBT, do not show a clear superiority of one with respect to the other. The number of CBT/MI sessions was found to directly and significantly correlate with alcohol abstinence ($P < 0.001$), and nonsignificantly with MD outcome (Riper et al. 2014). The effect sizes of CBT/MI treatments, however, appeared smaller compared to the ones observed in antidepressant treatments, as reviewed by Nunes and Levin (2004). Lastly, the effects of combined CBT/MI psychotherapy were compared to treatment as usual, with no additional information about the presence and/or type of pharmacological concomitant treatment.

A different approach has been investigated by the Building Recovery by Improving Goals, Habits, and Thoughts (BRIGHT) study, a community-based effectiveness trial that compares residential substance abuse treatment with residential treatment plus CBT for depression. The treatment consists of 16 two-hour sessions of group CBT. The results demonstrated better clinical outcome, with higher adherence to treatment and an improvement in severity of depressive symptoms at a 3-month follow-up, that persisted, even if in smaller proportions, at a 6-month follow-up (Watkins et al. 2011). This contribution warrants further investigation into group CBT and its application to the broader area of community-based treatment centers, such as primary care ones.

Then, with current available evidence, it can be stated that treatment of an MD and SUD must take both disorders into account: treatment of depression cannot replace the treatment of addiction, and conversely, treatment of addiction should not replace that of depression. Also, the literature indicates that a depressive episode should be treated as such even though the patient is an active substance user and that addiction should be addressed even if the patient is currently having a

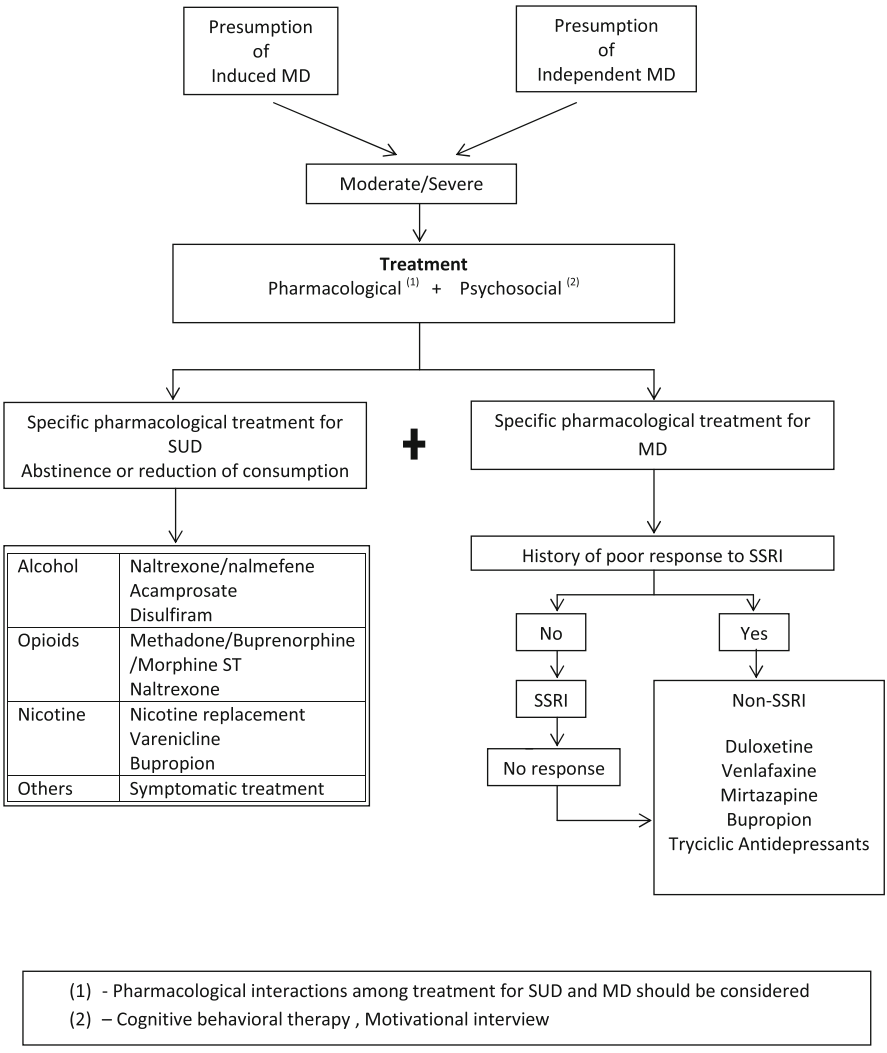

Fig. 8.1 Treatment algorithm for the management of Major Depression and Substance Use Disorder (1) Pharmacological interactions among treatment for SUD and MD should be considered (2) Cognitive behavioral therapy, Motivational interview

depressive episode. The treatment algorithm for the management of Major Depression and Substance Use Disorder is provided in Fig. 8.1.

8.5.3 Sequential, Parallel, or Integrated Treatment

It is relevant to point out that in many European countries substance abuse and mental illness are taken care of in two different and separate health networks. This implies that frequently patients with dual diagnosis are treated in separate facilities: one for drug dependence-related matters and another for psychiatric disorder ones. In many cases, abstinence from drug use is a requirement prior to the patient being admitted to treatment for depression. This attitude has now been definitively replaced by the so-called *integrated treatment* model. Such an approach embraces a simultaneous and coordinated treatment of both the addictive and the affective disorders in an effort to maximize treatment adherence and outcomes (Torrens et al. 2012).

Conclusions and Recommendations

Co-occurrence of MD and SUD is frequent, and those patients affected by dual disorders show severe psychopathological impairment as a worse medical and social outcome. It is extremely important to treat both depression and substance use disorders at the same time with an integrated model and not to approach each disorder separately following a sequential order. It is also of great priority to encourage the research of neurobiological mechanisms involved in dual disorders, in order to develop better treatments and more efficacious prevention strategies.

References

Araos P, Vergara-Moragues E, Pedraz M, Pavón FJ, Campos Cloute R, Calado M et al (2013) Psychopathological comorbidity in cocaine users in outpatient treatment. Adicciones 16(1): 15–26

Astals M, Domingo-Salvany A, Buenaventura CC, Tato J, Vazquez JM, Martin-Santos R et al (2008) Impact of substance dependence and dual diagnosis on the quality of life of heroin users seeking treatment. Subst Use Misuse 43(5):612–632

Beghi M, Rosenbaum JF, Cerri C, Cornaggia CM (2013) Risk factors for fatal and nonfatal repetition of suicide attempts: a literature review. Neuropsychiatr Dis Treat 9:1725–1736

Belmaker RH, Agam G (2008) Major depressive disorder. N Engl J Med 358(1):55–68

Blanco C, Alegria AA, Liu SM, Secades-Villa R, Sugaya L, Davies C et al (2012) Differences among major depressive disorder with and without co-occurring substance use disorders and substance-induced depressive disorder: results from the National Epidemiologic Survey on Alcohol and Related Conditions. J Clin Psychiatry 73(6):865–873

Boden JM, Fergusson DM (2011) Alcohol and depression. Addiction 106(5):906–914

Boschloo L, Vogelzangs N, Smit JH, van den Brink W, Veltman DJ, Beekman AT et al (2011) Comorbidity and risk indicators for alcohol use disorders among persons with anxiety and/or depressive disorders: findings from the Netherlands Study of Depression and Anxiety (NESDA). J Affect Disord 131(1–3):233–242

Boschloo L, Vogelzangs N, van den Brink W, Smit JH, Beekman AT, Penninx BW (2013) The role of negative emotionality and impulsivity in depressive/anxiety disorders and alcohol dependence. Psychol Med 43(6):1241–1253

Brady KT, Sinha R (2005) Co-occurring mental and substance use disorders: the neurobiological effects of chronic stress. Am J Psychiatry 162(8):1483–1493

Cappelleri JC, Bushmakin AG, Baker CL, Merikle E, Olufade AO, Gilbert DG (2005) Revealing the multidimensional framework of the Minnesota nicotine withdrawal scale. Curr Med Res Opin 21(5):749–760

Compton WM, Thomas YF, Stinson FS, Grant BF (2007) Prevalence, correlates, disability, and comorbidity of DSM-IV drug abuse and dependence in the United States: results from the national epidemiologic survey on alcohol and related conditions. Arch Gen Psychiatry 64(5): 566–576

Conner KR, McCarthy MD, Bajorska A, Caine ED, Tu XM, Knox KL (2012) Mood, anxiety, and substance-use disorders and suicide risk in a military population cohort. Suicide Life Threat Behav 42(6):699–708

Conner KR, Pinquart M, Duberstein PR (2008a) Meta-analysis of depression and substance use and impairment among intravenous drug users (IDUs). Addiction 103(4):524–534

Conner KR, Pinquart M, Holbrook AP (2008b) Meta-analysis of depression and substance use and impairment among cocaine users. Drug Alcohol Depend 98(1–2):13–23

Conner KR, Pinquart M, Gamble SA (2009) Meta-analysis of depression and substance use among individuals with alcohol use disorders. J Subst Abuse Treat 37(2):127–137

Cuenca-Royo AM, Torrens M, Sanchez-Niubo A, Suelves JM, Domingo-Salvany A (2013) Psychiatric morbidity among young-adults cannabis users. Adicciones 25(1):45–53

Funk KA, Bostwick JR (2013) A comparison of the risk of QT prolongation among SSRIs. Ann Pharmacother 47(10):1330–1341

Guillem E, Pelissolo A, Vorspan F, Bouchez-Arbabzadeh S, Lepine JP (2009) Sociodemographic profiles, addictive and mental comorbidity in cannabis users in an outpatient specific setting. Encéphale 35(3):226–233

Haddad P (1999) Do antidepressants have any potential to cause addiction? J Psychopharmacol 13(3):300–307

Hasin D, Samet S, Nunes E, Meydan J, Matseoane K, Waxman R (2006) Diagnosis of comorbid psychiatric disorders in substance users assessed with the Psychiatric Research Interview for Substance and Mental Disorders for DSM-IV. Am J Psychiatry 163(4):689–696

Hasin DS, Stinson FS, Ogburn E, Grant BF (2007) Prevalence, correlates, disability, and comorbidity of DSM-IV alcohol abuse and dependence in the United States: results from the National Epidemiologic Survey on Alcohol and Related Conditions. Arch Gen Psychiatry 64(7): 830–842

Herrero MJ, Domingo-Salvany A, Torrens M, Brugal MT (2008) ITINERE Investigators. Psychiatric comorbidity in young cocaine users: induced versus independent disorders. Addiction 103(2):284–293

Hughes JR, Hatsukami DK (1992) The nicotine withdrawal syndrome: a brief review and update. Int J Smok Cessation 1:21–26

John U, Meyer C, Rumpf HJ, Hapke U (2004) Smoking, nicotine dependence and psychiatric comorbidity–a population-based study including smoking cessation after three years. Drug Alcohol Depend 76(3):287–295

Krishnan V, Nestler EJ (2008) The molecular neurobiology of depression. Nature 455(7215): 894–902

Magidson JF, Wang S, Lejuez CW, Iza M, Blanco C (2013) Prospective study of substance-induced and independent major depressive disorder among individuals with substance use disorders in a nationally representative sample. Depress Anxiety 30(6):538–545

Maremmani AG, Dell'Osso L, Pacini M, Popovic D, Rovai L, Torrens M et al (2011) Dual diagnosis and chronology of illness in treatment-seeking Italian patients dependent on heroin. J Addict Dis 30(2):123–135

Marmorstein NR (2011) Associations between subtypes of major depressive episodes and substance use disorders. Psychiatry Res 186(2–3):248–253

Martín-Santos R, Fonseca F, Domingo-Salvany A, Ginés JM, Ímaz ML, Navinés R et al (2006) Dual diagnosis in the psychiatric emergency room in Spain. Eur J Psychiatry 20:147–156
Martin-Santos R, Torrens M, Poudevida S, Langohr K, Cuyas E, Pacifici R et al (2010) 5-HTTLPR polymorphism, mood disorders and MDMA use in a 3-year follow-up study. Addict Biol 15(1): 15–22
Mendelsohn C (2012) Smoking and depression–a review. Aust Fam Physician 41(5):304–307
Morgello S, Holzer CE 3rd, Ryan E, Young C, Naseer M, Castellon SA et al (2006) Interrater reliability of the Psychiatric Research Interview for Substance and Mental Disorders in an HIV-infected cohort: experience of the National NeuroAIDS Tissue Consortium. Int J Methods Psychiatr Res 15(3):131–138
Mueller TI, Lavori PW, Keller MB, Swartz A, Warshaw M, Hasin D et al (1994) Prognostic effect of the variable course of alcoholism on the 10-year course of depression. Am J Psychiatry 151(5):701–706
Nestler EJ, Carlezon WA Jr (2006) The mesolimbic dopamine reward circuit in depression. Biol Psychiatry 59(12):1151–1159
Nunes EV, Levin FR (2004) Treatment of depression in patients with alcohol or other drug dependence: a meta-analysis. JAMA 291(15):1887–1896
Pani PP, Vacca R, Trogu E, Amato L, Davoli M (2010) Pharmacological treatment for depression during opioid agonist treatment for opioid dependence. Cochrane Database Syst Rev 9: CD008373. doi(9):CD008373.
Pettinati HM, Oslin DW, Kampman KM, Dundon WD, Xie H, Gallis TL et al (2010) A double-blind, placebo-controlled trial combining sertraline and naltrexone for treating co-occurring depression and alcohol dependence. Am J Psychiatry 167(6):668–675
Pettinati HM, O'Brien CP, Dundon WD (2013) Current status of co-occurring mood and substance use disorders: a new therapeutic target. Am J Psychiatry 170(1):23–30
Riper H, Andersson G, Hunter SB, de Wit J, Berking M, Cuijpers P (2014) Treatment of comorbid alcohol use disorders and depression with cognitive-behavioural therapy and motivational interviewing: a meta-analysis. Addiction 109(3):394–406
Rodriguez-Llera MC, Domingo-Salvany A, Brugal MT, Silva TC, Sanchez-Niubo A, Torrens M et al (2006) Psychiatric comorbidity in young heroin users. Drug Alcohol Depend 84(1):48–55
Salo R, Flower K, Kielstein A, Leamon MH, Nordahl TE, Galloway GP (2011) Psychiatric comorbidity in methamphetamine dependence. Psychiatry Res 186(2–3):356–361
Samet S, Fenton MC, Nunes E, Greenstein E, Aharonovich E, Hasin D (2013) Effects of independent and substance-induced major depressive disorder on remission and relapse of alcohol, cocaine and heroin dependence. Addiction 108(1):115–123
Schuckit MA (2006) Comorbidity between substance use disorders and psychiatric conditions. Addiction 101(Suppl 1):76–88
Torrens M, Serrano D, Astals M, Perez-Dominguez G, Martin-Santos R (2004) Diagnosing comorbid psychiatric disorders in substance abusers: validity of the Spanish versions of the Psychiatric Research Interview for Substance and Mental Disorders and the Structured Clinical Interview for DSM-IV. Am J Psychiatry 161(7):1231–1237
Torrens M, Fonseca F, Mateu G, Farre M (2005) Efficacy of antidepressants in substance use disorders with and without comorbid depression. A systematic review and meta-analysis. Drug Alcohol Depend 78(1):1–22
Torrens M, Martin-Santos R, Samet S (2006) Importance of clinical diagnoses for comorbidity studies in substance use disorders. Neurotox Res 10(3–4):253–261
Torrens M, Gilchrist G, Domingo-Salvany A, psyCoBarcelona Group (2011a) Psychiatric comorbidity in illicit drug users: substance-induced versus independent disorders. Drug Alcohol Depend 113(2–3):147–156
Torrens M, Martínez-Sanvisens D, Martínez-Riera R, Bulbena A, Szerman N, Ruiz P (2011b) Dual diagnosis: focusing on depression and recommendations for treatment. Addict Disord Their Treat 10:50–59

Torrens M, Rossi PC, Martinez-Riera R, Martinez-Sanvisens D, Bulbena A (2012) Psychiatric co-morbidity and substance use disorders: treatment in parallel systems or in one integrated system? Subst Use Misuse 47(8–9):1005–1014

Vallecillo G, Mojal S, Roquer A, Martinez D, Rossi P, Fonseca F et al (2013) Risk of QTc prolongation in a cohort of opioid-dependent HIV-infected patients on methadone maintenance therapy. Clin Infect Dis 57(8):1189–1194

Valverde O, Celerier E, Baranyi M, Vanderhaeghen P, Maldonado R, Sperlagh B et al (2009) GPR3 receptor, a novel actor in the emotional-like responses. PLoS One 4(3):e4704

Valverde O, Torrens M (2012) CB1 receptor-deficient mice as a model for depression. Neuroscience 204:193–206

Vergara-Moragues E, Gonzalez-Saiz F, Lozano OM, Betanzos Espinosa P, Fernandez Calderon F, Bilbao-Acebos I et al (2012) Psychiatric comorbidity in cocaine users treated in therapeutic community: substance-induced versus independent disorders. Psychiatry Res 200(2–3): 734–741

Watkins KE, Hunter SB, Hepner KA, Paddock SM, de la Cruz E, Zhou AJ et al (2011) An effectiveness trial of group cognitive behavioral therapy for patients with persistent depressive symptoms in substance abuse treatment. Arch Gen Psychiatry 68(6):577–584

Wise RA (1989) Opiate reward: sites and substrates. Neurosci Biobehav Rev 13(2–3):129–133

Bipolar Affective Disorders and Alcohol Dependence: Comorbidity, Consequences, and Treatment

9

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Abstract

Alcohol use disorders such as dependence, abuse, or hazardous use are frequently seen as comorbid conditions in bipolar affective disorders. These comorbid disorders significantly mutually influence each other's severity and prognosis, result in a more severe course of both diseases and lead to more complications such as rapid cycling or mixed episodes prospectively. Individuals with a primary alcohol use disorder onset may have a better prognosis for the affective symptoms but for not drinking and drug use consequences.

Treatment options have been extended by a number of studies during the last half decade. In comorbid patients, cognitive behavioral therapy can be employed, when the patient is stabilized affectively using a mood stabilizer such as lithium. A significant reduction of alcohol use was reported from a study adding valproate to lithium, while other studies with antipsychotics or naltrexone and acamprosate did not yield any efficacy on affective symptoms or drinking patterns.

In summary, comorbid individuals with bipolar and alcohol and substance use disorders are severely and chronically affected by both diseases. Treatment options are increasing, including psychotherapy and treatment with mood stabilizers.

9.1 Introduction

Depending on the diagnostic system used and subject sample studied, bipolar affective disorders (BADs) in the general population are estimated to have a frequency of 1 % to maximum 5 %. In comparison, alcohol use disorders (AUD) like alcohol dependence in Europe and America have a lifetime prevalence of approx. 5–10 % (Angst et al. 2003; Angst 2008).

Both disorders are chronic and can considerably impair the affected persons in their social functioning and lifestyle. In addition, each of these disorders has a significantly increased rate in suicides and suicide attempts which then increase even more with the coexistence of both disorders (e.g., Cardoso et al. 2008; Oquendo et al. 2010).

9.2 Comorbidity of Bipolar Affective Disorders in Alcohol Use Disorder Patients

In comparison to the general population, affected persons with bipolar I disorder (at least one episode of depression and one of mania) are diagnosed with an AUD at least three times more frequently. In general the frequencies of AUDs in bipolar patients have been reported and vary from 6 % to 69 % but most studies reported rates of 30 % and more (Cassidy et al. 2001). Most affected individuals are

inpatients in treatment for BADs. More than 42 % of this group with bipolar I and II disorders (Bipolar II: at least one depressive and at least one hypomanic episode) had a lifetime diagnosis of an AUD (Farren and McElroy 2010). Alcohol is the most often used substance (in about 33 % of BAD patients), marihuana follows in 16 % of the affected persons.

Epidemiological studies support these findings. In the Epidemiological Catchment Area Study (ECA) (Regier et al. 1990) which was conducted at the beginning of the 1990s, 46 % of BAS subjects had an AUD. Besides, bipolar men were affected two to three times more often than bipolar women.

This information is complemented with data from the National Epidemiologic Survey of Alcohol and Related Conditions (NESARC) study conducted at the beginning of the last decade in the USA (Grant et al. 2005) which reported a frequency of AUDs (DSM IV) in bipolar I patients to be 23.6 % in the last 12 months and 58 % in lifetime. Substance use disorders (SUD) with illegal substances had a frequency of 12.9 % in the last year and 37.5 % in lifetime. Similar rates were reported in the Systematic Treatment Enhancement Program Bipolar Disorders (STEP BD) study in around one-third (32.2 %) of the 3750 Bipolar I or II patients in psychiatric treatment for Bipolar Disorder (Ostacher et al. 2010).

9.3 Reverse Side of the Coin: Bipolar Disorders in Alcohol Use Disorder Subjects

Conversely, the comorbidity of BAD in AUD subjects is lower. Affective disorders could be ascertained in 13.4 % of these patients. Data on this comorbidity is available from epidemiological studies. The National Comorbidity Survey (NCS) (Kessler et al. 1994) found that 6.5 % of the men dependent on alcohol and 10.6 % of the women had at least one manic episode in their history. However, this survey did not differentiate between manic episodes which appeared before the start of regular substance use, those which started only after the substance use and those which were possibly induced by substance use.

9.4 Consequences of Comorbidity

Of course persons affected by two simultaneous illnesses suffer from more significant consequences than when only one disorder occurs; either of these illnesses can considerably influence the lifestyle and quality of life of the affected persons. Numerous investigations showed that comorbid AUDs can influence the clinical course of BADs unfavorably (review in Sonne and Brady 2002). Persons affected with both BAD and AUD have an earlier onset of affective symptoms, more frequent rehospitalization due to relapses and a higher rate of complications of the affective disorder. Rapid cycling (more than four affective episodes within 1 year) and mixed states (when depressive and manic symptoms occur at the same time) which are seen as more severe and difficult-to-treat forms of BADs, increased

with comorbid AUDs. In addition, the affected persons were more often male, suffer from other psychic illnesses, showed lower treatment compliance and, in particular with persons with an AUD, a significantly higher rate in suicidal behavior and ideation (Oquendo et al. 2010).

Vice versa, this is also true. Persons with mixed episodes or rapid cycling, compared with bipolar I and II patients, have increased rates of AUDs (Soyka 2000). Persons with a bipolar depression and AUD were reported to have a higher risk for hypomanic, manic, and mixed episodes (Ostacher et al. 2010).

The temporal sequence of onset of each respective disorder may be of importance in the investigation on causes and consequences of the comorbidity. An affective disorder which precedes the onset of another psychic disorder is termed "primary affective disorder." Secondary psychiatric disorders succeed the onset of another (primary) psychiatric illness. When three groups of bipolar patients (group 1: bipolar without alcohol and SUD, group 2: onset of BAD precedes alcohol and SUDs, and group 3: onset of a SUD precedes BAD) were compared in retrospect, affected study participants in the second group showed a significantly earlier onset of affective symptoms than those in the other two groups. In comparison, affected patients in the third group reported more often suicidal behaviors than those in the other two groups (Feinman and Dunner 1996). Other investigations suggest that the onset of BADs more often precedes that of a SUD than vice versa. However, the affected subjects in whom the onset of alcohol and substance use precedes that of bipolar disorders, may have a milder course of disease with fewer episodes of affective symptoms (Sonne and Brady 2002).

A recently published study (Prisciandaro et al. 2012) examined the influence of depressive symptoms on craving and drinking behavior one week later in 30 comorbid patients. This data was obtained from an 8-week, placebo-controlled study (acamprosate versus placebo). The bipolar patients were well stabilized and treated with different mood stabilizers (antipsychotics, antiepileptics, or lithium).

Depressive symptoms correlated in this investigation significantly with craving and drinking behavior one week later. The lower drop-out rate was remarkable (23 of 30 patients completed the investigation).

Additional treatment with acamprosate showed significant improvements in the frequency and amount of consumption by the end of the study (week 7 and 8) without significantly influencing affective symptoms (Tolliver et al. 2010).

9.5 Relevance of Onset of Bipolar and Alcohol Use Disorders

The sequential onset of both disorders was examined in a prospective study lasting over 45 years in 144 patients with a first manifestation of a manic episode (Strakowski et al. 2005). Twenty-seven individuals in this group with primary alcohol dependence were found to be older, have less mixed episodes and a faster recovery from the affective index episode than others in the comparison groups. However, patients with primary bipolar illness showed comparably longer duration of affective symptoms and suffered more from consequences of alcohol

dependence in the 5 years they were under observation. There was no difference between the two groups regarding relapse of affective symptoms. Further, in a large multicenter study (Ostacher et al. 2010), the distinction between primary and secondary substance use was not validated when the age at onset of the bipolar disorder was controlled for. Therefore, age at onset of bipolar disorder may be the most salient factor in understanding whether or not there will be a negative relationship between mood and substance use symptoms in patients treated for bipolar illness (Ostacher et al. 2010).

It can be supposed that the sequential onset of both disorders, especially for AUDs in individuals with BAD, plays an important role. Possible consequences for the concept and planning of future therapy strategies with these patients should be considered. In terms of focus in therapy, patients with primary bipolar disorder should receive more attention on their affective symptoms and patients with primary alcohol dependence more on their drinking behavior.

9.6 Other Substance Use and Bipolar Affective Disorders

As with AUD, several epidemiological and clinical studies demonstrated that SUDs are highly prevalent among patients suffering from a mood disorder (Beaulieu et al. 2012). For instance, in a recent Canadian epidemiological study where sociodemographic variables, clinical variables, and depressive symptomatology were compared between patients with bipolar ($n = 467$) and major depressive disorder ($n = 4{,}145$), the authors reported an average past-year problematic SUD of 29 % (23.1–34.8 %) for BAD and 14.3 % (12.8–15.8 %) for major depression disorder (MDD) (Schaffer et al. 2010). The odds ratio (OR) for developing any SUD is 6.9 in patients with a lifetime bipolar I disorder, compared with the general population (Kessler et al. 2007). In particular early-onset BAD may be even more strongly associated with the development of a comorbid SUD (Goldstein et al. 2010). Vice versa, an existing SUD is considered a risk factor for the development of a bipolar I disorder. In that regard, cocaine use disorder predicts subsequent onset of bipolar one disorder (OR = 4.2), as does stimulant abuse (OR = 3.1) and dependence (OR = 5.7) (Kessler et al. 1999) while the onset of BAD after cannabis use was less pronounced (Strakowski et al. 2007).

9.7 Treatment Strategies on the Comorbidity of Bipolar Affective Disorders and Alcohol Use Disorders

Although patients affected by both disorders suffer severe impairments in their psychosocial functioning, treatment strategies combining psychotherapeutic and pharmacological procedures can reduce at least the severity and chronicity of both illnesses. For instance, it is easier for individuals with BAD and secondary AUD to limit their consumption of alcohol when their affective symptoms are pharmacologically (and psychiatrically) treated adequately; the contact to patients is regular

and the compliance good. Conversely, affected patients with primary AUD can learn to handle their affective symptoms better and be optimally treated pharmacologically if their excessive alcohol consumption were dealt with. However, treatment adherence and compliance are a challenge in this special group, since medications are not often taken as prescribed and appointments are not often kept. Outpatient contact and/or timely inpatient treatment for deteriorations in either one of the disorder are crucial as in other psychic disorders.

The American Psychiatric Association (APA) (2002) guidelines recommend concurrent (integrated) treatment of both alcohol use and BADs, not sequential treatment of one and then the other disorder. This is obvious because the illnesses mutually influence each other and the symptoms of one illness continue to exist if only the other were treated. In turn, this is more likely to lead to relapse of the illness treated first.

Therapy strategies which are based on "dual disorders" are especially favorable. These treatment strategies, introduced in the following sections, are increasingly widespread especially since they also reported sufficient success rates (Brady et al. 2007). However, specific proposals for bipolar disorders and alcohol dependence are rare in the German-speaking countries, compared to psychosis and addiction.

9.7.1 Pharmacological Options

An increasing number of studies on the use of pharmacological therapy alone and in combination with psychotherapy for bipolar disorders with comorbid AUD have been conducted in the last few years.

Table 9.1 gives an overview of recent studies on treatment using various substances for comorbid bipolar affective and AUDs.

However, the number of placebo-controlled or double-blind studies conducted are few even though such study approaches offer higher levels of evidence than observation studies in clinical cohorts. In addition, alcohol and SUDs are often unequivocal exclusion criterion in studies on therapeutic efficacy (Swann et al. 2005). In the past, lithium preparations and valproate (antiepileptic) were used most often for the treatment of bipolar disorders, carbamazepine (antiepileptic) is less often prescribed. Lithium has been shown to be less effective with comorbid patients (overview by Cerullo and Strakowski, 2007). Admittedly, the use of antiepileptics is also limited in these patients. Carbamazepine and valproate, for example, can cause induction of liver transaminases (ALAT, ASAT, γGT) and in rare cases liver failure. Patients with severe alcohol dependence often already suffer from liver function disorders.

Recently, controlled clinical studies were published. A placebo-controlled double- blind study on 59 individuals with comorbid bipolar and AUDs was conducted for over 24 weeks (Salloum et al. 2005). Besides improvement of the affective symptoms, less drinking days and lower consumption were shown in the valproate group, which in turn correlated with the plasma valproate levels. Thus, valproate

Table 9.1 Clinical studies on treatment of comorbid bipolar disorders and alcohol and substance dependence

Study	Design	Intervention	Inclusion criteria	Alcohol or substance use disorders	Results
Geller et al. (1998)	RCT, double-blind	Lithium	12 bipolar I; 5 bipolar II disorders	Alcohol or substance dependence	Improvement of alcohol and substance use disorder and affective symptoms
Schmitz et al. (2002)	Open-label	Cognitive therapy and relaxation techniques	46 bipolar disorder	Alcohol or substance use disorders	Improvement of affective but not alcohol use symptoms
Brown et al. (2002)	Open-label	Naltrexone	34 bipolar disorder	Alcohol dependence	Improvement of alcohol use disorder and affective symptoms
Brown et al. (2002, 2003a, b)	Open-label	Quetiapine	17 outpatients with bipolar disorder	Cocaine or stimulant use	Significant improvements in craving and mood symptoms; days/week of cocaine use decreased non-significantly, and urine drug screens did not change
Brown et al. (2003)	Open-label	Lamotrigine	22 bipolar I; 7 bipolar II; 1 bipolar disorder not otherwise specified	Cocaine dependence	Improvement of affective but not alcohol use symptoms
Brown et al. (2005)	Open-label	Aripiprazole	18 bipolar I; 1 bipolar II; 1 schizo-affective disorders	Alcohol or substance use disorders	Improvement of alcohol and substance use disorder and affective symptoms
Salloum et al. (2005)	RCT, double-blind	Valproate (as add on to Lithium)	59 bipolar I disorders	Alcohol dependence	Improvement of alcohol use disorder but not affective symptoms
Brown et al. (2006a, b)	Open-label	Quetiapine	14 bipolar I; 3 bipolar II disorders	Cocaine dependence	Improvement of affective but not alcohol use symptoms

(continued)

Table 9.1 (continued)

Study	Design	Intervention	Inclusion criteria	Alcohol or substance use disorders	Results
Drake et al. (2004)	Open-label	Integrated dual treatment of disorders	51 bipolar disorder	Alcohol or substance use disorders	Improvement of alcohol use disorder but not affective symptoms
Brown et al. (2005)	Open-label	Aripiprazole	abuse (alcohol, $n = 17$; cocaine, $n = 9$; opioids, $n = 3$; and cannabis, $n = 3$) in BD patients ($n = 19$)	Multiple alcohol and substance use disorders	Decreased alcohol and cocaine craving. Number of days of alcohol or cocaine use per week and the number of cocaine-positive urine screens were not significantly reduced.
Albanese and Suh (2006)	Open-label	Risperidone	Bipolar ($n = 9$) or Major depression ($n = 6$) patients	Cocaine dependence	may decrease cocaine craving and use; no assessment of comorbid alcohol use disorder
Brown et al. (2007)	RCT, double blind, add-on	Citicoline up to 2,000 mg/d as add on	44 outpatients with a history of mania or hypomania	Cocaine dependence	Significantly lower probability of a cocaine-positive urine compared with placebo but no significant difference was observed on mood symptoms.
Nejtek et al. (2008)	RCT, head to head comparison	Risperidone versus Quetiapine	Quetiapine $n = 42$; Risperidon $n = 38$	cocaine or metham-phetamine use in bipolar disorder	positive improvements in drug craving ($P < 0.0005$) and in overall drug use ($P = 0.03$) in both treatment arms
Weiss et al. (2000, 2007, 2009)	Open-label	Integrated Group therapy	50 bipolar I; 10 bipolar II; 2 bipolar disorder not otherwise specified	Alcohol or substance use disorders	Improvement of alcohol use disorder but not affective symptoms
Stedman et al. (2010)	RCT, double-blind	Quetiapine as add on for Lithium/Divalproex	362 bipolar I disorder	Alcohol dependence	No influence of both alcohol use and affective symptoms

Brown et al. (2008)	RCT, double-blind	Quetiapine	102 bipolar I disorder	Alcohol dependence	Improvement of affective but not alcohol use symptoms
Brown et al. (2009)	RCT, double-blind	Naltrexon and Cognitive therapy	50 bipolar I; 10 bipolar II; 2 bipolar disorder not otherwise specified	Alcohol dependence	Improvement of alcohol use disorder but not affective symptoms
Tolliver et al. (2012)	RCT, double-blind	Various affective relapse prevention medication; Acamprosat vs. Placebo as add on	33 bipolar I and II disorder	Alcohol dependence	No improvement of alcohol use frequency and amount, no influence on affective symptoms

RCT randomized controlled trial

remains as one of the possible pharmacological strategies to treat comorbid patients. Yet another complementary strategy is the use of antipsychotics in comorbid patients. The effectiveness of aripiprazole was initially tested in a relatively small group of 18 comorbid individuals with bipolar or schizo-affective disorders with an AUD for more than 12 weeks (Brown et al. 2005). Although all affective symptoms improved, results on alcohol consumption remained unsatisfactory. However, craving for alcohol and the purchase of alcoholic beverages decreased at this time. The same study group then used quetiapine in dosages more than 600 mg/d for over 12 weeks on 115 comorbid patients in another study (Brown et al. 2008), 102 of these patients could be examined at least once prospectively. Other than depressive symptoms, neither the manic symptoms nor characteristics of alcohol dependence showed any improvements.

A subsequent study combined both pharmacological treatments mentioned above. Bipolar patients dependent on alcohol were treated with either lithium or valproate combined with quetiapine in flexible dosage (300–800 mg/d) or placebo (Stedman et al. 2010). Three hundred sixty-two patients were randomized for treatment of 12 weeks ($n = 176$ with quetiapine as add on, $n = 178$ with placebos). No significant effect on the characteristics of alcohol dependence could be observed.

Naltrexone (NTX), which has been shown to be effective in relapse prevention of alcohol dependence especially in the USA, was examined in three studies. Initial investigations on comorbid patients with NTX alone or in combination with disulfiram reported favorable effects on several characteristics of consumption, e.g., amount of alcohol consumed (Petrakis et al. 2005) as well as affective symptoms, craving, and consumption days (Brown et al. 2006a, b).

Naltrexone was then examined by the latter research group for its effectiveness in comorbid individuals (Brown et al. 2009). Fifty affected individuals with comorbid bipolar and AUD were examined with 50 mg/d NTX (as an add-on to mood stabilizers) or placebo for over 12 weeks. Effects of the additional NTX on drinking days, craving, and liver enzymes, however, showed only a statistical trend.

The results of pharmacologic strategies on the treatment of comorbid persons remain conflicting. The best results were reported with valproate but these were no longer seen when valproate was combined with quetiapine. Other substances such as aripiprazole or NTX were tested only in small studies or the effectiveness showed only a statistical trend.

9.7.2 Are There Effective Psychotherapeutic Approaches?

Psychotherapy requires a high personal and personnel commitment in the treatment of addiction as well as bipolar disorders. Therefore, it is encouraging to find studies with favorable results in the treatment of persons with addiction and affective disorders (Farren and Mc Elroy 2008). In this research group, 232 comorbid patients with an alcohol dependence and an affective disorder (among whom 102 were individuals with BADs), were treated inpatient with cognitive behavioral

therapy for 4 weeks. Part of the therapy included psychoeducation on both disorders. A 6-month follow-up was conducted and scientifically evaluated. Both groups (depressive and bipolar patients) showed a significant reduction of amount consumed after 3 and 6 months, but no difference was found between these groups. Similar results were found for the consumption of illegal substances which, at baseline, was higher in bipolar patients compared to the depressive persons. Obviously, this therapeutic expense also increased the patients' compliance.

More than half the depressive and more than ¾ of the bipolar study participants were treated with antidepressants or mood stabilizers. Though the study provided no information on specific substances, at the start of the study 67 % of depressive patients received an antidepressant versus 38 % of the bipolar patients. These figures continued at discharge from therapy (59 % of the depressive versus 41 % of the bipolar) and 3 months after (51 % of the depressive versus 46 % of the bipolar). With over 93 % recourse, these results can be considered highly positive even in the absence of a control group with similar therapy. A 5-year follow-up of the same group found a significant long-term benefit of inpatient stay, particularly in those who engaged in postdischarge supportive therapy. A significant number of those who reduced their drinking by 6 months achieved complete abstinence by 5 years (Farren et al. 2014).

Another randomized controlled trial compared 20 weeks of integrated group therapy or group drug counseling with 3 months of posttreatment follow-up (Weiss et al. 2007). Sixty-two patients with bipolar disorder and current substance dependence, treated with mood stabilizers for $\geq$2 weeks, were randomly assigned to integrated group therapy ($n = 31$) or group drug counseling ($n = 31$). Significantly fewer days of substance use for integrated group therapy patients during treatment and follow-up were reported. Integrated group therapy, as a new treatment developed specifically for patients with bipolar disorder and substance dependence, was concluded to be a promising approach to reduce substance use in this population.

Therefore, this therapeutic strategy is judged to be promising even when it was not from a controlled clinical trial. Still, the therapeutic and aftercare expenses are too high for them to be established in every national health system.

9.7.3 Specific Treatment Approaches in Other Comorbid Substance Use and Bipolar Disorders

In general, there is a paucity of studies on comorbid substance use and bipolar disordered patients. As mentioned above, alcohol was the primary substance in most trials, and the remaining treatment studies focused mainly on cocaine use. The typical research paradigm for studying pharmacotherapy in these trials was to give a double-blind medication, primarily to treat the substance dependence after the patient was stabilized on a medication for the bipolar illness (Pettinati et al. 2013).

9.7.3.1 Mood Stabilizer

In general, there are few studies which evaluated the use of mood stabilizers in comorbid substance use and bipolar disordered patients (recent review by Pettinati et al. 2013). A reduction of depressive symptoms (assessed by HAMD-17) was observed in 2 open-label studies of cocaine dependence. An open-label study ($n = 30$) and a replication study ($n = 32$) examining lamotrigine as monotherapy (up to 300 mg/d) or as an adjunct to other medications (up to 12.5 mg/d in patients taking valproic acid) in BAD, demonstrated efficacy in reducing self-report cravings and cocaine use (Brown et al. 2003a, b, 2006a, b).

A 6-month, double-blind, placebo-controlled comparison RCT of lithium monotherapy and lithium plus valproic acid was conducted in patients with BD comorbid with alcohol, cannabis, or cocaine abuse or dependence and rapid cycling during the last 12 months ($n = 149$) (Kemp et al. 2009). Only a small group of patients ($n = 31$; 21 %) met criteria of a minimum of 4 consecutive weeks of stabilization with lithium (blood level $\geq .8$ mEq/L) plus valproic acid (blood level ≥ 50 μg/mL) and were then randomly assigned to the double-blind phase of the study. There was a trend toward improvement of substance abuse outcomes. However, given the small sample size, no statistical difference was reported for the 2 treatment groups. Thus, adding valproic acid to lithium is a first-choice treatment recommendation for cannabis and cocaine abuse disorders comorbid with BAD, whereas valproic acid monotherapy or valproic acid added to other ongoing medications other than lithium are second-choice recommendations (Beaulieu et al. 2012).

9.7.3.2 Antipsychotics

Aripiprazole was studied in a small, 12-week, open-label study of polysubstance abuse (alcohol, $n = 17$; cocaine, $n = 9$; opioids, $n = 3$; and cannabis, $n = 3$) in BD patients ($n = 19$) (Brown et al. 2005). Aripiprazole improved mood (depressive and manic) symptoms. It also not only decreased alcohol but also cocaine craving. However, number of days of alcohol or cocaine use per week and the number of cocaine-positive urine screens were not significantly reduced.

One 20-week, double-blind, head-to-head RCT comparing quetiapine (mean dose: 301.9 mg/d; $n = 42$) and risperidone (mean dose: 3.1 mg/d; $n = 38$) for cocaine or methamphetamine use in BAD found positive improvements in drug craving and in overall drug use in both treatment arms (Nejtek et al. 2008). Moreover, a positive outcome on mood, cocaine craving, and cocaine use also was reported in two other studies of quetiapine in patients with BD comorbid with cocaine (Brown et al. 2002, 2003a, b) or stimulant use (Brown et al. 2003a, b).

Admittedly, the absence of a placebo arm in these studies makes the interpretation of these results more difficult. Therefore, second-choice recommendation was assigned to the add-on use of quetiapine in treating cocaine, amphetamines, and methamphetamines in BAD.

A small, open-label, naturalistic study of risperidone treatment (1.18 mg/d) in cocaine-dependent BD ($n = 9$) or MDD ($n = 6$) patients with or without psychotic features found that risperidone was safe and well-tolerated and may decrease

cocaine craving and use (Albanese and Suh 2006). Six out of 9 BAD patients and all six MDD patients had comorbid AUD, but no specific results were obtained on AUD outcomes. As previously reported in the section on quetiapine, both risperidone (mean dose: 3 mg/d; $n = 38$) and quetiapine (mean dose: 301.9 mg/d; $n = 42$) was associated with decreased drug craving and overall drug use in a 20-week, double-blind RCT in BD patients with comorbid cocaine or methamphetamine use (Nejtek et al. 2008).

Other Medication

Citicoline, a nutritional supplement was assessed in a 12-week, placebo-controlled RCT as an add-on medication (citicoline up to 2,000 mg/d) in 44 outpatients with a history of mania or hypomania and cocaine dependence (Brown et al. 2007). All the patients were previously treated regarding their affective symptoms with a mood stabilizer. Citicoline use was associated with significantly lower probability of a cocaine-positive urine compared with placebo but no significant difference was observed on mood symptoms. A second-choice recommendation is assigned because of the lack of statistical difference on mood symptoms between the treatment and placebo arms. A larger study of citicoline in patients with BAD I and cocaine dependence is ongoing, as well as studies on methamphetamine and cannabis use to establish the efficacy of citicoline for these SUDs.

9.7.3.3 Psychotherapy

As with comorbid alcohol use and bipolar disordered patients, the integrated group therapy developed by Weiss and colleagues (Weiss et al. 2000, 2007, 2009) based on CBT components, has been studied in a pilot study and two separate RCTs ($n = 168$) but all by the same group of investigators. This technique has been developed specifically for bipolar patients with a comorbid SUD, and consists of 12–20 group sessions, which was compared with either group drug counseling or no treatment. As with comorbid bipolar and AUD patients, results consistently indicated a superiority of that treatment in terms of decreased drug use and increased total and consecutive abstinent days, even at 8-month follow-up. This specific treatment fulfills criteria for level 2 evidence, and provides positive results in the BD plus SUD patients.

In summary, few psychotherapeutic interventions have been studied in a randomized study design and only by one research group. This makes the process of assessing clinical efficacy of cognitive behavioral therapy or other approaches quite difficult. In fact, the most recent Cochrane review on psychotherapy of mental illness and SUDs examined 25 RCTs and concluded that it was impossible to rule in favor of any specific psychosocial treatment, because of a large array of methodological differences and difficulties impeding data pooling as well as interpretation (Cleary et al. 2008).

Clearly, evidence from RCTs for psychosocial treatment is lacking in comorbid bipolar and SUDs, but clinicians facing the task of treating these difficult cases need some guidance. When considering the programmatic nature of these treatments, Mueser et al. (2003) suggested that quasiexperimental evidence could be

considered sufficient to define evidence-based practices for the purposes of clinical implementation for persons with mental illness (Gabe 2000; Drake et al. 2001).

Conclusion

In persons with bipolar disorders, alcohol and SUDs (alcohol or substance dependence or harmful use) are common. The occurrence of one disorder has an unfavorable influence on the other. Pharmacological and psychotherapeutic approaches which deal with this comorbidity are increasing and showing significant improvements in both. The efficacious approaches include a mood stabilizer (valproate) and cognitive behavioral therapy for AUD and bipolar subjects. In comparison, while there is some evidence for mood stabilizers, antipsychotics and cognitive therapy reduced craving and drug use in subjects with stimulant and cocaine use disordered bipolar patients.

References

Albanese MJ, Suh JJ (2006) Risperidone in cocaine-dependent patients with comorbid psychiatric disorders. J Psychiatr Pract 12:306–311

American Psychiatric Association (2002) Guidelines for treatment of bipolar disorders. Am J Psychiatry 159:1–50

Angst J (2008) Bipolar disorder–methodological problems and future perspectives. Dialogues Clin Neurosci 10:129–139

Angst J, Gamma A, Benazzi F et al (2003) Diagnostic issues in bipolar disorder. Eur Neuropsychopharmacol 13(Suppl 2):S43–S50

Beaulieu S, Saury S, Sareen J, Tremblay J, Schütz CG, McIntyre RS, Schaffer A (2012) Canadian Network for Mood and Anxiety Treatments (CANMAT) Task Force. The Canadian Network for Mood and Anxiety Treatments (CANMAT) task force recommendations for the management of patients with mood disorders and comorbid substance use disorders. Ann Clin Psychiatry 24:38–55

Brady KT, Verduin ML, Tolliver BK (2007) Treatment of patient's comorbid for addiction and other psychiatric disorders. Curr Psychiatry Rep 9:374–380

Brown ES, Beard L, Dobbs L, Rush AJ et al (2006a) Naltrexone in patients with bipolar disorder and alcohol dependence. Depress Anxiety 23:492–495

Brown ES, Carmody TJ, Schmitz JM, Caetano R, Adinoff B, Swann AC, John Rush A et al (2009) A randomized, double-blind, placebo-controlled pilot study of naltrexone in outpatients with bipolar disorder and alcohol dependence. Alcohol Clin Exp Res 33:1863–1869

Brown ES, Garza M, Carmody TJ (2008) A randomized, double-blind, placebo-controlled add-on trial of quetiapine in outpatients with bipolar disorder and alcohol use disorders. J Clin Psychiatry 69:701–705

Brown ES, Gorman AR, Hynan LS (2007) A randomized, placebo-controlled trial of citicoline add-on therapy in outpatients with bipolar disorder and cocaine dependence. J Clin Psychopharmacol 27:498–502

Brown ES, Jeffress J, Liggin JD et al (2005) Switching outpatients with bipolar or schizoaffective disorders and substance abuse from their current antipsychotic to aripiprazole. J Clin Psychiatry 66:756–760

Brown ES, Nejtek VA, Perantie DC et al (2003a) Cocaine and amphetamine use in patients with psychiatric illness: a randomized trial of typical antipsychotic continuation or discontinuation. J Clin Psychopharmacol 23:384–388
Brown ES, Nejtek VA, Perantie DC et al (2003b) Lamotrigine in patients with bipolar disorder and cocaine dependence. J Clin Psychiatry 64:197–201
Brown ES, Nejtek VA, Perantie DC et al (2002) Quetiapine in bipolar disorder and cocaine dependence. Bipolar Disord 4:406–411
Brown ES, Perantie DC, Dhanani N et al (2006b) Lamotrigine for bipolar disorder and comorbid cocaine dependence: a replication and extension study. J Affect Disord 93:219–222
Cardoso BM, Kauer Sant'Anna M, Dias VV et al (2008) The impact of co-morbid alcohol use disorder in bipolar patients. Alcohol 42:451–457
Cassidy F, Ahearn EP, Carroll BJ (2001) Substance abuse in bipolar disorder. Bipolar Disord 3:181–188
Cerullo MA, Strakowski SM (2007) The prevalence and significance of substance use disorders in bipolar type I and II disorder. Subst Abuse Treat Prevent Pol 2:29
Cleary M, Hunt G, Matheson S, et al. (2008) Psychosocial interventions for people with both severe mental illness and substance misuse. Cochrane Database Systematic Reviews: CD001088
Drake RE, Essock SM, Shaner A et al (2001) Implementing dual diagnosis services for clients with severe mental illness. Psychiatr Serv 52:469–476
Drake RE, Xie H, McHugo GJ, Shumway M et al (2004) Three-year outcomes of long-term patients with co-occurring bipolar and substance use disorders. Biol Psychiatry 56:749–756
Farren CK, Mc Elroy S (2008) Treatment response of bipolar and unipolar alcoholics to an inpatient dual diagnosis program. J Affect Disord 106:265–272
Farren CK, McElroy S (2010) Predictive factors for relapse after an integrated inpatient treatment programme for unipolar depressed and bipolar alcoholics. Alcohol Alcohol 45:527–533
Farren CK, Murphy P, McElroy S (2014) 5-year follow-Up of depressed and bipolar patients with alcohol use disorder in an Irish population. Alcohol Clin Exp Res 38:1049–1058
Feinman JA, Dunner DL (1996) The effect of alcohol and substance abuse on the course of bipolar affective disorder. J Affect Disord 37:43–49
Gabe M (2000) Mental health: a report of the Surgeon General. Home Care Providers 5:117
Geller B, Cooper TB, Sun K et al (1998) Double-blind and placebo-controlled study of lithium for adolescent bipolar disorders with secondary substance dependency. J Am Acad Child Adolesc Psychiatry 37:171–178
Goldstein BI, Bukstein OG (2010) Comorbid substance use disorders among youth with bipolar disorder: opportunities for early identification and prevention. J Clin Psychiatry 71(3):348–358
Grant BF, Hasin DS, Stinson FS (2005) Co-occurrence of 12-month mood and anxiety disorders and personality disorders in the US: results from the national epidemiologic survey on alcohol and related conditions. J Psychiatr Res 39:1–9
Kessler RC, Stang P, Wittchen HU, Stein M, Walters EE (1999) Lifetime co-morbidities between social phobia and mood disorders in the US National Comorbidity Survey. Psychol Med 29 (3):555–567
Kemp DE, Gao K, Ganocy SJ, Elhaj O, Bilali SR, Conroy C, Findling RL, Calabrese JR (2009) A 6-month, double-blind, maintenance trial of lithium monotherapy versus the combination of lithium and divalproex for rapid-cycling bipolar disorder and Co-occurring substance abuse or dependence. J Clin Psychiatry 70(1):113–121
Kessler RC, McGonagle KA, Zhao S et al (1994) Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States. Results from the National Comorbidity Survey. Arch Gen Psychiatry 51:8–19
Kessler RC, Rubinow DR, Holmes C, Abelson JM, Zhao S (2007) The epidemiology of DSM-III-R bipolar I disorder in a general population survey. Psychol Med 27(5):1079–1089

Mueser KT, Torrey WC, Lynde D et al (2003) Implementing evidence-based practices for people with severe mental illness. Behav Modif 27:387–411

Nejtek VA, Avila M, Chen LA et al (2008) Do atypical antipsychotics effectively treat co-occurring bipolar disorder and stimulant dependence? A randomized, double-blind trial. J Clin Psychiatry 69:1257–1266

Oquendo MA, Currier D, Liu SM et al (2010) Increased risk for suicidal behavior in comorbid bipolar disorder and alcohol use disorders: results from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). J Clin Psychiatry 71:902–909

Ostacher MJ, Perlis RH, Nierenberg AA (2010) STEP-BD Investigators. Impact of substance use disorders on recovery from episodes of depression in bipolar disorder patients: prospective data from the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD). Am J Psychiatry 167:289–297

Petrakis IL, Poling J, Levinson C, VA New England VISN I MIRECC Study Group et al (2005) Naltrexone and disulfiram in patients with alcohol dependence and comorbid psychiatric disorders. Biol Psychiatry 57:1128–1137

Pettinati HM, O'Brien CP, Dundon WD (2013) Current status of co-occurring mood and substance use disorders: a new therapeutic target. Am J Psychiatry 170:23–30

Prisciandaro JJ, DeSantis SM, Chiuzan C et al (2012) Impact of depressive symptoms on future alcohol use in patients with co-occurring bipolar disorder and alcohol dependence: a prospective analysis in an 8-week randomized controlled trial of acamprosate. Alcohol Clin Exp Res 36(3):490–496

Regier DA, Farmer ME, Rae DS et al (1990) Comorbidity of mental disorders with alcohol and other drug abuse. Results from the Epidemiologic Catchment Area (ECA) Study. JAMA 2649:2511–2518

Salloum IM, Cornelius JR, Daley DC et al (2005) Efficacy of valproate maintenance in patients with bipolar disorder and alcoholism: a double-blind placebo-controlled study. Arch Gen Psychiatry 62(1):37–45

Schaffer A, Cairney J, Veldhuizen S, Kurdyak P, Cheung A, Levitt A (2010) A population-based analysis of distinguishers of bipolar disorder from major depressive disorder. J Affect Disord 125(1–3):103–110

Schmitz JM, Averill P, Sayre S, McCleary P, Moeller FG, Swann A. (2002) Cognitive-behavioral treatment of bipolar disorder and substance abuse: a preliminary randomized study. Addictive Disorders and Their Treatment. 1:17–24.

Sonne SC, Brady T (2002) Bipolar disorders and alcoholism. Alcohol Res Health 26:103–108

Soyka M (2000) Substance misuse, psychiatric disorder and violent and disturbed behaviour. Br J Psychiatry 176:345–350

Stedman M, Pettinati HM, Brown ES et al (2010) A double-blind, placebo-controlled study with quetiapine as adjunct therapy with lithium or divalproex in bipolar I patients with coexisting alcohol dependence. Alcohol Clin Exp Res 34:1822–1831

Strakowski SM, DelBello MP, Fleck DE, Adler CM, Anthenelli RM, Keck PE Jr, Arnold LM, Amicone J (2007) Effects of co-occurring cannabis use disorders on the course of bipolar disorder after a first hospitalization for mania. Arch Gen Psychiatry 64(1):57–64

Strakowski SM, DelBello MP, Fleck DE et al (2005) Effects of co-occurring alcohol abuse on the course of bipolar disorder following a first hospitalization for mania. Arch Gen Psychiatry 62:851–858

Swann AC, Dougherty DM, Pazzaglia PJ et al (2005) Increased impulsivity associated with severity of suicide attempt history in patients with bipolar disorder. Am J Psychiatry 162:1680–1687

Tolliver BK, Desantis SM, Brown DG et al (2010) A randomized, double-blind, placebo-controlled clinical trial of acamprosate in alcohol-dependent individuals with bipolar disorder: a preliminary report. Bipolar Disord 14:54–63

Weiss RD, Griffin ML, Greenfield SF et al (2000) Group therapy for patients with bipolar disorder and substance dependence: results of a pilot study. J Clin Psychiatry 61:361–367

Weiss RD, Griffin ML, Jaffee WB et al (2009) A "community-friendly" version of integrated group therapy for patients with bipolar disorder and substance dependence: a randomized controlled trial. Drug Alcohol Depend 104:212–219

Weiss RD, Griffin ML, Kolodziej ME (2007) A randomized trial of integrated group therapy versus group drug counseling for patients with bipolar disorder and substance dependence. Am J Psychiatry 164:100–107

Personality Disorder and Addiction

10

Marc Walter

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Abstract

Personality disorder and substance use disorder very commonly co-occur. Depending on the sample and setting, comorbid substance use disorder can be diagnosed in approximately every second patient suffering from a personality disorder. Comorbid personality disorder seems to be more prevalent in drug use disorder than in alcohol use disorder. The association between substance use disorder and borderline or antisocial personality disorder is particularly frequent. These comorbidities are generally characterised by severe addiction problems and by an unfavourable clinical course.

The differential indication for the treatment of patients with personality disorder and comorbid substance use disorder is of particular importance. For most patients with personality disorders, psychotherapy is the treatment of choice. Pharmacotherapy is helpful in an acute crisis and for other comorbid psychiatric disorders such as depression and psychosis. Three different evidence-based psychotherapies have been examined for comorbid patients (dialectical behaviour therapy; dynamic deconstructive psychotherapy; dual-

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focused schema therapy). There have been no controlled trials of pharmacotherapy for patients with personality disorder and substance use disorder.

In conclusion, the principle should generally be applied that the two disorders should be treated together. However, further research is needed to improve the specific treatment options for patients with personality disorder and substance use disorder.

10.1 Introduction

A personality disorder is defined as an enduring pattern of inner experience and behaviour that markedly deviates from the expectations of the individual's culture. A personality disorder is pervasive and inflexible, has an onset in adolescence or early adulthood, is stable over time, and leads to distress or impairment (APA 2013).

For the diagnosis of personality disorder, some important principles should be considered. The diagnosis should not be stigmatised, nor caused by the therapist's situational and personal concern or anger. The diagnosis may only be made if the patient suffers from personality problems, exhibits interpersonal problems, or is in conflict with ethics, or law and order.

Table 10.1 lists the ten specific personality disorders according to the current approach of DSM-5 (Sect. II). In an alternative model developed for the DSM-5 (Sect. III), personality disorders are characterised by impairments in personality functioning and personality traits. The disturbances in self and interpersonal functioning are seen here as the core of personality psychopathology, and personality disorders are evaluated on a continuum (APA 2013).

Personality disorders in the DSM-5 classification of the APA closely resemble the ICD-10 classification of the WHO with respect to diagnosis and criteria (Simms 1992). However, they are not identical. Whereas the ICD is especially used in clinical settings throughout Europe, the DSM is employed in most American and European research studies on personality disorders. The main difference between the two classifications is probably the diagnosis of the schizotypical personality disorder in DSM-5, which is diagnosed as a form of a schizophrenic psychosis in

Table 10.1 Classification of personality disorders according to DSM-5

Cluster A	Cluster B	Cluster C
Paranoid personality disorder	Antisocial personality disorder	Avoidant personality disorder
Schizoid personality disorder	Borderline personality disorder	Dependent personality disorder
Schizotypical personality disorder	Histrionic personality disorder	Obsessive-compulsive personality disorder
	Narcissistic personality disorder	

the ICD-10. The essential feature of the schizotypical personality disorder according to DSM is a pervasive pattern of social deficits, marked by cognitive and perceptual distortions, rather than a period of psychotic symptoms, which is generally seen as typical of schizophrenic psychosis. This diagnostic difference may be one reason why the schizotypical personality disorder is less often diagnosed in Europe than in the USA.

Another difference between both classifications is the division of the borderline personality disorder (called unstable personality disorder) into two subtypes in the ICD-10. According to ICD-10, one subtype (the impulsive type) cannot be diagnosed together with the antisocial personality disorder (called dissocial personality disorder). Thus, this common comorbidity in clinical settings cannot be diagnosed in the ICD-10.

Two specific personality disorders are more often diagnosed together with substance use problems: the borderline personality disorder (BPD) and the antisocial personality disorder (ASPD). Both disorders are connected to higher impulsivity and aggressive behaviour (Walter et al. 2011) and are often part of the specific dual disorder of personality disorder and substance use disorder.

ASPD is characterised by a pattern of disregard for and violation of the rights of others, and BPD by a pattern of interpersonal and affective instability and impulsivity. Neurobiology results indicate that ASPD patients often exhibit impaired emotional modulation (Herpertz et al. 2007) and a reduction in structural volume, mainly in the prefrontal cortex (Narayan et al. 2007). BPD is mainly due to a negative self-image (Dammann et al. 2011) and disturbed emotional regulation (Gunderson 2011).

10.2 Epidemiology

Epidemiological studies have shown that the prevalence in the general population of personality disorders is approximately 10 %. The rates vary between 4 % and 20 %, depending on the samples included. In individuals with a personality disorder, the risk of comorbid substance use disorder (SUD) is increased fivefold for alcohol use disorders and twelvefold for drug use disorder (Trull et al. 2010).

The comorbidity of personality disorders in patients with SUD is between 34 % and 73 % (Verheul 2001). These are most commonly cluster B personality disorders, particularly BPD (Walter et al. 2009). In a sample with BPD patients, half of the patients also exhibited an alcohol and/or a drug use disorder (McGlashan et al. 2000).

In patients with alcohol dependence, different specific personality disorders were identified, including BPD and narcissistic, compulsive, and paranoid personality disorders. The co-occurrence of one or more personality disorders was found to be positive correlated with the severity of addiction (Preuss et al. 2009). In patients with alcohol dependence and cannabis use disorders, BPD, ASPD, and schizotypal personality disorder were diagnosed most often (Hasin et al. 2011).

Table 10.2 Prevalence rates of personality disorders in patients with SUD

Study	Sample size	Diagnostic instruments	Any personality disorder	ASPD
Khantzian and Treece (1985)	133	Clinical	65 %	34.6 %
Strain et al. (1991)	66	Clinical	–	30.3 %
Abbott et al. (1994)	144	SCID	45.8 %	31.3 %
Brooner et al. (1997)	716	SCID	34.8 %	25.1 %
Verheul (2001) (Review)	>100	Interview	56.5 % median	22.9 % median
Trull et al. (2010)	>40,000	AUDADIS-IV	–	26.6 %

Note: *ASPD* Antisocial personality disorder, *SUD* Substance use disorder, *SCID* Structured clinical interview for DSM-IV personality disorders, *AUDADIS-IV* Alcohol use disorder and associated disabilities interview schedule-IV

In a recent study, 46 % of patients with SUD also had a personality disorder—16 % ASPD and 13 % BPD (Langås et al. 2012).

Table 10.2 shows the prevalence rates for personality disorders and ASPD, as reported for patients being treated for SUD.

Thus, comorbidity between personality disorder and SUD is common; this comorbidity is mainly related to ASPD and BPD and is often associated with severe addiction problems. In addition, there are also clear indications that—even though the types of personality disorder in alcohol and drug dependence are similar—the prevalence of any specific comorbid personality disorder may be slightly higher in drug-dependent than in alcohol-dependent patients.

10.3 Aetiology

There are various different hypotheses to explain the frequent comorbidity of personality disorders and SUD, including secondary substance abuse in patients with a primary diagnosis of a personality disorder, the existence of common biological vulnerability factors such as problems with impulsivity and impulse control, and the possibility that repeated trauma cause personality changes that may be associated with the diagnosis of personality disorder.

The best current empirical model for the aetiology of comorbidity postulates a primary personality disorder, followed by the secondary development of a SUD. Especially in BPD, ASPD, and in the narcissistic personality disorder, the self-medication hypothesis is extended to the self-regulation of emotions hypothesis and thus provides a partial explanation of substance use. Patients with cluster B personality disorders such as BPD or ASPD usually begin early with excessive

substance use. It was shown that these patients start using intravenous drugs significantly earlier than patients without comorbid personality disorder (Cohen et al. 2007).

It has also been proposed that there are common biological vulnerability factors, and indeed neuroimaging studies have shown similar findings for patients with personality disorders and with SUD. Current findings are primarily non-specific and are also found in other psychiatric disorders. One striking similarity between patients with ASPD, alcohol, cocaine, and heroin dependence is the reduction in the volume of grey matter in the brain areas of the limbic system such as the striatum and amygdala as well as in the prefrontal cortex (Makris et al. 2008). These areas are known to be involved in the regulation and control of emotions and craving (the desire to use drugs). In both disorders—personality disorders and SUD— these results may be linked to clinical deficits and difficulties in impulse control. Impulsivity in cocaine-dependent patients is positively correlated with the reduction in volume (Moreno-López et al. 2012). Family studies have shown that not only drug-dependent patients, but also their healthy family members had impulsive personality traits and deficits in executive functioning (Ersche et al. 2012).

In general, increased impulsivity is associated with lower dopamine autoreceptor binding and with greater stimulant-induced dopamine release in the striatum (Buckholtz et al. 2010). This result may provide an explanation of why patients with cluster B personality disorders are also more vulnerable to the consumption of psychotropic substances. Higher impulsivity in these patients leads to greater dopamine release in the brain, with corresponding positive substance effects after intake such as relaxation and euphoria (Blum et al. 2013).

10.4 Clinical Course

In general, patients with personality disorders and comorbid SUDs differ from those without comorbid SUDs. They have earlier addiction problems, are younger at entry into an addiction-specific treatment, often consume illegal substances, and have more social problems and lower psychosocial functioning (Langås et al. 2012).

Moreover, the clinical course is, as expected, empirically worse for patients with personality disorder and comorbid SUD. Even when their clinical course had improved, patients with SUD and comorbid ASPD exhibited more severe addiction and mental health problems than those without comorbid personality disorder (Galen et al. 2000). Moreover, it was found that comorbid antisocial, borderline,

or schizotypical personality disorder were a significant predictor for persistent drug use over several years, whereas other comorbid mental disorders had no influence on the course of drug problems (Fenton et al. 2012).

A further finding shows how important the diagnosis of a personality disorder for the course of addiction-specific treatment is: Comorbid personality disorder did not remit after treatment of SUD (Verheul et al. 2000). Conversely, comorbid SUD is associated with poorer outcome in patients with borderline personality disorder (Zanarini et al. 2004).

Overall, it can be assumed that treatment of SUD alone has little reciprocal effect on the course of the comorbid personality disorder, so addiction treatment should increasingly concentrate on the treatment of the specific concurrent personality disorder.

10.5 Treatment

10.5.1 Psychotherapy

Psychotherapy is accepted as the treatment of choice for personality disorders. In patients with the diagnosis of personality disorder, disorder-specific psychotherapies should be used whenever possible. In the treatment of BPD and other severe personality disorders, disorder-specific psychotherapies have been proven to be highly effective. This is particularly the case for dialectical behaviour therapy (DBT) (Linehan 1993), for which there are the most positive studies with the highest level of evidence. Furthermore, there is good evidence for transference-focused psychotherapy (TFP), mentalization-based psychotherapy, and schema therapy (Gunderson 2011).

Three different psychotherapies for patients with the dual disorder of personality disorder and SUD are now supported by good evidence from randomised-controlled trials: DBT, dynamic deconstructive psychotherapy (DDP) and dual-focused schema therapy (DFST) (Pennay et al. 2011).

The standard DBT approach was first adapted for use in patients with borderline personality disorder and comorbid drug dependence. This partially adapted DBT for BPD and opioid dependence was found to be more effective than other therapeutic approaches in the treatment of women (Linehan et al. 2002). But even standard DBT reduces borderline symptoms and improves emotion regulation in patients with dual disorders (van den Bosch et al. 2002; Verheul et al. 2003). It currently remains unclear whether substance problems are positively influenced by standard DBT in patients with dual disorders. Adapted DBT is similar in some respects to specific therapies for substance abuse problems such as motivational interviewing (Miller and Rollnick 2002) and relapse prevention (Marlatt and

Gordon 1985). Relapse is seen here as a typical phenomenon of addiction, and not as a failure of the patient; relapse and the risk situation should be generally handled with behavioural analyses, in order to achieve forms of coping other than substance use (Dimeff and Linehan 2008).

In addition, psychodynamically oriented DDP has given positive study results. There were changes in the areas of psychosocial functioning, parasuicidal behaviour, depression, dissociation, and above all, a greater reduction in alcohol consumption than in the control group (Gregory et al. 2008). However, the study is limited by the inclusion of alcohol-dependent patients and its relatively small size. DDP usually involves a single 1 h individual therapy session per week for 12–18 months. DDP show similarities to TFP treatment. The primary focus of TFP is on the dominant affect-laden themes that emerge in the relationship between patient and therapist (Clarkin et al. 2006). DDP has been developed for the treatment of BPD, ASPD and concurrent SUD; it attempts to remediate three main neurocognitive deficits, which are responsible for adaptive processing of emotional experiences: association, attribution, and alterity (Gregory et al. 2010). DDP therapists also encourage the use of family therapy interventions, self-help groups, and education.

In two controlled studies, positive effects were found with DFST in patients with personality disorder and addiction (Ball et al. 2011). At least in the first study, it was unclear how many substances were consumed, and whether all patients were classified as substance dependent (Ball et al. 2005). DFST integrates cognitive behavioural coping skills for substance use with targeted interventions for early maladaptive schemas (i.e., enduring negative themes about oneself, others, and events), affective reactions, relational problems, and maladaptive behavioural coping styles (Young 1994). In contrast to DBT, DFST is not limited to BPD but can be applied to all serious personality disorders and is designed to last 6 months. In the first 2 months of therapy, addiction coping skills are integrated with identification and education about personality, schemas, relationships, and coping. During the remaining 4 months, DFST focuses on cognitive, experiential, behavioural, and relational change strategies.

Table 10.3 lists the characteristics of these three psychotherapies for the dual disorder of personality disorder and SUD.

Finally, it should be noted that, although all three specific psychotherapies for the dual disorder of personality disorder and SUD (DBT, DDP, DFST) have provided positive results in the first randomised controlled studies, their value in clinical practice has not yet been fully assessed. This is particularly true for the comparison between these specific approaches for dual disorders with disorder-specific treatments for personality disorders. In the coming years, further research will show which treatment method is particularly effective for which dual disorder.

Table 10.3 Psychotherapy for patients with personality disorder and SUD

Psychotherapy	Duration	Treatment target	Setting	Patients	Comorbidity
Dialectical behaviour therapy (DBT)	12 months	Decreasing abuse of substances, increasing community reinforcement of healthy behaviours	Weekly individual psychotherapy, weekly group skills training; weekly consultation between clinicians	Opiate-dependent women with borderline personality disorder	Cocaine dependence, ASPD, depression, anxiety
Dynamic deconstructive psychotherapy (DDP)	12 months	Integration of polarised and distorted attributions towards self and others	Weekly individual psychotherapy, independent group therapy	Alcohol-dependent patients with borderline personality disorder	Illegal drug use, ASPD depression, anxiety
Dual-focused schema therapy (DFST)	6 months	Cognitive behavioural coping skills for substance use and targeted interventions for early maladaptive schemas	Weekly individual psychotherapy, three weekly group psycho-education	Opiate-dependent methadone maintained patients with personality disorders	Illegal drug use, depression, anxiety

Note: *SUD* Substance use disorder, *ASPD* Antisocial personality disorder

10.5.2 Pharmacotherapy

In personality disorders, psychopharmacological treatments are generally indicated when comorbid mental disorders such as depressive disorder occur or for the purposes of emergency medication during agitation and psychotic episodes. Medications such as antidepressants or second-generation antipsychotics are generally promising for this purpose (Herpertz et al. 2007).

When comorbid alcohol dependence is diagnosed, evidence-based medication can be used to prevent alcohol relapse such as acamprosate and naltrexone (Kiefer et al. 2003). Acamprosate is approved for the maintenance of abstinence in alcohol-dependent patients. This acts by modulating glutamatergic transmission and is intended to reduce the desire to use alcohol (craving). Naltrexone, a selective opioid receptor antagonist, is also approved for relapse prevention in alcohol dependence. It reduces the craving for alcohol by competitively inhibiting endorphin-mediated dopamine release. It has been suggested that naltrexone does not only maintain abstinence but also prevents uncontrolled drinking.

When comorbid heroin or opioid dependence occurs, substitution treatment is often helpful. The Swiss Society of Addiction Medicine (SSAM) recommends substitution treatment with methadone and buprenorphine and has described this substitution treatment as the therapy of choice for severe opioid dependence (SSAM 2006). Substitution treatment with opioid agonists such as methadone or buprenorphine may lead to psychosocial stabilisation in patients with severe heroin dependence and comorbid personality disorder.

Research on the psychopharmacological treatment of dual disorder personality disorder and SUD is still in its infancy. No controlled studies are currently available, but there is some evidence that mood stabilisers and some second-generation antipsychotics may also positively influence craving and alcohol consumption (Gianoli et al. 2012).

Conclusions

Personality disorder and substance use disorder very commonly co-occur. In particular, borderline personality disorder, antisocial personality disorder, and comorbid substance use disorder are frequently associated. At least half of patients in treatment for substance use or in psychotherapy treatment have this dual disorder.

Beside the disorder-specific treatment for personality disorders, there are three different psychotherapy treatments that showed better therapy outcomes than treatment as usual (TAU) groups: dialectical behaviour therapy, dynamic deconstructive psychotherapy, and dual-focused schema therapy. The studies have shown a decrease in substance use, a decrease in psychopathological symptoms like depression and anxiety, and improvements in psychosocial functioning during treatment. There is currently insufficient evidence to recommend one treatment rather than another. There have been no controlled trials of pharmacotherapy for this dual disorder. However, psychosocial treatment (e.g. relapse prevention) combined with acamprosate and naltrexone can be

used in alcohol dependence. Moreover, in severe heroin dependence, opioid agonists should be substituted to improve the clinical outcome.

In general, it should be noted that the two disorders—personality disorder and substance use disorder—should be treated together in an integrated treatment setting and team. Further research is needed to examine effective treatment options for concurrent personality disorder and substance use disorder.

References

Abbott PJ, Weller SB, Walker SR (1994) Psychiatric disorders of opiate addicts entering treatment: preliminary data. J Addict Dis 13:1–11

American Psychiatric Association (2013) Diagnostic and statistical manual of mental disorders, 5th edn. (DSM-5). American Psychiatric Publishing

Ball SA, Cobb-Richardson P, Connolly AJ, Bujosa CT, O'Neall TW (2005) Substance abuse and personality disorders in homeless drop-in center clients: symptom severity and psychotherapy retention in a randomized clinical trial. Compr Psychiatry 46:371–379

Ball SA, Maccarelli LM, LaPaglia DM, Ostrowski MJ (2011) Randomized trial of dual-focused vs. single-focused individual therapy for personality disorders and substance dependence. J Nerv Ment Dis 199:319–328

Blum J, Gerber H, Gerhard U, Schmid O, Petitjean S, Riecher-Rössler A, Wiesbeck GA, Borgwardt SJ, Walter M (2013) Acute effects of heroin on emotions in heroin-dependent patients. Am J Addict 22:598–604

Brooner RK, King VL, Kidorf M, Schmidt CW, Bigelow GE (1997) Psychiatric and substance use comorbidity among treatment-seeking opioid abusers. Arch Gen Psychiatry 54:71–80

Buckholtz JW, Treadway MT, Cowan RL, Woodward ND, Li R, Ansari MS, Baldwin RM, Schwartzman AN, Shelby ES, Smith CE, Kessler RM, Zald DH (2010) Dopaminergic network differences in human impulsivity. Science 329:532

Clarkin JF, Yeomans FE, Kernberg OF (2006) Psychotherapy of borderline personality disorder. Focusing on object relations. American Psychiatric Publishing, Arlington

Cohen P, Chen H, Crawford TN, Brook JS, Gordon K (2007) Personality disorders in early adolescence and the development of later substance use disorders in the general population. Drug Alcohol Depend 88(Suppl 1):71–84

Dammann G, Hügli C, Selinger J, Gremaud-Heitz D, Sollberger D, Wiesbeck GA, Küchenhoff J, Walter M (2011) The self-image in patients with borderline personality disorder. J Pers Disord 25:517–527

Dimeff LA, Linehan MM (2008) Dialectical behavior therapy for substance abusers. Addict Sci Clin Pract 4:39–47

Ersche KD, Turton AJ, Chamberlain SR, Müller U, Bullmore ET, Robbins TW (2012) Cognitive dysfunction and anxious-impulsive personality traits are endophenotypes for drug dependence. Am J Psychiatry 169:926–936

Fenton MC, Keyes K, Geier T, Greenstein E, Skodol A, Krueger B, Grant BF, Hasin DS (2012) Psychiatric comorbidity and the persistence of drug use disorders in the United States. Addiction 107:599–609

Galen LW, Brower KJ, Gillespie BW, Zucker RA (2000) Sociopathy, gender, and treatment outcome among outpatient substance abusers. Drug Alcohol Depend 61:23–33

Gianoli MO, Jane JS, O'Brien E, Ralevski E (2012) Treatment for comorbid borderline personality disorder and alcohol use disorders: a review of the evidence and future recommendations. Exp Clin Psychopharmacol 20:333–444

Gregory RJ, Chlebowski S, Kang D, Remen AL, Soderberg MG, Stepkovitch J, Virk S (2008) A controlled trial of psychodynamic psychotherapy for co-occurring borderline personality disorder and alcohol use disorder. Psychotherapy (Chic) 45:28–41

Gregory RJ, DeLucia-Deranja E, Mogle JA (2010) Dynamic deconstructive psychotherapy versus optimized community care for borderline personality disorder co-occurring with alcohol use disorders: a 30-month follow-up. J Nerv Ment Dis 198:292–298

Gunderson JG (2011) Borderline personality disorder. N Engl J Med 364:2037–2042

Hasin D, Fenton MC, Skodol A, Krueger R, Keyes K, Geier T, Greenstein E, Blanco C, Grant B (2011) Personality disorders and the 3-year course of alcohol, drug, and nicotine use disorders. Arch Gen Psychiatry 68:1158–1167

Herpertz SC, Zanarini M, Schulz CS, Siever L, Lieb K, Möller HJ (2007) WFSBP Task Force on Personality Disorders. World Federation of Societies of Biological Psychiatry (WFSBP) guidelines for biological treatment of personality disorders. World J Biol Psychiatry 8:212–244

Khantzian EJ, Treece C (1985) DSM-III psychiatric diagnosis of narcotic addicts. Recent findings. Arch Gen Psychiatry 150:1067–1071

Kiefer F, Jahn H, Tarnaske T et al (2003) Comparing and combining naltrexone and acamprosate in relapse prevention of alcoholism: a double-blind, placebo-controlled study. Arch Gen Psychiatry 60:92–99

Langås AM, Malt UF, Opjordsmoen S (2012) In-depth study of personality disorders in first-admission patients with substance use disorders. BMC Psychiatry 12:180

Linehan MM (1993) Cognitive-behavioral treatment in borderline personality disorder. Guilford, New York

Linehan MM, Dimeff LA, Reynolds SK, Comtois KA, Welch SS, Heagerty P, Kivlahan DR (2002) Dialectical behavior therapy versus comprehensive validation therapy plus 12-step for the treatment of opioid dependent women meeting criteria for borderline personality disorder. Drug Alcohol Depend 67:13–26

Miller WR, Rollnick S (2002) Motivational interviewing: preparing people for change, 2nd edn. Guilford, New York

Makris N, Oscar-Berman M, Kim S, Hodge SM, Kennedy DN, Caviness VS, Phil D, Marinkovic K, Breiter HC, Gasic GP, Harris GJ (2008) Decreased volume of the brain reward system in alcoholism. Biol Psychiatry 64:192–202

Marlatt GA, Gordon JR (1985) Relapse prevention: a self-control strategy for the maintenance of behavior change. Guilford, New York

McGlashan TH, Grilo CM, Skodol AE, Gunderson JG, Shea MT, Morey LC, Zanarini MC, Stout RL (2000) The Collaborative Longitudinal Personality Disorders Study: baseline Axis I/II and II/II diagnostic co-occurrence. Acta Psychiatr Scand 102:256–264

Moreno-López L, Catena A, Fernández-Serrano MJ, Delgado-Rico E, Stamatakis EA, Pérez-García M, Verdejo-García A (2012) Trait impulsivity and prefrontal gray matter reductions in cocaine dependent individuals. Drug Alcohol Depend 125:208–214

Narayan VM, Narr KL, Kumari V, Woods RP, Thompson PM, Toga AW, Sharma T (2007) Regional cortical thinning in subjects with violent antisocial personality disorder or schizophrenia. Am J Psychiatry 164:1418–1427

Pennay A, Cameron J, Reichert T, Strickland H, Lee NK, Hall K, Lubman DI (2011) A systematic review of interventions for co-occurring substance use disorder and borderline personality disorder. J Subst Abuse Treat 41:363–373

Preuss UW, Johann M, Fehr C, Koller G, Wodarz N, Hesselbrock V, Wong WM, Soyka M (2009) Personality disorders in alcohol-dependent individuals: relationship with alcohol dependence severity. Eur Addict Res 15:188–195

Schweizerische Gesellschaft für Suchtmedizin (SSAM, 2006). Medizinische Empfehlungen für substitutionsgestützte Behandlungen (SGB) bei Opioidabhängigkeit. Bern.

Simms GO (1992) ICD-10 Classification of mental and behavioural disorders: Clinical Descriptions and Diagnostic Guidelines. Bertrams.

Strain EC, Brooner RK, Bigelow GE (1991) Clustering of multiple substance use and psychiatric diagnosis in opiate addicts. Drug Alcohol Depend 27:127–134

Trull TJ, Jahng S, Tomko RL, Wood PK, Sher KJ (2010) Revised NESARC personality disorder diagnoses: gender, prevalence, and comorbidity with substance dependence disorders. J Pers Disord 24:412–426

Verheul R, Kranzler HR, Poling J, Tennen H, Ball S, Rounsaville BJ (2000) Axis I and Axis II disorders in alcoholics and drug addicts: fact or artifact? J Stud Alcohol 61:101–110

Verheul R (2001) Co-morbidity of personality disorders in individuals with substance use disorders. Eur Psychiatry 16:274–282

Verheul R, Van Den Bosch LM, Koeter MW, De Ridder MA, Stijnen T, Van Den Brink W (2003) Dialectical behaviour therapy for women with borderline personality disorder: 12-month, randomised clinical trial in The Netherlands. Br J Psychiatry 182:135–140

van den Bosch LM, Verheul R, Schippers GM, van den Brink W (2002) Dialectical behavior therapy of borderline patients with and without substance use problems. Implementation and long-term effects. Addict Behav 27:911–923

Walter M, Gunderson JG, Zanarini MC, Sanislow C, Grilo CM, McGlashan TH, Morey LC, Yen S, Stout R, Skodol A (2009) New onsets of substance use disorders in borderline personality disorder over seven years of follow-ups. Addiction 204:97–103

Walter M, Wiesbeck GA, Dittmann V, Graf M (2011) Criminal recidivism in offenders with personality disorders and substance use disorders over 8 years of time at risk. Psychiatry Res 186:443–445

Young JE (1994) Cognitive therapy for personality disorders: a schema-focused approach. Professional Resource Exchange Inc., Sarasota

Zanarini MC, Frankenburg FR, Hennen J, Reich DB, Silk KR (2004) Axis I comorbidity in patients with borderline personality disorder: 6-year follow-up and prediction of time to remission. Am J Psychiatry 161:2108–2114

Comorbidity of Anxiety Disorders and Substance Use

11

Michael Soyka

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Abstract

Generalized anxiety disorder, panic disorder with and without agoraphobia, social phobia, and specific phobias are frequently associated with substance use disorders. Since anxiety symptoms may occur as a consequence of withdrawal from drugs such as alcohol, opioids, or benzodiazepines or as a result of intoxication, the differential diagnosis between substance-induced anxiety disorders and comorbid psychiatric disorders can be difficult. Epidemiologic studies indicate a two to threefold increased risk for alcohol use disorders in patients with anxiety disorders; specifically, the prevalence of alcohol dependence but not abuse is increased. The increased risk for substance use can be explained only in part by self-medication or tension reduction. The best option for the treatment of comorbid patients might be standard treatment for substance use plus cognitive–behavioral therapy.

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List of Abbreviations

CBT	Cognitive–behavioral therapy
GAD	Generalized anxiety disorder
OR	Odds ratio
PD	Panic disorder
PTSD	Posttraumatic stress disorder
SAD	Social anxiety disorder

11.1 Definition of Anxiety Disorders

Comorbidity of substance use with psychiatric disorders is of relevance for the diagnosis, prognosis, and treatment of substance use disorders. A significant comorbidity of substance use with affective disorder, especially bipolar disorder, and schizophrenia is well established (Kessler et al. 2005; Marmorstein et al. 2010; Merikangas et al. 2003). More recently, comorbidity with anxiety disorders has emerged as a focus (Grant et al. 2009).

Anxiety disorders can be subtyped as generalized anxiety disorder (GAD), panic disorder (PD) with and without agoraphobia, social phobia, and specific phobias (Bandelow et al. 2008). Obsessive–compulsive disorder and posttraumatic stress disorder (PTSD) will not be addressed in this chapter. According to DSM-5, GAD is characterized by an array of mental and somatic symptoms, including excessive worry—persisting for 6 months or longer—combined with autonomic, musculoskeletal, gastrointestinal, and respiratory symptoms. Current diagnostic criteria require prolonged feelings of anxiety and worry accompanied by at least three of the following six key symptoms: restlessness, fatigue, impaired concentration, irritability, muscle tension, and disruptions in patterns of sleep. PD is characterized by recurrent panic attacks with intense fear or discomfort, accompanied by at least four of 13 somatic and mental symptoms (14 in ICD-10). A panic attack usually reaches a peak within 10 min and lasts for about 30–45 min. Typically, patients are afraid they have a serious medical condition such as myocardial infarction. About two-thirds of patients with PD also have agoraphobia. This disorder is characterized by fear of places or situations from which escape might be difficult or in which help may not be available in the event of having an unexpected panic attack. Typical risk situations include standing in a crowd or in line, being outside the home alone, or travelling on a bus, aircraft, train, or car. These situations are avoided or endured with marked distress.

Key features of specific phobias are excessive or unreasonable fear of single objects or situations (e.g., heights, animals, seeing blood, etc.). Social phobia (social anxiety disorder; SAD) is characterized by persistent, unreasonable fear of being observed or evaluated negatively by others in social performance or

interaction situations and is associated with somatic and cognitive symptoms. The feared situations are avoided or endured with anxiety or distress. These situations include fear of speaking in public or to unfamiliar people or being exposed to possible scrutiny by others. Blushing or related symptoms may occur.

The pathophysiology of GAD and other anxiety disorders and their association with substance use disorders is not well understood. There is some evidence for a modest genetic risk. Impaired serotonergic and GABAergic neurotransmission have been discussed as key factors in GAD. Both neurotransmitters play a role also in mediating the effects of alcohol. Alcohol enhances GABAergic neurotransmission, and chronic alcohol intake is associated with a serotonergic deficit. Other relevant neurotransmitters involved in stress reactivity and alcohol consumption are norepinephrine, opioids, cholecystokinin, corticotrophin-releasing factors, and neuropeptide Y (Brady and Sinha 2005); impairments of the benzodiazepine receptor are probably also involved. More recently, the role of neuropeptide S in the basolateral amygdala and the relevance of neuropeptide S for the anxiolytic effects of alcohol have been stressed (Enquist et al. 2012). Recently, the role of corticotrophin-releasing hormone-2 receptor gene variants for HPA activation and alcohol consumption in the animal model was demonstrated (Yong et al. 2014). A dysfunction of the hypothalamic–pituitary stress axis has repeatedly been described in patients with anxiety disorders, and multiple lines of evidence suggest that alcoholics react differently to healthy controls to anxiety-related stimuli and may have a disruption of affect regulation (Yang et al. 2013). The prefrontal cortex is one of the key structures in the neurobiology of anxiety disorders (Bishop et al. 2004).

11.2 Epidemiology of Anxiety Disorders

Anxiety disorders are very frequent in the general population. In the US National Comorbidity Survey, the lifetime prevalence for any anxiety disorder was 28.8 %, and the 12-month prevalence was 18.1 %. GAD has a 12-month prevalence of 3.1 % in the USA and a lifetime prevalence of 5.7 %–6.4 % in the USA and Europe. Women have a two- to threefold increased risk for GAD. For agoraphobia without PD, lifetime and 12-month prevalence rates are 1.4 % and 0.8 %, respectively; for PD, 4.7 % and 2.7 %; for specific phobia, 12 % and 6.8 %; and for seasonal affective disorder (SAD), 12.1 % and 6.8 %. Recently the 12-month prevalence for anxiety disorders within the European Union was estimated at 14.0 % with 61.5 Million individuals affected (Baldwin et al. 2014).

11.2.1 Comorbidity with Substance Use Disorders

Most studies on the association of anxiety disorders with substance use are cross-sectional, and a few are longitudinal (Robinson et al. 2011). Epidemiologic studies indicate a two- to threefold increased risk for alcohol use disorders in patients with

anxiety disorders. Grant et al. (2005) reported data from the National Epidemiologic Survey on Alcohol and Related Conditions, which studied a large representative sample ($N = 43{,}093$) of the adult US population. Prevalence estimates for 12-month and lifetime GAD were 2.1 % and 4.1 %, respectively. Higher rates were found for males. GAD was highly comorbid with substance use in general and with other anxiety, mood, and personality disorders. Specifically, the odds ratio (OR) for any alcohol use disorder was 2.0 for 12-month prevalence and 2.2 for lifetime prevalence. There are interesting and significant differences between comorbidity of anxiety disorders with harmful alcohol use and alcohol dependence. While the comorbidity with alcohol abuse was not increased in this study (ORs 1.0 and 1.1 for 12-month and lifetime prevalence, respectively), the ORs for alcohol dependence were significant (3.1 and 2.8, respectively). Similar results were found also for other drugs of abuse: Data indicate an association of GAD with dependence on nicotine or drugs but not with abuse of nicotine or drugs. The relationship was strongest for drugs (ORs 9.9 and 5.2, respectively). In addition, as demonstrated in previous studies there was also evidence for a strong association of GAD with other mood and anxiety disorders. Further analysis of the database from this study revealed marked sex differences: Men with GAD had significantly higher rates of comorbid alcohol and drug use disorders and reported greater use of alcohol and drugs to help relieve GAD symptoms.

Again, an association of alcohol dependence, but not harmful use, with anxiety disorders (and depression) was shown in a Dutch Study (Boschloo et al. 2011). This study included a sample of 2,329 people with lifetime DSM-IV anxiety disorders or depressive disorders or both and 652 controls. Prevalence rates for alcohol dependence in persons with combined anxiety/depression were 20.3 % (controls: 5.5 %). Prevalence of alcohol abuse was similar in all groups (about 12 %). A number of independent risk factors for alcohol dependence were identified: Male gender, vulnerability factors such as a family history of alcohol dependence or anxiety/depression, childhood trauma, smoking, drug dependence, and early onset of anxiety/depression. There is also some evidence that having a comorbid anxiety disorder is associated with increased substance use severity (Schneier et al. 2010).

The database is far less extensive for drug abuse. In a large national epidemiologic survey in the US, 12-month prevalence estimates were 1.4 % and lifetime prevalence rates 7.7 %, which clearly exceeded the rates of drug dependence (0.6 % and 2.6 %, respectively). Twelve-month prevalence for drug use disorders was associated with any anxiety disorder (OR 2.7); with any PD (OR 3.9; PD with agoraphobia: OR 5.6, without: OR 3.1); with social phobia, OR 2.6; with specific phobia, OR 2.3; and with GAD, OR 4.5. When adjusted for demographic characteristics and other psychiatric disorders, any anxiety disorder was associated with drug use disorders with an OR of 2.1, with drug abuse with an OR of 1.5, and with drug dependence with an OR of 2.8. For drug dependence, GAD had an OR of 2.5. These data correspond in part to studies in alcohol use disorders showing that drug dependence rather than abuse is associated with anxiety disorders, specifically GAD.

11.2.2 Course of Comorbidity

The chronological relationship between the onset of anxiety disorders and substance use disorders is complex. Substance-induced anxiety symptoms frequently occur during detoxification from alcohol or benzodiazepines or during intoxication with cannabis or psychostimulants (cocaine, amphetamine) but often improve or vanish within a few weeks. Long-term longitudinal studies in patients with anxiety disorders did not indicate an association of phobias with the onset of alcohol use disorders but rather a modest association between adult subclinical-specific phobias and later-onset alcohol use disorders (OR 3.2); the association was stronger in women than men. Zimmermann et al. (2003) reported 4-year follow-up data from a prospective community survey in 3,021 adolescents. Baseline social phobia and panic attacks significantly predicted subsequent alcohol problems in young adults. This chronological order has recently been confirmed in a longitudinal Dutch study showing that current anxiety disorder significantly predicted first incidence of alcohol dependence (Boschloo et al. 2013).

Flensborg-Madsen et al. (2011) examined the effects of alcohol intake (not alcohol use disorders) on the risk of psychiatric disorders. This prospective cohort study included participants from the Copenhagen City Heart Study ($N = 18{,}146$). Participants were followed for up to 26 years. Alcohol intake was measured by self-report, while psychiatric diagnoses were measured through registers. For women, drinking above sensible limits increased the risk for psychiatric disorders in general and especially for anxiety disorders (risk: 2.00). For men, a weekly low to moderate alcohol intake seemed to have a protective effect against developing a psychiatric disorder. Risk for anxiety disorders was lower in men drinking more than 14 drinks per week (OR 0.79). The authors claimed an "apparent protective effect" of alcohol among men as a sign of mental and social well-being and normal functioning.

Grant et al. (2009) studied sociodemographic and psychopathologic predictors of the first incidence of DSM-IV substance use and mood and anxiety disorders by examining data from the WAVE 2 National Epidemiologic Survey on Alcohol and Related Conditions. One-year incidence rates were highest for alcohol abuse (1.02), alcohol dependence (1.70), major depressive disorder (1.51), and GAD (1.12). Incidence rates were greater among men for substance use disorders and greater among women for mood and anxiety disorders, except bipolar disorder, and social phobia. Age was inversely related to all disorders. Interestingly, substance use disorders did not predict any incident mood or anxiety disorder, whereas baseline bipolar I predicted incident drug abuse and baseline PD predicted incident drug dependence. Although these results may be consistent with the self-medication hypothesis, other mechanisms such as shared liability arising from the same genetic or environmental risk factors cannot be excluded (2009).

Melchior et al. (2014) recently reported additional data from the US national Epidemiologic Survey on Alcohol and Related Conditions . Of 34,632 people included, 3.2 % had a diagnosis of lifetime illegal drug use disorder; 21.2 %, a comorbid mood disorder; 11.8 %, a comorbid anxiety disorder; and 45.9 %, comorbid mood and anxiety disorders. In contrast, recent data from the National

Comorbidity Survey of a nationally representative sample of the US adult population showed that substance dependence temporally precedes several anxiety disorders, particularly PD (OR 2.62, Goodwin and Stein 2013). The ORs for social phobia (OR 1.7) and agoraphobia (OR 1.78) were smaller. Conversely, the anxiety disorder appeared first in more than 50 % of substance use disorder cases, in nearly 40 % of PTSD cases, and in nearly 30 % of GAD cases. Similarly, a lifetime history of social phobia, PTSD, or GAD significantly predicts lifetime substance dependence (OR 1.51 for social phobia, 2.06 for PTSD, and 1.45 for GAD).

The database for drug use is more limited. Liang et al. (2011) performed a retrospective cohort study on data from the 2007 National Survey of Mental Health and Wellbeing (MHW) in 8,841 adult Australians. Previously, Teesson et al. (2009) had reported data from this study indicating that 19 % of males and 8 % of females with an anxiety disorder had a coexisting substance use disorder and 26 % of males and 11 % of females with an affective disorder had a coexisting substance use disorder. Overall prevalence for drug dependence was 2.56 %. Individuals with an affective disorder or anxiety disorder were at higher risk of harmful use and drug dependence (males: 9.3 %; females: 3.9 %). Again, the self-medication theory or common genetic factors were discussed to explain these findings.

11.2.3 Gender Issues

In general, substance use disorders are more prevalent in men, and anxiety disorders are more prevalent in women (Kessler et al. 2005). Women with substance use disorders are more likely to have a comorbid anxiety disorder than men (60.7 % versus 35 %, Kessler et al. 1997) There is some evidence that comorbid anxiety disorders complicate treatment of substance use in women. Farris et al. (2012) studied 260 women treated within an alcohol program and found that lifetime anxiety diagnosis was linked to poorer drinking outcomes post treatment, although women with comorbid anxiety disorders drank less than nonanxious patients before treatment.

11.3 Reasons for Comorbidity of Anxiety Disorders and Substance Use: Self-medication Theory

Community-based epidemiologic studies show a 2.2-fold greater risk for anxiety disorders among individuals with alcohol dependence than among the general population. The lifetime prevalence for anxiety disorders among alcoholics is 6–20 %. The risk is highest for social and specific phobias.

Self-medication or tension reduction has been discussed as a possible explanation for substance use in anxiety disorders (Robinson et al. 2011). The relaxing, tension- and stress-reducing, and sedating effects of alcohol in particular are well established. Short-term consumption of alcohol or benzodiazepines diminishes anxiety in patients with PD (Kushner et al. 1996). Although the chronological

relationship or primary–secondary distinction between the onset of anxiety symptoms and substance use varies considerably, many studies indicate that the onset of anxiety precedes substance use in many cases (Falk et al. 2008; Merikangas et al. 1998). This has been explained by means of cognitive processes and the expectancy of the drug's effect. In contrast, long-term use of alcohol and possibly other drugs may induce anxiety disorders. Substance use may worsen psychiatric symptoms (Schuckit and Hesselbrock 1994). Anxiety is a frequent symptom also in alcohol and drug withdrawal, but there is no clear experimental evidence for the induction of anxiety disorders by alcoholism. In SAD, clinical findings on the interrelationship with alcohol use are inconsistent. Finally, anxiety symptoms may be part of a protracted withdrawal syndrome, a still rather ill-defined syndrome. The empirical basis for this association is lacking.

Anxious patients may start to use alcohol or drugs to reduce anxiety and medicate their distress. Among individuals drawn from a nationally representative survey of US citizens ($N = 25{,}342$), only 20 % of anxious patients endorsed drinking to control anxiety symptoms. This subgroup of patients drank more alcohol, had a higher cross-sectional rate of alcohol dependence and was at a higher risk for developing new alcohol dependence over 4 years compared to anxious nonself-medicators.

An important study on the role of self-medication in the development of comorbid anxiety and substance use disorders was recently published by Robinson et al. (2011). This group performed a longitudinal, nationally representative survey in 34,653 adults in two waves (2001–2002 and 2004–2005). The National Epidemiologic Survey on Alcohol and Related Conditions assessed DSM-IV psychiatric disorders, self-medication, and sociodemographic variables. The main outcome measures were incident substance use disorders in participants with baseline anxiety disorders and incident anxiety disorders in those with baseline substance use disorders. Logistic regression analyses revealed that self-medication conferred a heightened risk of new-onset substance use disorders in those with baseline anxiety disorders (OR 2.50–4.99). Self-medication was associated with an increased risk of social phobia (adjusted odds ratio 2.13 in baseline alcohol use disorders and 3.17 in baseline drug use disorders). These results highlight the complex interrelationship between anxiety disorders and substance use. Self-medication in anxiety disorders confers a risk of incident substance use disorders and, conversely, self-medication in substance use disorders was found to be associated with incident social phobia.

Apart from social phobia, PD was the only other anxiety disorder that predicted self-medication. George et al. (1990) had already proposed that the use of alcohol may kindle or condition panic attacks.

Alcohol or drug use disorders may also cause or trigger anxiety. Anxiety and inner restlessness are frequent symptoms in alcohol or drug withdrawal. Repeated withdrawal syndromes may trigger or kindle anxiety disorders. This theory has not been studied in great detail. A number of molecular and epigenetic mechanisms may underlie anxiety disorders in substance using patients. The amygdala is the most relevant key structure mediating the genetic predisposition to anxiety and alcoholism.

Finally, anxiety and substance use disorders share some common causes. For example, sexual abuse and childhood trauma can constitute a risk for both. Animal studies indicate a genetic linkage between anxiety disorders and alcohol use disorders. A family history of alcoholism seems to be associated with alcohol and anxiety disorders in offspring.

11.4 Prevention and Therapy

Anxiety and substance use disorders usually start in adolescence or early adulthood, although onset is not restricted to this age. Prevention strategies, which include early diagnosis and intervention, should be aimed at younger individuals. As to adult populations, Boschloo et al. (2013) stress the importance of addiction prevention strategies for anxious patients in mental health settings. Of importance in their longitudinal study they found that in addition to an anxiety disorder diagnosis, subthreshold alcohol problems and recent negative life events also, independently, predicted alcohol dependence incidence, a finding providing some clinical characteristics that might help to identify persons at an increased risk for developing alcohol dependence.

Treatment-seeking in dual disorder patients is rather low, but it increases with the severity of personal problems related to substance use and is highest in those with anxiety and depression. Studies have found that individuals with a comorbid anxiety and substance use disorder have a poorer treatment response and outcome, have more personal and social problems and impairment and generate greater costs than other patients (Farris et al. 2012; Kushner et al. 1996); however, not all studies came to the same conclusions (Marquenie et al. 2006).

In some cases, anxiety symptoms decrease after detoxification, and no specific treatments are necessary (Hintz and Mann 2005; Schuckit and Hesselbrock 1994). Persisting anxiety disorders are associated with a less favorable outcome. Schellekens et al. (2014) recently studied 189 alcoholic men prospectively recruited from an inpatient detoxification clinic. Comorbid anxiety disorders were associated with a higher risk for relapse, among others.

A number of psychological interventions have been studied and shown efficacy in anxiety disorders in general including exposure therapy, cognitive therapy, and cognitive–behavioral therapy (Baldwin et al. 2014). The first step is often some form of psychoeducation and information about the diagnosis, etiology, and treatment options.

Persisting anxiety disorders independent from substance use should be treated with psychotherapy. Exposure therapy (usually in the form of gradual exposure in vivo, but also performed as "flooding") and response prevention are very effective in specific phobias, SAD, and agoraphobia. In this treatment setting, patients are usually confronted with a feared situation, for example, using an underground train in agoraphobia or imagining and nearing a feared animal. Cognitive–behavioral treatment approaches have been proposed for panic attacks and other symptoms that cannot be treated with exposure. The efficacy of

cognitive–behavioral therapy (CBT) across anxiety disorders was shown in a large meta-analysis of 108 studies (Norton and Price 2007). CBT is based on cognitive models emphasizing the role of worrying, metacognitions, and avoidance behavior. A more recent review of meta-analytic findings confirmed the efficacy of CBT also in anxiety disorders, although few of these studies included a placebo condition (Olatunji et al. 2010). For anxiety disorders, studies comparing CBT with a wait-list control group found significantly larger effect sizes than those comparing CBT with an attention placebo. The evidence for psychodynamic therapies in anxiety disorders is very limited. Both individual and group therapies are used in anxiety disorders.

Psychological interventions in comorbid anxiety and substance use disorders have not been studied in great detail. The basic question is whether to address one disorder or the other or to offer integrated treatment programs. Schade et al. (2005) reported results of a randomized controlled trial in 96 abstinent alcohol-dependent patients with comorbid social phobia or agoraphobia who were treated with an intensive 32-week psychosocial relapse-prevention program alone or in combination with CBT for anxiety and an optional selective serotonin reuptake inhibitor. In this study, additional anxiety therapy improved anxiety symptoms but not alcohol relapse rates. Avants et al. (1998) studied outpatient methadone maintenance patients who received either case management plus CBT (MA-) or case management plus an intensive manualized program (MAplus) and subdivided patients into groups on the basis of the severity of their social anxiety (severe and mild). The more severely affected patients were more often abstinent from heroin and showed a stronger decrease in anxiety symptoms and less risk behavior when participating in the MA-group, while there were no differences between MA-patients. The authors suggested that SAD patients in a methadone program might benefit more from less intensive programs.

Ballie and Sannibal (2007) reviewed six randomized controlled trials of treatment for comorbid anxiety and substance use disorder. They concluded that for patients with more than moderate substance dependence there is clear and consistent evidence that standard treatment for substance use disorders has the best outcomes. Treating anxiety first and "removing self-medication rationalizations" for drinking was considered to be a rational approach in many dual disorder patients and to perhaps lead to greater treatment compliance when focusing on alcohol. Special CBT approaches to reduce the expectancies for tension reduction from alcohol may help to reduce anxiety symptoms.

A smaller ($N = 55$) but randomized Norwegian study recently showed that integrated treatment in patients with substance use disorders co-occurring with anxiety and/or depression compared to treatment as usual increased motivation for substance use treatment after 12 months significantly in the intervention group, while substance use was decreased in both groups (Wüsthoff et al. 2014). In the intervention group, therapists were trained in motivational interviewing and CBT.

Numerous pharmacological agents are used for the treatment of anxiety disorders including many antidepressants (Baldwin et al. 2014). Benzodiazepines can be given for acute symptoms but caution is warranted for longer treatment,

especially in dual disorder patients. For a more indepth review of the pharmacological treatment of anxiety and SUD the reader is referred to Chap. 19.

Conclusion

In conclusion, the comorbidity of anxiety and substance use disorders is high. Anxiety symptoms may decline after detoxification. Persisting anxiety disorders are of prognostic relevance and should be addressed in comprehensive treatment settings.

References

Avants SK, Margolin A, Kosten TR, Rounsaville BJ, Schottenfeld RS (1998) When is less treatment better? The role of social anxiety in matching methadone patients to psychosocial treatments. J Consult Clin Psychol 66(6):924–931

Baldwin DS et al (2014) Evidence-based pharmacological treatment of anxiety disorders, post-traumatic stress disorder and obsessive-compulsive disorder: a revision of the 2005 guidelines from the British Association for Psychopharmacology. J Psychopharmacol 28(5):403–439

Ballie A, Sannibal C (2007) Anxiety and drug and alcohol problems. In: Baker A, Velleman R (eds) Clinical handbook of co-existing mental health and drug and alcohol problems. Routledge, London, pp 197–217

Bandelow B, Zohar J, Hollander E, Kasper S, Moller HJ, Allgulander C, Vega J (2008) World Federation of Societies of Biological Psychiatry (WFSBP) guidelines for the pharmacological treatment of anxiety, obsessive-compulsive and post-traumatic stress disorders—first revision. World J Biol Psychiatry 9(4):248–312. doi:10.1080/15622970802465807

Bishop S, Duncan J, Brett M, Lawrence AD (2004) Prefrontal cortical function and anxiety: controlling attention to threat-related stimuli. Nat Neurosci 7(2):184–188. doi:10.1038/nn1173

Boschloo L, Vogelzangs N, Smit JH, van den Brink W, Veltman DJ, Beekman AT, Penninx BW (2011) Comorbidity and risk indicators for alcohol use disorders among persons with anxiety and/or depressive disorders: findings from the Netherlands Study of Depression and Anxiety (NESDA). J Affect Disord 131(1–3):233–242. doi:10.1016/j.jad.2010.12.014

Boschloo L, Vogelzangs N, van den Brink W, Smit JH, Veltman DJ, Beekman AT, Penninx BW (2013) Depressive and anxiety disorders predicting first incidence of alcohol use disorders: results of the Netherlands Study of Depression and Anxiety (NESDA). J Clin Psychiatry 74(12):1233–1240. doi:10.4088/JCP.12m08159

Brady KT, Sinha R (2005) Co-occurring mental and substance use disorders: the neurobiological effects of chronic stress. Am J Psychiatry 162(8):1483–1493. doi:10.1176/appi.ajp.162.8.1483

Enquist J, Ferwerda M, Madhavan A, Hok D, Whistler JL (2012) Chronic ethanol potentiates the effect of neuropeptides in the basolateral amygdala and shows increased anxiolytic and antidepressive effects. Neuropsychopharmacology 37(11):2436–2445. doi:10.1038/npp.2012.102

Falk DE, Yi HY, Hilton ME (2008) Age of onset and temporal sequencing of lifetime DSM-IV alcohol use disorders relative to comorbid mood and anxiety disorders. Drug Alcohol Depend 94(1–3):234–245. doi:10.1016/j.drugalcdep.2007.11.022

Farris SG, Epstein EE, McCrady BS, Hunter-Reel D (2012) Do co-morbid anxiety disorders predict drinking outcomes in women with alcohol use disorders? Alcohol Alcohol 47(2):143–148. doi:10.1093/alcalc/agr155

Flensborg-Madsen T, Becker U, Gronbaek M, Knop J, Sher L, Mortensen EL (2011) Alcohol consumption and later risk of hospitalization with psychiatric disorders: prospective cohort study. Psychiatry Res 187(1–2):214–219. doi:10.1016/j.psychres.2010.11.016

George DT, Nutt DJ, Dwyer BA, Linnoila M (1990) Alcoholism and panic disorder: is the comorbidity more than coincidence? Acta Psychiatr Scand 81(2):97–107

Goodwin RD, Stein DJ (2013) Anxiety disorders and drug dependence: evidence on sequence and specificity among adults. Psychiatry Clin Neurosci 67(3):167–173. doi:10.1111/pcn.12030

Grant BF, Goldstein RB, Chou SP, Huang B, Stinson FS, Dawson DA, Compton WM (2009) Sociodemographic and psychopathologic predictors of first incidence of DSM-IV substance use, mood and anxiety disorders: results from the Wave 2 National Epidemiologic Survey on Alcohol and Related Conditions. Mol Psychiatry 14(11):1051–1066. doi:10.1038/mp.2008.41

Grant BF, Hasin DS, Stinson FS, Dawson DA, June Ruan W, Goldstein RB, Huang B (2005) Prevalence, correlates, co-morbidity, and comparative disability of DSM-IV generalized anxiety disorder in the USA: results from the National Epidemiologic Survey on Alcohol and Related Conditions. Psychol Med 35(12):1747–1759. doi:10.1017/S0033291705006069

Hintz T, Mann K (2005) Comorbidity in alcohol use disorders: focus on mood, anxiety and personality. In: Rössler W, Stohler R (eds) Dual diagnosis. The evolving conceptual framework. Karger, Basel, pp 65–91

Kessler RC, Chiu WT, Demler O, Merikangas KR, Walters EE (2005) Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. Arch Gen Psychiatry 62(6):617–627. doi:10.1001/archpsyc.62.6.617

Kessler RC, Crum RM, Warner LA, Nelson CB, Schulenberg J, Anthony JC (1997) Lifetime co-occurrence of DSM-III-R alcohol abuse and dependence with other psychiatric disorders in the National Comorbidity Survey. Arch Gen Psychiatry 54(4):313–321

Kushner MG, Mackenzie TB, Fiszdon J, Valentiner DP, Foa E, Anderson N, Wangensteen D (1996) The effects of alcohol consumption on laboratory-induced panic and state anxiety. Arch Gen Psychiatry 53(3):264–270

Liang W, Chikritzhs T, Lenton S (2011) Affective disorders and anxiety disorders predict the risk of drug harmful use and dependence. Addiction 106(6):1126–1134. doi:10.1111/j.1360-0443.2011.03362.x

Marmorstein NR, Iacono WG, Malone SM (2010) Longitudinal associations between depression and substance dependence from adolescence through early adulthood. [Research Support, N.I.H., Extramural]. Drug Alcohol Depend 107(2–3):154–160. doi:10.1016/j.drugalcdep.2009.10.002

Marquenie LA, Schade A, Van Balkom AJ, Koeter M, Frenken S, van den Brink W, van Dyck R (2006) Comorbid phobic disorders do not influence outcome of alcohol dependence treatment. Results of a naturalistic follow-up study. Alcohol Alcohol 41(2):168–173. doi:10.1093/alcalc/agh252

Melchior M, Prokofyeva E, Younès N, Surkan PJ, Martins SS (2014) Treatment for illegal drug use disorders: the role of comorbid mood and anxiety disorders. BMC Psychiatry 14:89. doi:10.1186/1471-244X-14-89

Merikangas KR, Mehta RL, Molnar BE, Walters EE, Swendsen JD, Aguilar-Gaziola S, Kessler RC (1998) Comorbidity of substance use disorders with mood and anxiety disorders: results of the International Consortium in Psychiatric Epidemiology. Addict Behav 23(6):893–907

Merikangas KR, Zhang H, Avenevoli S, Acharyya S, Neuenschwander M, Angst J (2003) Longitudinal trajectories of depression and anxiety in a prospective community study: the Zurich Cohort Study. Arch Gen Psychiatry 60(10):993–1000. doi:10.1001/archpsyc.60.9.993

Norton PJ, Price EC (2007) A meta-analytic review of adult cognitive-behavioral treatment outcome across the anxiety disorders. J Nerv Ment Dis 195(6):521–531

Olatunji BO et al (2010) Efficacy of congnitive behavioural therapy for anxiety disorders: a review of meta-analytic findings. J Psychiatr 33:517–577

Robinson J, Sareen J, Cox BJ, Bolton JM (2011) Role of self-medication in the development of comorbid anxiety and substance use disorders: a longitudinal investigation. [Research Support, Non-U.S. Gov't]. Arch Gen Psychiatry 68(8):800–807. doi:10.1001/archgenpsychiatry.2011.75

Schade A, Marquenie LA, van Balkom AJ, Koeter MW, de Beurs E, van den Brink W, van Dyck R (2005) The effectiveness of anxiety treatment on alcohol-dependent patients with a comorbid phobic disorder: a randomized controlled trial. Alcohol Clin Exp Res 29(5):794–800

Schellekens AF, de Jong CA, Buitelaar JK, Verkes RJ (2014) Co-morbid anxiety disorders predict early relapse after inpatient alcohol treatment. Eur Psychiatry. doi:10.1016/j.eurpsy.2013.08.006

Schneier FR, Foosel TE, Hasin DS et al (2010) Social anxiety disorder and alcohol use disorder co-morbidity in the National Epidemiologic Survey on Alcohol and related Conditions. Psychol Med 40:977–988

Schuckit MA, Hesselbrock V (1994) Alcohol dependence and anxiety disorders: what is the relationship? Am J Psychiatry 151(12):1723–1734

Teesson M, Slade T, Mills K (2009) Comorbidity in Australia: findings of the 2007 National Survey of Mental Health and Wellbeing. [Research Support, Non-U.S. Gov't]. Aust N Z J Psychiatry 43(7):606–614. doi:10.1080/00048670902970908

Wüsthoff LE, Waal H, Gråwe RW (2014) The effectiveness of integrated treatment in patients with substance use disorders co-occurring with anxiety and/or depression–a group randomized trial. BMC Psychiatry 14:67. doi:10.1186/1471-244X-14-67

Yang H, Devous MD, Briggs RW, Spence JS, Xiao H, Kreyling N, Adinoff B (2013) Altered neural processing of threat in alcohol-dependent men. Alcohol Clin Exp Res 37(12):2029–2038. doi:10.1111/acer.12187

Yong W, Spence JP, Eskay R, Fitz SD, Damadzic R, Lai D, Liang T (2014) Alcohol-preferring rats show decreased corticotropin-releasing hormone-2 receptor expression and differences in HPA activation compared to alcohol-nonpreferring rats. Alcohol Clin Exp Res 38(5):1275–1283. doi:10.1111/acer.12379

Zimmermann P, Wittchen HU, Hofler M, Pfister H, Kessler RC, Lieb R (2003) Primary anxiety disorders and the development of subsequent alcohol use disorders: a 4-year community study of adolescents and young adults. Psychol Med 33(7):1211–1222

Posttraumatic Stress Disorders and Addiction

12

Ingo Schäfer and Willemien Langeland

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Abstract

Disorders related to stress or trauma are common among patients with substance use disorders (SUD). In clinical samples of patients with SUD, the prevalence of lifetime Posttraumatic Stress Disorder (PTSD) ranges from 26 % to 52 %, and from 15 % to 41 % for current PTSD. A substantial number of these patients suffer from the consequences of severe and prolonged interpersonal trauma usually referred to as "Complex PTSD". Another common consequence of repeated interpersonal trauma in childhood are dissociative symptoms that may or may not co-occur with PTSD in SUD patients. While several hypotheses can explain the relationships between SUD and PTSD, the self-medication hypothesis has the strongest empirical support. Patients with both disorders have a more severe clinical profile than SUD patients without PTSD, poorer adherence to treatment, a shorter duration of abstinence, and worse outcomes across a variety of measures. Their clinical needs often make a treatment approach necessary that integrates SUD specific and trauma specific interventions. Several trauma treatments focusing on the present (i.e. providing skills training and psycho-education) and, more recently, also past-focused (i.e. exposure-based) treatments have been evaluated in SUD patients with co-occurring PTSD. Some of them outperformed SUD treatment-as-usual on PTSD and/or substance use outcomes. Findings on the effects of medication in patients with SUD and co-occurring PTSD are scarce and remain inconclusive.

12.1 Introduction

Trauma or stress-related disorders, especially Posttraumatic Stress Disorder (PTSD), have become one of the best-researched comorbidities in the field of substance abuse. What these disorders have in common is a history of trauma exposure. Patients with substance use disorders (SUD) report extensively high numbers of traumatic experiences. The majority of these patients was not traumatised by one discreet incident, such as a car accident, a rape, or a criminal assault, but was repeatedly exposed to traumatic stressors and many are still exposed to ongoing victimisation. Most patients report traumatic events in childhood, such as sexual and physical abuse, which can be followed by further experiences of interpersonal violence over the lifespan, often perpetuated by their ongoing substance abuse.

Traumatic exposure may be followed by a variety of clinical presentations grouped as posttraumatic stress disorders that are seen as a spectrum of disorders. The mental health consequences of traumatic experiences are of importance for both the development of SUD and for their course and outcome. In this chapter we will briefly outline the diagnostic criteria for trauma spectrum disorders. We will give an overview of findings related to their prevalence among patients with SUD,

potential relationships between both groups of disorders, and clinical aspects, including evidence-based treatments for patients with this comorbidity. Given the large volume of literature on trauma and posttraumatic stress disorders, we restrict the term *trauma* to events that satisfy PTSD Criterion A according to DSM-5. Moreover, we focus on relationships between SUD and posttraumatic stress disorders rather than on trauma per se.

12.2 Posttraumatic Stress Disorder and Other Trauma-Related Disorders

Fortunately, many individuals show resilient responses to severe stress and potentially traumatic events. In a substantial number of people, however, these experiences lead to the development of posttraumatic stress disorders. The spectrum or continuum of trauma-related disorders includes Acute Stress Disorder (ASD), Posttraumatic Stress Disorder (PTSD), and reactions that typically arise from severe and prolonged experiences of interpersonal trauma that often begin already early in life, usually referred to as "Complex PTSD". There is some overlap between this construct and the "dissociative subtype of PTSD" that has recently been included in DSM-5. Finally, high levels of dissociative symptoms, also in the absence of PTSD, and Dissociative Disorders are in most cases a consequence of early and complex trauma. In this short overview we will focus on the more severe clinical conditions (complex) PTSD and Dissociative Disorders.

12.2.1 Posttraumatic Stress Disorder

The most common diagnosis in the field of trauma-related disorders is Posttraumatic Stress Disorder (PTSD). A diagnosis of PTSD requires exposure to a traumatic event in which a person experiences or witnesses (an) event(s) that involves real or threatened bodily harm (DSM-5 American Psychiatric Association 2013). In DSM-IV, PTSD was defined by three trauma symptom clusters: *intrusions* (recurrent and intrusive distressing trauma memories including images, perceptions, thoughts, flashbacks and distressing dreams of the event, and a numbing of general responsiveness), *avoidance* (avoiding reminders of past trauma, an inability to recall an important aspect of the trauma, a diminished interest in significant activities, detachment from others, a restricted sense of affect, and a sense of foreshortened future), and *hyperarousal and hypervigilance* (sleeping difficulties, irritability, inability to concentrate, and exaggerated startle responses). To meet full criteria for a diagnosis of PTSD, the individual must experience symptoms for at least 1 month (after 3 months "chronic PTSD") and the symptoms must cause clinically significant distress or impairment in social, occupational, or other areas of functioning. In DSM-5, the 3 clusters of DSM-IV symptoms are divided into 4 clusters: *intrusions*, *avoidance*, *negative alterations in cognitions and mood* (persistent and distorted blame of self or others, persistent negative emotional

state) and *alterations in arousal and reactivity* (also including reckless or destructive behaviour). All of these symptoms may aggravate the clinical picture of traumatised SUD patients and interfere with treatment for substance abuse.

Research has clearly shown that the diagnosis of PTSD does not encompass the entirety of mental health consequences of trauma exposure, especially after repeated traumatisation and early adverse experiences prior to the onset of PTSD. As a consequence a "dissociative subtype of PTSD" has been included in DSM-5. Compared to individuals with PTSD alone (simple PTSD), patients with a diagnosis of the dissociative subtype of PTSD have higher levels of psychiatric comorbidity, especially comorbid personality disorders, increased functional impairment and increased suicidality. There is some overlap between this new subtype of PTSD in DSM-5 and the concept of "Complex PTSD" that has been proposed for ICD-11.

12.2.2 Complex PTSD

After repeated interpersonal traumatic experiences in childhood, PTSD symptoms may be complicated by sustained and pervasive disturbances in emotion regulation, in the experience of a diminished and defeated sense of self, altered systems of meaning, and in difficulties maintaining relationships. This syndrome has been labelled "PTSD with associated features" in DSM-IV-TR and "PTSD with personality change" in ICD-10 and is known by clinicians as "complex PTSD" or "Disorders of Extreme Stress Not Otherwise Specified (DESNOS)". It has now been proposed to officially include this diagnosis into the section on disorders specifically related to trauma and stress in ICD-11 (Maercker et al. 2013). In addition to the three core elements of PTSD, the proposed diagnosis includes enduring disturbances in the domains of affect, self, and interpersonal relationships. It is assumed that Complex PTSD is distinguishable from personality disorders by its restricted symptom profile and its responsiveness to specific treatments that differ from those for personality disorders and from those for PTSD.

The recognition of the range of interrelated problems associated with a history of early severe interpersonal trauma is an important development with much relevance for the field of substance abuse. Complex PTSD may interfere with engagement in treatment, participation in and learning from structured treatment activities, and with the ability to inhibit substance cravings and impulsive substance-seeking behaviours while sustaining substance-free relationships, and relapse prevention behaviours.

12.2.3 Dissociative Disorders

Another common consequence of repeated interpersonal trauma in childhood are high levels of dissociative symptoms and, at the more extreme end of this symptom spectrum, dissociative disorders. According to the DSM-IV (APA 1994), the essential feature of dissociation is a disruption of the normal integrative functions

of consciousness, memory, identity, and perception of the environment. DSM-IV recognises five distinct dissociative disorders, i.e. dissociative amnesia, dissociative fugue, dissociative identity disorder (DID), and depersonalization disorder as well as atypical dissociative disorders (i.e. dissociative disorder not otherwise specified; DDNOS). The DSM-5 classification reduces the number of these disorders by including dissociative fugue as specifier of dissociative amnesia rather than a separate diagnosis. Derealisation is included in the name and symptom structure of what was previously called depersonalisation disorder and is now called depersonalisation/derealisation disorder. Moreover, several changes to the criteria for dissociative identity disorder have been made: Certain possession-form phenomena and functional neurological symptoms to account for more diverse presentations of the disorder have been included; symptoms of disruption of identity may now be reported as well as observed; and gaps in the recall of events may occur for everyday events, not just for traumatic events.

Dissociative symptoms or disorders can, in the same way as simple and complex PTSD, aggravate the clinical picture of traumatised SUD patients and interfere with treatment for substance abuse. Dissociative symptoms or disorders can aggravate the clinical picture of traumatised SUD patients and interfere with treatment for substance abuse in the same way as simple and complex PTSD can.

12.3 Prevalence of the Dual Disorder of SUD and Posttraumatic Stress Disorders

12.3.1 SUD in Individuals with Posttraumatic Stress Disorders

Among people with lifetime PTSD, lifetime SUD is estimated at 21–43 %, compared to 8–25 % in those without PTSD (Jacobsen et al. 2001). According to US population data, among women who experience PTSD in their lifetime, 28 % develop an alcohol use disorder and 27 % develop a drug use disorder. Among men, 52 % and 35 % respectively, develop an alcohol or drug use disorder (Kessler et al. 1995). In a population-based study from Australia (Mills et al. 2006), 34 % of those with PTSD also had a substance use disorder, most commonly an alcohol use disorder (24 %). Even higher rates are found in clinical populations. For example, up to 75 % of combat veterans with lifetime PTSD also meet criteria for lifetime alcohol abuse or dependence (Jacobsen et al. 2001). In a study among women presenting for treatment with Complex PTSD and other severe consequences of childhood sexual abuse, one-third of the participants (33 %) had a lifetime history of substance abuse (Levitt and Cloitre 2005). And up to 59 % of patients with dissociative disorders also meet criteria for alcohol dependence (Langeland et al. 2005).

12.3.2 Posttraumatic Stress Disorders in Individuals with SUD

Conversely, the prevalence of PTSD is markedly elevated among individuals with SUD. In clinical SUD samples, the prevalence of lifetime PTSD ranges from 26 % to 52 % and from 15 % to 41 % for current PTSD (Schäfer and Najavits 2007). These rates are considerably higher than those observed in general population surveys where rates of current PTSD usually do not exceed 9 %. The prevalence of PTSD varies per sample. For example, current PTSD is more prevalent in females than in males—typically about twice the rate (e.g. Dom et al. 2007; Driessen et al. 2008). Moreover, some substances of abuse show a higher association with PTSD than others (e.g. "harder drugs" and polydrug use compared to alcohol or cannabis). In European samples, the prevalence of current PTSD among treatment seeking alcohol dependent patients was 15–25 % (e.g. Driessen et al. 2008; Schäfer et al. 2007), while the prevalence among patients with (additional) drug dependence was 29–36 % (Driessen et al. 2008).

As the diagnosis of complex PTSD (ICD-11) or a dissociative subtype (DSM-5) is just about to be included in the diagnostic systems, no studies using these categories in SUD patients exist so far. A wealth of studies, however, indicates that SUD patients reporting early and complex trauma (i.e. chronic exposure or exposure to different forms of childhood interpersonal trauma) suffer from characteristics of these diagnoses including disturbances in emotion regulation, interpersonal problems, altered sense of self, and chronic suicidality (Hien et al. 2005).

The few studies on the prevalence of dissociative disorders in patients with SUD need to be interpreted with care. A study from Turkey using the Structured Clinical Interview for DSM-IV dissociative disorders reported a current prevalence rate of 17 % (Karadag et al. 2005), others reported even higher rates. It has been proposed that lower levels of dissociative symptoms (and probably also dissociative disorders) are found in alcohol-dependent patients as compared to patients with drug use disorders (for overviews see Langeland et al. 2005; Schäfer et al. 2007). This was confirmed in a study among a larger sample of patients with different SUD where higher levels of dissociation were observed in patients with (additional) drug dependence as compared to patients with mere alcohol dependence (Schäfer et al. 2010). However, when severity of traumatic events in childhood, PTSD, age and gender were included in the analysis, the influence of the type of substance abuse did not prove to be statistically significant. The variable most strongly related to dissociative symptoms was severity of traumatic events in childhood, in particular emotional abuse, even after controlling for PTSD and other potential confounders.

12.4 Relationships Between Posttraumatic Stress Disorders and SUD

The question of pathways or mechanisms is crucial for understanding the relationship between trauma exposure, posttraumatic stress disorders, and substance use disorders (e.g. Hien et al. 2005). A better understanding of pathways from trauma to addiction and the complex symptom interplay that exists between trauma-related disorders and SUD can inform interventions addressing trauma and substance abuse. Four predominant hypotheses have been proposed to explain the ways in which PTSD or other trauma-related disorders often co-occur with SUD:

1. Self-medication hypothesis: Individuals with trauma-related symptoms use substances to control their emotional pain.
2. High-risk hypothesis: Substance use, drug use in particular, is a high-risk behaviour leading to a lifestyle that increases the risk for trauma exposure.
3. Susceptibility hypothesis: Substance users, drug users in particular, are more susceptible to PTSD or other trauma-related disorders following exposure to traumatic events.
4. Third factor hypothesis: There is no direct relationship, but the association appears because both conditions derive from a third common factor, such as genetics (influence of other variables).

Figure 12.1 depicts a model to explain ways in which posttraumatic stress disorders could lead to addiction problems.

While these models are not mutually exclusive, the self-medication model is the model with the strongest empirical support. Findings supporting the self-medication

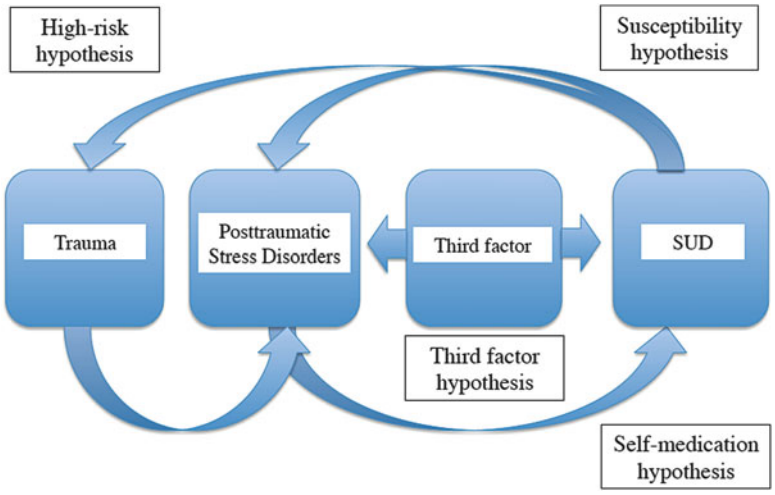

Fig. 12.1 Relationships between posttraumatic stress disorders and SUD

model come from different types of studies. A frequent approach is to compare the motivation for using substances in SUD patients with and without PTSD. In many studies, greater use of substances in patients with co-occurring PTSD was associated with situations involving unpleasant emotions, physical discomfort and interpersonal conflicts compared to situations involving pleasant or neutral situations. Similar associations were found between PTSD status and reasons for relapse in recently abstinent patients. In a series of laboratory studies, Coffey and colleagues found that clients who were alcohol and cocaine dependent with a comorbid diagnosis of PTSD reported greater drug and alcohol craving following the presentation of trauma-related stimuli as compared to neutral stimuli, and that PTSD severity was predictive of craving elicited by trauma-related stimuli and drug-related stimuli (Coffey et al. 2002). Moreover, alcohol craving and distress in response to trauma images decreased in patients receiving six sessions of trauma-focused imaginal exposure, but did not change in control patients (Coffey et al. 2002).

12.5 Clinical Aspects and Relationships with Outcome

12.5.1 Clinical Differences in Patients with PTSD

Patients with both PTSD and SUD have a more severe clinical profile than patients with SUD only, especially when trauma occurred early in their lives (see Schäfer and Najavits 2007). They have earlier onset of substance abuse and more years of problematic use, they report more polydrug use, and they have greater severity of current substance use. Patients with SUD and co-occurring PTSD also report worse physical health, lower well-being, and more interpersonal problems. Finally, patients with both disorders are more likely to meet criteria for additional psychiatric disorders, especially major depression and anxiety disorders (Langeland et al. 2004). Large epidemiological surveys also find high rates of other co-occurring disorders among those with PTSD and SUD. In one such study (Mills et al. 2006), almost two-thirds of those with PTSD and SUD had an additional affective disorder, and about half had a comorbid anxiety disorder. Personality disorders were also highly prevalent (62 %). All of these disorders were significantly more frequent in individuals with PTSD and SUD as compared to those with SUD alone or neither disorder. Also, consistent with findings from clinical studies, individuals with PTSD and SUD experienced poorer physical health and greater disability than those with SUD alone.

In addition to worse physical health and more psychiatric comorbidity, patients with complex PTSD present the typical manifestations of this disorder. They suffer from impulsivity and suicidal ideation, self-destructive behaviour, and vulnerability to revictimisation (Hien et al. 2005).

12.5.2 Treatment Utilisation and Outcome

Studies on the relationship between a history of trauma and treatment utilisation in patients with SUD are inconclusive. In a large sample of German outpatients with alcohol dependence, a history of sexual violence was related to higher use of SUD services in female but not in male victims (Schäfer et al. 2009). Victims of both genders were significantly younger at first contact with addiction treatment. Other authors reported that patients with a history of childhood sexual abuse seek less treatment for SUD, at least in institutional contexts (e.g. Peltan and Cellucci 2011). Simpson (2002) reported that with greater severity of childhood sexual abuse, the number of treatments for mental health problems increased, yet the number of substance abuse treatment episodes decreased. She suggested that there may not be a consistent relationship between childhood trauma and SUD treatment utilisation because of the relationship between traumatic experiences and utilisation of other services. While several studies reported a poorer outcome of treatment in patients with a history of childhood trauma (see Schäfer et al. 2009) others could not confirm this relationship. Recently contingency management (Petry et al. 2011) and self-help approaches (Makin-Byrd et al. 2011) have even been reported to have a higher efficacy in SUD patients with abuse histories. With regard to contingency management, one potential mechanism could be that this approach is especially effective in patients with more severe psychopathology, which is often the case in victims of sexual abuse (Petry et al. 2011).

In accordance with the findings among patients with other co-occurring disorders, there seems to be a relatively high lifetime utilisation rate of SUD services in substance abuse patients with PTSD (e.g. Najavits et al. 2004). When they engage in SUD treatment, patients with co-occurring PTSD have a poorer adherence to treatment than patients without the disorder, a shorter duration of abstinence, and worse outcomes across a variety of measures (Schäfer and Najavits 2007). Ouimette et al. (2003) conducted a 5-year follow-up study on one hundred male patients with co-occurring PTSD who attended SUD treatment. Patients who received PTSD treatment in the first 3 months following discharge and those who received treatment for a longer duration in the first year were more likely to be remitted 5 years later. The importance of treating symptoms of PTSD in SUD patients is further supported by studies showing that reductions of PTSD severity during treatment were likely to be associated with substance use improvement whereas substance use symptom reduction had little impact on symptoms of PTSD (e.g. Hien et al. 2010a, b). While the negative influence of comorbid PTSD on treatment outcome is clear, more research is needed on other potential factors. For instance, SUD patients with and without comorbid PTSD are also known to differ on other proximal determinants of treatment response, such as social support and coping strategies.

12.6 Assessment

The substantial prevalence rates of traumatic events among individuals with SUD point to the need to assess those entering substance abuse treatment programmes for traumatic experiences and trauma-related disorders. Asking if trauma has occurred can give clients a meaningful context to understand their behaviours and can empower them to search for and find the kind of help that best suits them. Many professionals, however, hesitate to assess for traumatic experiences and identify trauma-related disorders in their clients. The reasons include insufficient training, discomfort to ask about traumatic events, a high caseload, and fears that inquiring about trauma could cause harm to patients. With regard to the latter point, it is important to note that asking if a traumatic event has occurred and assessing its impact is not the same as opening up and exploring the trauma in detail, which should only be done by clinicians with more advanced training. If the difference between asking about trauma for screening and going into detail and "unpack" the trauma is clearly explained to the client, screening for trauma can be performed safely. When asking about trauma, especially about childhood abuse, it is essential to ask specific questions with clear examples, for instance "When you were a child, did an adult ever hurt or punish you in a way that left bruises, cuts or scratches?" or "When you were a child, did anyone ever do something sexual that made you feel uncomfortable?" (Read et al. 2007). Other principles of asking for trauma and responding to disclosures of trauma can be found in Box 12.1.

Box 12.1. Principles of asking and responding (mod. from Read et al. 2007)

Principles of Asking for Trauma

- Ask all clients/patients
- At initial assessment (or if in crisis, as soon as person is settled)
- In context of a general psychosocial history
- Preface with brief normalising statement
- Use specific questions with clear examples of what you are asking about
- Do not gather all the details, stop client empathetically if necessary

Principles of Responding to Disclosures of Trauma

- Affirm that it was a good thing to tell
- Offer support (make sure you know what is available)
- Ask whether the client relates the abuse to their current difficulties
- Check current safety—from on-going abuse
- Check emotional state at end of session
- Offer follow-up/"check-in"

With regard to the consequences of trauma, clinicians should consider the full context of a patient's presentation when formulating their diagnosis. The diagnosis of PTSD may be appropriate in some cases, but not all, especially not in the aftermath of early traumatisation. Despite the evidence that a majority of women and many men who are seeking treatment for addictions have been exposed to early and multiple traumatic experiences, standard treatment programmes do not typically assess or target the associated impairments of PTSD, which greatly complicates the prognosis. In practice, integrating interventions that specifically target the associated features are often recommended for these patients.

For most types of assessments (screening tools, questionnaires, and interviews) there is good evidence that they are also valid and reliable in individuals with SUD (for overview see Winters et al. 2014). However, if patients are assessed when actively using substances or during the period of detoxification, the cut-scores of some measures, especially self-rating measures of PTSD and dissociation, need to be adapted. While PTSD symptoms and dissociative symptoms can decrease or increase during detoxification, it has been suggested that major changes in symptoms should be completed within two weeks after termination of active use. Nevertheless, it remains difficult to determine the exact effects of withdrawal or comorbid psychopathology on self-rating instruments. Symptoms of PTSD and dissociation should therefore be assessed repeatedly in the course of treatment to enhance the diagnostic validity. Moreover, it is recommended to give preference to diagnostic interviews over self-ratings. The gold standard for PTSD assessment is the *Clinician-Administered PTSD Scale* (CAPS) which is currently updated to match the DSM-5 criteria for PTSD. Further gold standard measures are the *Structured Clinical Interview for Dissociative Disorders-Revised* (SCID-D-R) for Dissociative Disorders, and the *Structured Interview for Disorders of Extreme Stress* (SIDES) for complex PTSD. Future clinical practice and research should include thorough assessment of trauma and neglect history and all DSM-5 trauma-related disorders as well as ICD-11 Complex PTSD, using validated instruments recommended in international guidelines (Cloitre et al. 2012; ISSTD 2011). The following website provides an overview of existing measures, many of which have been translated into different European languages: http://www.ptsd.va.gov/professional/pages/assessments/assessment.asp.

12.7 Psychotherapy for Posttraumatic Stress Disorders and SUD

12.7.1 General Principles of Treatment

Although effective treatments for both posttraumatic stress disorders (e.g. prolonged exposure, eye movement desensitisation, and reprocessing) and SUD (e.g. cognitive behavioural therapy, motivational enhancement techniques) are available, the literature for co-occurring posttraumatic stress disorders and SUD is still limited. The initial debate focused on the sequence of treatments. Early

authors suggested that PTSD treatment should only be initiated after a period of abstinence had been achieved. More recently, preference is given to integrated treatments that conceptualise posttraumatic stress disorders and SUD as one large issue and plan treatment accordingly. While it is unclear if integrated treatments have a superior efficacy in patients with SUD and PTSD as compared to one efficacious treatment alone (Torchalla et al. 2012), the clinical needs of patients with SUD and posttraumatic stress disorders often make an integrated approach necessary. It has become widely accepted that the treatment of posttraumatic stress symptoms is a prerequisite for becoming abstinent in many patients. On the other hand, a certain stability of SUD is needed for some interventions, namely trauma exposure.

While SUD specific interventions are needed all along the way of treatment, a phase-based approach has been proven helpful to organise trauma-specific interventions. This approach follows the three stages of trauma therapy: (1) stabilising and managing responses; (2) grieving and processing traumatic memories; (3) reconnecting with the world. All patients need, and can benefit from, the present-focused interventions of the first phase of treatment. This phase includes getting a "road map" of the healing process, establishing safety, mobilising all available resources for healing, and learning how to regulate one's emotions and manage symptoms. The second phase (including past-focused interventions, i.e. processing traumatic memories by means of trauma exposure) is essential to resolve symptoms of PTSD, but the moment when patients can enter this phase depends on the severity and complexity of the posttraumatic stress disorder. In more complex patients, a longer period of stabilisation will be necessary and in some patients (e.g. some patients with complex PTSD, DID or DDNOS) treatment is restricted to present-focused approaches. The following paragraphs summarise the available evidence for manualised present-focused and past-focused treatments of posttraumatic stress disorders in patients with SUD.

12.7.2 Present-Focused Treatments

Different treatment approaches focusing on the present (i.e. providing skills training and psycho-education) can be of help in SUD patients with posttraumatic stress disorders. Some of these programmes, e.g. "Dialectical Behaviour Therapy for patients with SUD" (Dimeff and Linehan 2008) have not yet been evaluated in patients with PTSD. In a recent overview, van Dam et al. (2012) could identify four present-focused treatments for concurrent PTSD and SUD with at least one effectiveness study: *CBT for PTSD in SUD treatment*, *Substance dependency-posttraumatic stress disorder therapy*, *Transcend*, and *Seeking Safety*. They conclude that the first three programmes showed no effects or that it was not possible to draw firm conclusions because of the design of the respective studies. A relatively good evidence base exists for the manualised group treatment *Seeking Safety* (Najavits 2002). The programme has been evaluated in a larger number of studies including six randomised controlled trials (RCTs). It offers 25 topics to teach

coping skills for PTSD and SUD in four domains (cognitive, behavioural, interpersonal, and case management) and has been translated into several European languages (see www.seekingsafety.org). An important assumption of the programme is that safety has the highest priority when recovering from posttraumatic stress disorders and SUD. Safety is defined as abstinence from substances, reduction in self-destructive behaviour, establishment of a network of supportive people, and self-protection from dangers associated with the disorders (e.g., HIV-risk, and domestic violence). Randomised controlled trials showed that *Seeking Safety* can lead to significant improvements in SUD and PTSD symptom severity. In the RCTs, the programme was more effective than the usual treatment for substance abuse and of equal effectiveness as other cognitive–behavioural interventions for SUD. In some of the controlled trials, *Seeking Safety* outperformed the control on PTSD but not SUD, in another on SUD but not PTSD, and in some on both PTSD and SUD (Najavits and Hien 2013). An advantage of the treatment is the possibility to provide clients with trauma-specific stabilisation in an early phase of treatment, when abstinence is difficult to achieve or to maintain. It can be followed, if necessary, by past-focused (i.e. exposure-based) treatments.

12.7.3 Past-Focused Treatments

In recent years, several past-focused approaches have been evaluated in patients with PTSD and SUD. Most models (e.g. Mills et al. 2012; van Dam et al. 2013; Sannibale et al. 2013) took the approach of combining an existing empirically validated treatment developed for PTSD (such as *prolonged exposure)* and SUD (such as *relapse prevention*). More recently, the author of the present-focused model *Seeking Safety* developed a past-focused model (*Creating Change*) where exposure is broadened to a gentler version. It also includes extensive preparation and decision-making tools for deciding whether a client is ready for exposure (Najavits and Johnson 2014). It is important to note that all models with past-focused (i.e. exposure-based) components also incorporated present-focused approaches (Najavits and Hien 2013). They were delivered in individual rather than group modality, and most tended to be restricted to a more narrow sample than the studies on present-focused treatment approaches. All studies of past-focused models showed positive results but mainly on symptoms of PTSD. For instance, *prolonged exposure* combined with *relapse prevention* (COPE; Mills et al. 2012), outperformed the control SUD treatment-as-usual on PTSD at 9-month follow-up but did not outperform the usual treatment on the SUD variables. One of the most important results of the existing studies is that exposure-based models can be used with many SUD clients without notable negative outcomes when they are adapted to their needs.

To provide better guidance for the clinical management of patients with posttraumatic stress disorders and SUD, future studies need to address how these

behavioural treatments can be optimally combined with pharmacological treatments.

12.8 Pharmacotherapy

So far, only few studies examined the effects of pharmacological treatments in patients with co-occurring PTSD and SUD. In one study, Trafton et al. (2006) assessed the effects of opioid substitution therapy among 255 opioid-dependent veterans. In this prospective observational trial, substitution therapy was as effective at reducing substance use in patients with comorbid PTSD as it was in patients without the disorder. One year after treatment both groups showed similar reductions in substance use, but PTSD patients received higher doses of opiate medication and attended more psychosocial treatment sessions. Another study found no significant benefit of the antidepressant sertraline over placebo in 94 alcohol-dependent patients with PTSD with regard to their alcohol consumption and symptoms of PTSD after 12 weeks of treatment (Brady et al. 2005). In a post-hoc cluster analysis of this study, a significant improvement became apparent in sertraline-treated participants with less severe alcohol dependence and early-onset PTSD.

Petrakis et al. (2006) compared the effects of disulfiram and naltrexone to placebo in male veterans with alcohol dependence and different comorbid psychiatric disorders. Patients received either disulfiram or no disulfiram and were, in addition to that, randomised to naltrexone or placebo, resulting in four different study groups. Of the 93 patients with co-occurring PTSD, individuals receiving naltrexone, disulfiram, or both medications had better outcomes after 12 weeks of treatment than the placebo group in terms of drinking days per week and consecutive days of abstinence. In addition, favourable effects on PTSD symptoms were observed in patients on disulfiram compared to those on naltrexone. However, as the authors point out, several limitations make the interpretation of these results difficult, including the potentially confounding effect of abstinence and the open administration of disulfiram. Nevertheless, the findings of this study suggest that both medications are safe and effective for alcohol-dependent patients with PTSD and should be considered for clinical management. In a more recent study of these authors (Petrakis et al. 2012), 88 patients with alcohol dependence and co-occurring PTSD received either paroxetine or desipramine and were, in addition to that, randomised to naltrexone or placebo. After 12 weeks, no differences were found between both antidepressants with regard to symptoms of PTSD but desipramine outperformed paroxetine on alcohol use outcomes. No additional effects of naltrexone were found.

Other promising pharmacotherapies of comorbid PTSD and SUD include, for instance, quetiapine, an antipsychotic medication (Monnelly et al. 2004) and topiramate, an antiseizure medication (Alderman et al. 2009), but the safety and efficacy of these medications for the treatment of posttraumatic stress disorders and SUD need to be tested in controlled clinical trials.

Conclusions

Trauma-related disorders are a common comorbidity among patients with SUD. Patients with both disorders have a more severe clinical profile and a worse overall outcome. Therefore, traumatic experiences and their clinical consequences should be routinely assessed in clinical practice and patients with trauma-related comorbidity should be offered specific treatments. Given that many patients suffer from the consequences of early and complex trauma, the typical features associated with these experiences need to be covered. Often, an integrated approach will be necessary to adequately address both disorders. While treatment approaches focusing on the present (i.e. providing skills training and psycho-education) will be beneficial for most patients, including those with dissociative disorders, past-focused (i.e. exposure-based) treatments should (additionally) be offered to SUD patients with co-occurring PTSD. More research is needed on the potential effects of medication in this group of patients.

References

Alderman CP, McCarthy LC, Condon JT, Marwood AC, Fuller JR (2009) Topiramate in combat-related posttraumatic stress disorder. Ann Pharmacother 43(4):635–641. doi:10.1345/aph.1L578

Brady KT, Sonne S, Anton RF, Randall CL, Back SE et al (2005) Sertraline in the treatment of co-occurring alcohol dependence and posttraumatic stress disorder. Alcohol Clin Exp Res 29 (3):395–401

Cloitre M, Courtois CA, Ford JD, Green BL, Alexander P (2012) The ISTSS Expert Consensus Treatment Guidelines for Complex PTSD in Adults. www.istss.org/AM/Template.cf. Accessed: 27 Jan 2014

Coffey SF, Saladin ME, Drobes DJ, Brady KT, Dansky BS, Kilpatrick DG (2002) Trauma and substance cue reactivity in individuals with comorbid posttraumatic stress disorder and cocaine or alcohol dependence. Drug Alcohol Depend 65(2):115–127

Dimeff LA, Linehan MM (2008) Dialectical behavior therapy for substance abusers. Addict Sci Clin Pract 4(2):39–47

Dom G, De Wilde B, Hulstijn W, Sabbe B (2007) Traumatic experiences and posttraumatic stress disorders: differences between treatment-seeking early- and late-onset alcoholic patients. Compr Psychiatry 48(2):178–185. doi:10.1016/j.comppsych.2006.08.004

Driessen M, Schulte S, Luedecke C, Schaefer I, Sutmann F et al (2008) Trauma and PTSD in patients with alcohol, drug, or dual dependence: a multi-center study. Alcohol Clin Exp Res 32 (3):481–488. doi:10.1111/j.1530-0277.2007.00591.x

Hien D, Cohen L, Campbell A (2005) Is traumatic stress a vulnerability factor for women with substance use disorders? Clin Psychol Rev 25(6):813–823

Hien DA, Campbell AN, Ruglass LM, Hu MC, Killeen T (2010a) The role of alcohol misuse in PTSD outcomes for women in community treatment: a secondary analysis of NIDA's Women and Trauma Study. Drug Alcohol Depend 111(1–2):114–119. doi:10.1016/j.drugalcdep.2010.04.011

Hien DA, Jiang H, Campbell AN, Hu MC, Miele GM et al (2010b) Do treatment improvements in PTSD severity affect substance use outcomes? A secondary analysis from a randomized clinical trial in NIDA's Clinical Trials Network. Am J Psychiatry 167(1):95–101. doi:10.1176/appi.ajp.2009.09091261

International Society for the Study of Trauma and Dissociation (ISSTD) (2011) Guidelines for treating dissociative identity disorder in adults, third revision: summary version. J Trauma Dissociation 12(2):115–187. doi:10.1080/15299732.2011.537247

Jacobsen LK, Southwick SM, Kosten TR (2001) Substance use disorders in patients with post-traumatic stress disorder: a review of the literature. Am J Psychiatry 158(8):1184–1190

Karadag F, Sar V, Tamar-Gurol D, Evren C, Karagoz M et al (2005) Dissociative disorders among inpatients with drug or alcohol dependency. J Clin Psychiatry 66(10):1247–1253

Kessler RC, Sonnega A, Bromet E, Hughes M, Nelson CB (1995) Posttraumatic stress disorder in the National Comorbidity Survey. Arch Gen Psychiatry 52(12):1048–1060

Langeland W, Draijer N, van den Brink W (2004) Psychiatric comorbidity in treatment-seeking alcoholics: the role of childhood trauma and perceived parental dysfunction. Alcohol Clin Exp Res 28(3):441–447

Langeland W, van den Brink W, Draijer N (2005) Gender and the relationship between childhood trauma, dissociation and alcohol dependence. Zeitschrift für Psychotraumatologie und Psychologische Medizin 3:29–40

Levitt JT, Cloitre M (2005) A clinician's guide to STAIR/MPE: treatment for PTSD related to childhood abuse. Cogn Behav Pract 12(1):40–52. doi:10.1016/s1077-7229(05)80038-0

Maercker A, Brewin CR, Bryant RA, Cloitre M, Reed GM et al (2013) Proposals for mental disorders specifically associated with stress in the International Classification of Diseases-11. Lancet 381(9878):1683–1685. doi:10.1016/S0140-6736(12)62191-6

Makin-Byrd K, Cronkite RC, Timko C (2011) The influence of abuse victimization on attendance and involvement in mutual-help groups among dually diagnosed male veterans. J Subst Abuse Treat 41(1):78–87. doi:10.1016/j.jsat.2011.02.001

Mills KL, Teesson M, Back SE, Brady KT, Baker AL et al (2012) Integrated exposure-based therapy for co-occurring posttraumatic stress disorder and substance dependence: a randomized controlled trial. JAMA 308(7):690–699

Mills KL, Teesson M, Ross J, Peters L (2006) Trauma, PTSD, and substance use disorders: findings from the Australian National Survey of Mental Health and Well-Being. Am J Psychiatry 163(4):652–658. doi:10.1176/appi.ajp.163.4.652

Monnelly EP, Ciraulo DA, Knapp C, LoCastro J, Sepulveda I (2004) Quetiapine for treatment of alcohol dependence. J Clin Psychopharmacol 24(5):532–535

Najavits LM (2002) Seeking safety: a treatment manual for PTSD and substance abuse. Guilford, New York

Najavits LM, Hien D (2013) Helping vulnerable populations: a comprehensive review of the treatment outcome literature on substance use disorder and PTSD. J Clin Psychol 69 (5):433–479. doi:10.1002/jclp.21980

Najavits LM, Johnson KM (2014) Pilot study of creating change, a new past-focused model for PTSD and substance abuse. Am J Addict 23(5):415–422

Najavits LM, Sonn J, Walsh M, Weiss RD (2004) Domestic violence in women with PTSD and substance abuse. Addict Behav 29(4):707–715. doi:10.1016/j.addbeh.2004.01.003

Ouimette P, Moos RH, Finney JW (2003) PTSD treatment and 5-year remission among patients with substance use and posttraumatic stress disorders. J Consult Clin Psychol 71(2):410–414

Peltan JR, Cellucci T (2011) Childhood sexual abuse and substance abuse treatment utilization among substance-dependent incarcerated women. J Subst Abuse Treat 3:215–224. doi:10.1016/j.jsat.2011.03.004

Petrakis IL, Poling J, Levinson C, Nich C, Carroll K et al (2006) Naltrexone and disulfiram in patients with alcohol dependence and comorbid post-traumatic stress disorder. Biol Psychiatry 60(7):777–783. doi:10.1016/j.biopsych.2006.03.074

Petrakis IL, Ralevski E, Desai N, Trevisan L, Gueorguieva R et al (2012) Noradrenergic versus serotonergic antidepressant with or without naltrexone for veterans with PTSD and comorbid alcohol dependence. Neuropsychopharmacology 37(4):996–1004. doi:10.1038/npp.2011.283

Petry NM, Ford JD, Barry D (2011) Contingency management is especially efficacious in engendering long durations of abstinence in patients with sexual abuse histories. Psychol Addict Behav 25(2):293–300. doi:10.1037/a0022632

Read J, Hammersley P, Rudegeair T (2007) Why, when and how to ask about childhood abuse. Adv Psychiatr Treat 13:101–110

Sannibale C, Teesson M, Creamer M, Sitharthan T, Bryant RA et al (2013) Randomized controlled trial of cognitive behaviour therapy for comorbid post-traumatic stress disorder and alcohol use disorders. Addiction 108(8):1397–1410. doi:10.1111/add.12167

Schäfer I, Langeland W, Hissbach J, Luedecke C, Ohlmeier MD et al (2010) Childhood trauma and dissociation in patients with alcohol dependence, drug dependence, or both-A multi-center study. Drug Alcohol Depend 109(1–3):84–89. doi:10.1016/j.drugalcdep.2009.12.012

Schäfer I, Najavits LM (2007) Clinical challenges in the treatment of patients with posttraumatic stress disorder and substance abuse. Curr Opin Psychiatry 20(6):614–618. doi:10.1097/YCO.0b013e3282f0ffd9

Schäfer I, Reininghaus U, Langeland W, Voss A, Zieger N et al (2007) Dissociative symptoms in alcohol-dependent patients: associations with childhood trauma and substance abuse characteristics. Compr Psychiatry 48(6):539–545. doi:10.1016/j.comppsych.2007.05.013

Schäfer I, Verthein U, Oechsler H, Deneke C, Riedel-Heller S et al (2009) What are the needs of alcohol dependent patients with a history of sexual violence? A case-register study in a metropolitan region. Drug Alcohol Depend 105(1–2):118–125. doi:10.1016/j.drugalcdep.2009.06.020

Simpson TL (2002) Women's treatment utilization and its relationship to childhood sexual abuse history and lifetime PTSD. Subst Abuse 23(1):17–30. doi:10.1023/a:1013678626447

Torchalla I, Nosen L, Rostam H, Allen P (2012) Integrated treatment programs for individuals with concurrent substance use disorders and trauma experiences: a systematic review and meta-analysis. J Subst Abuse Treat 42(1):65–77. doi:10.1016/j.jsat.2011.09.001

Trafton JA, Minkel J, Humphreys K (2006) Opioid substitution treatment reduces substance use equivalently in patients with and without posttraumatic stress disorder. J Stud Alcohol 67 (2):228–235

van Dam D, Ehring T, Vedel E, Emmelkamp PM (2013) Trauma-focused treatment for posttraumatic stress disorder combined with CBT for severe substance use disorder: a randomized controlled trial. BMC Psychiatry 13:172. doi:10.1186/1471-244X-13-172

van Dam D, Vedel E, Ehring T, Emmelkamp PM (2012) Psychological treatments for concurrent posttraumatic stress disorder and substance use disorder: a systematic review. Clin Psychol Rev 32(3):202–214. doi:10.1016/j.cpr.2012.01.004

Winters LE, Karow A, Reimer J, Fricke S, Kuhnigk O, Schäfer I (2014) Psychometric properties of the Posttraumatic Diagnostic Scale (PDS) in alcohol-dependent patients. Subst Abus 35 (3):262–267

ADHD and Addiction

13

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Abstract

Attention-deficit hyperactivity disorder (ADHD) is characterized by symptoms of inattention and/or hyperactivity and impulsivity. It is frequently present in substance use disorder (SUD) patients; estimates of the prevalence of ADHD vary between 14 % and 23 % in SUD populations. The high comorbidity is partly based on communal underlying neurobiological characteristics such as a shared genetic background of the two disorders. Neuropsychological correlates of both disorders include a dysfunction of the motivational/reward system and impulsivity. In general, patients with this type of comorbidity represent a more severe subgroup of SUD patients with more additional comorbidity and a more disadvantageous prognosis and higher treatment drop-out than SUD patients without ADHD. It is important to detect and treat ADHD in SUD patients, and substance use disorder treatment centers can play an important role in this by screening for ADHD. Treatment options may include medication, although convincing evidence of effect in SUD populations is yet lacking, and cognitive behavioral therapy. As problems of SUD and ADHD can be intertwined, it is appropriate to start ADHD treatment during SUD treatment, ideally after initial stabilization of substance use. As this patient group is characterized by high complexity, further research and development of integrated treatment programs are warranted.

13.1 ADHD

Attention-Deficit Hyperactivity Disorder (ADHD) is one of the most common psychiatric disorders in childhood, affecting approximately 4–8 % of children in the general population (Faraone et al. 2003). Although symptoms wane in some patients in adulthood, the majority of patients continue to be impaired by their symptoms (Faraone et al. 2006), leading to a prevalence of 1–5 % in adulthood (Simon et al. 2009).

ADHD is characterized by symptoms of attention deficit and/or hyperactivity and impulsivity. Three different subtypes exist: patients who exhibit mainly attention-deficit symptoms have the attention-deficit subtype, whereas patients experiencing mainly hyperactivity and impulsivity symptoms are diagnosed with the hyperactive/impulsive subtype. The majority of the clinical population has symptoms in both domains and is diagnosed with the combined subtype (Wilens et al. 2009). In line with recent changes in the classification of psychiatric disorders in which axis I and II are no longer distinguished, the difference between ADHD and personality disorders in terms of its lifelong impact can be debated, as ADHD starts at young age and its symptoms often persist in adulthood. ADHD can lead to functional impairments in all domains of life. It is associated with lower level of education, higher level of unemployment, but also higher rates of unsuccessful marriages, criminality, and road traffic accidents (Biederman et al. 2006; Shaw et al. 2012). Altogether, these consequences are responsible for a reduced quality of

life, which is also caused by the fact that ADHD is often accompanied by comorbid disorders. Antisocial personality disorder, borderline personality disorder, mood disorders, and anxiety disorders are frequently present and have an impact on the prognosis (Wilens et al. 2004; Barkley and Brown 2008). Substance use disorders (SUDs) are also an important comorbid disorders in ADHD patients, affecting 15 % of adult ADHD patients (Kessler et al. 2006).

Several treatment options for adult ADHD exist. Pharmacological treatment with stimulants such as methylphenidate is by far the most described treatment modality, resulting in symptom improvement in a majority of patients (Mészáros et al. 2009). Although symptoms of for example inattention can be improved by medication, medication offers no solution for the fact that planning and organization skills are often not developed to their full potential. Recently, therapists and researchers in the field have focused on developing a cognitive behavioral therapy (CBT) for ADHD patients that addresses these functional skills (Safren et al. 2010). More research is needed to corroborate their promising results and also to investigate other treatment options.

In this chapter, we will provide an overview of the epidemiology of SUD patients with comorbid ADHD and of the neurobiological correlates of this type of comorbidity. We will then focus on the clinical presentation, treatment, and prognosis of these patients, and end with recommendations for future research.

13.2 Epidemiology of ADHD in SUD Patients

Several studies have shown that children with ADHD have a greater risk of developing SUD later in life than children without ADHD (Charach et al. 2011). Not surprisingly, the prevalence of ADHD in SUD patients is much higher than in the general population; a meta-analysis of predominantly American studies estimated the prevalence of ADHD in SUD patients to be 23.1 % (van Emmerik-van Oortmerssen et al. 2012) and in the largest study so far in 3,558 SUD patients in 10 mostly European countries, prevalence rates ranged from 5.4 to 31.3 % depending on country (van de Glind et al. 2014). The latter study found significant differences between countries, with Scandinavian countries having a higher ADHD prevalence than for example southern European countries. Also, differences were found between patients with different types of SUD, as a lower ADHD prevalence was found among alcohol-dependent patients compared to illicit drug-dependent patients. Altogether, these findings suggest that ADHD is a frequently present comorbid disorder in SUD patients. Several factors contribute to this high co-occurrence of both disorders. In the next paragraph, genetic and neurobiological mechanisms explaining the high comorbidity are discussed.

13.3 Neurobiology of ADHD

Pathophysiology underlying ADHD has been extensively investigated in the past two decades and the field is growing rapidly. Along with technical advances, exciting results from both genetic and brain imaging studies are emerging. This section briefly presents important findings regarding the neurobiological underpinnings in ADHD.

13.3.1 Genetic Factors

ADHD has a strong heritable component. The mean estimated heritability is 76 % in twin studies (Faraone et al. 2005). In familial studies, parents and siblings of ADHD patients show increased risk of ADHD. This risk is more strongly associated in index patients with persisting ADHD compared to remitted ADHD (Franke et al. 2012). A number of risk genes for ADHD have been identified but results have yet been inconsistent. The most replicated findings involve dopamine (DA) and serotonin transmission (Cortese and Castellanos 2012).

To date research has shown that ADHD involves multiple genes of moderate effect in complex interaction with environmental factors. For example, health complications early in life may modulate the genetic risk for ADHD (Plomp et al. 2009).

ADHD subtypes based solely on DSM-IV symptom criteria have been criticized as providing too heterogeneous samples for the purpose of genetic studies. Identifying endophenotypes based on neuropsychological deficits is suggested to offer more well-defined subtypes of ADHD (Franke et al. 2012) (for definition of endophenotypes, see (Castellanos and Proal 2012).

13.3.2 Neuropsychological Functioning

Over the years, several theories about core cognitive deficits in ADHD have been formulated based on results from neuropsychological studies and behavioural observations; focussing, for example on deficits in executive functioning (Pennington and Ozonoff 1996) or a dual pathway model of executive function deficits and reward deficiency (Sonuga-Barke 2003). Barkley proposed that executive function deficits seen in children with ADHD are secondary to failure in inhibition (Barkley 1997).

Meta-analysis of studies investigating neuropsychological functioning in ADHD show that, compared to controls, individuals with ADHD most consistently display differences in response inhibition, vigilance, spatial working memory, signal detection (arousal), set shifting, and some measures of planning (Nigg 2005).

13.3.3 Results from Imaging Studies

Results from both structural (Castellanos et al. 2002) and functional imaging studies (Bush et al. 1999) have repeatedly shown involvement of fronto-striatal-cerebellar networks in the neurobiology of ADHD, implicating neurotransmission involving DA and noradrenaline (NA). Prefrontal cortex (PFC) is rich in DA and NA receptors and has a vital role in cognitive control by regulating information received from sensory cortices and attention based on the relevance of incoming information. PFC is also important for sustaining attention over delay and shifting attention based to task demands. In addition, it has an important role in regulating behaviour and emotion (Durston et al. 2011).

Functional brain imaging studies have initially investigated subjects performing cognitive tasks challenging e.g. attention, working memory, and response inhibition thus activating brain areas of interest, comparing individuals with ADHD to controls or medicated individuals to non-medicated. Recently, interesting results are emerging from imaging studies investigating brain activity during resting state suggesting a more diffuse connectivity between functional networks in individuals with ADHD (Swanson et al. 2011).

Few imaging studies have been able to prospectively follow up individuals, who were diagnosed with ADHD as children, from childhood to adulthood. In a prospective study of 59 boys (aged 6–12 when diagnosed with ADHD) and 80 comparisons who underwent MRI after approximately 33 years of initial diagnosis, a reduction in brain gray matter was found in areas involved in attention, emotion regulation, and motivation (Proal et al. 2011). These results were independent of current diagnosis and the authors suggest that remission in ADHD is linked to compensatory maturation of prefrontal, cerebellar, and thalamic circuitry.

Recently, based on findings from brain imaging studies, involvement of several large-scale brain systems in ADHD has been proposed instead of focusing mainly on the influence of prefrontal brain regions (Castellanos and Proal 2012). The suggested brain systems include: (1) the fronto-parietal network, also referred to as an executive control circuit involved in goal directed behaviour, (2) the dorsal and ventral attentional networks, which form the key components of the attention regulatory system; especially the dorsal attentional network is implicated in ADHD, (3) the visual network, which is important in sustained attention and interacts with the dorsal attentional network, (4) the motor network; ADHD children often exhibit motoric hyperactivity, and (5) the default network, the activity of which is diminished during a task and increased during rest. Diminished suppression of the default network during tasks is related to lapses in attention [For a detailed account see Castellanos and Proal (2012)].

Disruptive externalizing disorders (CD, ODD, SUD and ADHD) that commonly co-exist share behavioural symptoms and neuropsychological dysfunctions and it has been suggested that they involve common genetic networks (Arcos-Burgos et al. 2012). Brain circuits involved in addiction vulnerability include those of reward, memory, executive function, and motivation, all of which play a role in

ADHD as well. Deficient DA transmission reported in ADHD is also implicated in vulnerability to addiction (Volkow et al. 2012).

To conclude, ADHD is a highly heritable disorder and its pathophysiology involves fronto-striatal-cerebellar networks and DA and NA neurotransmission (while not excluding other potential neurophysiological mechanisms). Results from imaging studies also support the notion that ADHD and SUD share some common neurobiological underpinnings.

13.4 Clinical Presentation of ADHD

Table 13.1 lists the ADHD symptoms of inattention and hyperactivity/impulsivity. A DSM5 ADHD diagnosis in adulthood can be established if a patient (retrospectively) meets all criteria in childhood as well as in adulthood. These criteria are: symptom criterion (i.e. at least six symptoms of inattention and/or six symptoms of hyperactivity and impulsivity in childhood, and five symptoms of inattention and/or hyperactivity/impulsivity in adulthood); age criterion (age of onset before 12); pervasiveness criterion (symptoms are present in at least two domains of life); impairment criterion (symptoms lead to a significant impairment); and diagnostic category (symptoms are not better explained for by the presence of another disorder).

While the core symptoms of inattention, hyperactivity, and impulsivity are well pronounced in children, the presentation is generally more subtle in adults. Hyperactivity at an adult age for instance is not expressed in running and climbing excessively, but rather as inner restlessness, inability to relax, over talkativeness, or avoiding going to theatres, etc. This makes it more difficult to recognize the symptoms, especially since the description of symptoms in the DSM is sometimes more suitable for a childhood situation than for adults.

As mentioned before, ADHD is often accompanied by comorbid disorders. This is also true for SUD patients with ADHD: in comparison to SUD patients without ADHD they even suffer more often from additional psychiatric disorders, such as antisocial personality disorder, borderline personality disorder, depression or anxiety disorders. In fact, the majority of SUD patients with ADHD have at least one more comorbid disorder (van Emmerik-van Oortmerssen et al. 2014), which contributes to the fact that this is a subgroup of SUD patients with more severity.

Although in childhood, ADHD is more often recognized in boys, the rates of ADHD for men and women are more equal in adult populations and are equal in adult SUD populations as well.

Table 13.1 ADHD symptoms of inattention and hyperactivity/impulsivity

Inattention symptoms	
1	Often fails to give close attention to details or makes careless mistakes in schoolwork, work, or other activities
2	Often has difficulty sustaining attention in tasks or play activities
3	Often does not seem to listen when spoken to directly
4	Often does not follow through on instructions and fails to finish schoolwork or duties in the workplace (not due to oppositional behavior or failure to understand)
5	Often has difficulty organizing tasks or activities
6	Often avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort (like schoolwork or homework)
7	Often loses things necessary for tasks or activities (e.g. toys, school assignments, pencils, books, or tools)
8	Is often easily distracted by extraneous stimuli
9	Is often forgetful in daily activities
Hyperactivity/impulsivity symptoms	
1	Often fidgets with hands or feet or squirms in seat
2	Often leaves seat in classroom or in other situations in which remaining in seat is expected
3	Often runs about or climbs excessively in situations in which it is not appropriate (in adolescents and adults, may be limited to subjective feelings of restlessness)
4	Often has difficulty playing or engaging in leisure activities quietly
5	Is often "on the go" or often acts as if "driven by a motor"
6	Often talks excessively
7	Often blurts out answers before the questions have been completed
8	Often has difficulty awaiting turn
9	Often interrupts or intrudes on others (e.g., butts into conversations and games)

13.5 Screening and Diagnostic Assessment of ADHD

Typically, in many SUD patients with ADHD the disorder has not been identified by health-care workers, so substance abuse treatment centres may often be the first to recognize the ADHD symptoms and perform diagnostic assessment. Screening and diagnostic assessment is however hampered by a number of important difficulties. As an example, ongoing substance use can mask ADHD symptoms, but it may also mimic ADHD symptoms that are no longer present when the effects of substance use have faded. The same holds for withdrawal symptoms such as restlessness and concentration problems. Several ADHD screening instruments exist, of which the ASRS-v1.1 has been validated in a population of SUD patients (van de Glind et al. 2013). It is important to remember that a diagnosis cannot be based on a simple screening, so in case of a positive result of the screening instrument, diagnostic assessment is indicated. This is usually postponed until after a period of several weeks of abstinence when interfering intoxication/withdrawal symptoms have been minimized. However, valuable information can also be

obtained if careful attention is given to childhood ADHD symptoms and to ADHD symptoms in past periods of abstinence, even if a patient is not abstinent at the time of assessment. It is generally recommended to involve an informant, such as a parent, to collect additional information on childhood symptoms; similarly, a partner or other significant person can shed light on adulthood symptoms. Structured interviews such as the Conners' Adult ADHD Diagnostic Interview for DSM-IV (CAADID) (Epstein et al. 2001) and DIVA (Kooij and Francken 2010) are helpful in obtaining all necessary diagnostic information in a standardized way.

ADHD symptoms need not only be differentiated from substance use disorders, but also from bipolar disorders, depressive and anxiety disorders, and borderline personality disorder, all of which share overlapping symptoms with ADHD. For example adults with ADHD often exhibit low self-esteem, low mood, affective lability and irritability, which may be confused with dysthymia, bipolar disorder, or borderline personality disorder (Kooij et al. 2010). Diagnosing ADHD is further complicated by the fact that these differential diagnoses can also be present as comorbidities.

Although ADHD is associated with deviations in neuropsychological functions when groups of ADHD patients and normal controls are compared, these deviations are relatively unspecific and neuropsychological tests are not sensitive enough as diagnostic tools on an individual level. They may, however, provide useful information about a person's cognitive functioning that is important for treatment planning. This is apparent for example in patients with severe learning difficulties.

13.6 Treatment of ADHD in SUD Patients

An important first step in the treatment of ADHD in SUD patients is psychoeducation about the disorder. For patients who have experienced ADHD-related problems from childhood on, it is a relief to learn that there is a condition explaining these problems. Often they have been told that they are lazy and they may have developed a low self-esteem because of failing tasks. Realizing that ADHD is involved in the origin of these difficulties is very valuable information for many patients. It is important to explain that ADHD is a lifelong condition, and treatment is aimed at reducing symptoms and learning how to cope with symptoms. In this paragraph, treatment options for ADHD are described, as well as their efficacy in SUD patients with ADHD.

13.6.1 Pharmacological Treatment

Stimulant medications such as methylphenidate are an effective treatment option for adults with ADHD (Mészáros et al. 2009). Methylphenidate blocks the dopamine transporters in the brain, which leads to enhanced dopamine levels and reduced ADHD symptoms. Dextroamphetamine, which is also a stimulant, exerts its effect through increased synaptic dopamine release. Although stimulant

medication is effective in 70 % of adult ADHD patients (Kooij et al. 2010), the effect of stimulant medication is not as clear in SUD patients with ADHD. Most randomized controlled trials to date did not find a convincing effect of methylphenidate on ADHD symptoms or SUD problems (e.g. Levin et al. 2007; Konstenius et al. 2010). The reasons for this putative lack of effect are not yet clear, but a possible explanation could be that direct toxic effects of drugs have altered dopamine neurotransmission in such a way that methylphenidate is not able to exert its effect anymore (Crunelle et al. 2013). It has also been suggested that higher doses may be warranted in a SUD population (Levin et al. 2007). This is supported by results from a recent study showing that methylphenidate in doses up to 180 mg improved ADHD-symptoms, reduced relapse and improved retention to treatment in amphetamine dependent men recently released from prison (Konstenius et al. 2014) Thus, although the first choice pharmacological therapy for ADHD is methylphenidate, it is important to realize that this medication may not be effective in many SUD patients with ADHD. Still a treatment with methylphenidate can be considered if a patient wants to try the option. In that case, it is important that a patient first becomes abstinent of substances, so the effect of medication is not disturbed by intoxication or withdrawal from substances and that agreements are made in advance on how long the effect is monitored before deciding if there is any effect or not.

The regular treatment dose of methylphenidate is 0.5–1.0 mg/kg/day. Before starting treatment, a somatic check-up is required with specific attention for cardiac problems, epilepsy, thyroid problems, and registration of blood pressure and heart frequency, which is repeated during treatment. Methylphenidate is available as immediate-release and several forms of sustained release. Immediate release preparations have a short effect span and should be administered four to five times a day. One of the side effects of this type of stimulants is the rebound effect: ADHD symptoms worsen as the medication effect declines. The sustained-release formula is prescribed once or twice daily, which is more convenient and feasible for most patients. Rebound effects occur less frequent and less pronounced. Another advantage of this medication formula is the lower abuse liability, in contrast to the immediate release form, which can be inhaled through the nose or injected. Compared to oral administration, sniffing or injecting methylphenidate results in a faster increase of extracellular dopamine, which evokes a reinforcing ‘high’. In patients where abuse is a particular concern, it is probably wiser to prescribe the sustained release form.

Other medication options for the treatment of ADHD include atomoxetine and bupropion. Atomoxetine inhibits noradrenaline re-uptake and is considered an appropriate second-line alternative for stimulants. There is only limited information on the effects of atomoxetine in SUD patients with ADHD, but the scarce studies to date showed disappointing effects on ADHD symptoms. Only one double-blind RCT (Wilens et al. 2008) found that atomoxetine treatment was superior to placebo in improving ADHD symptoms in recently abstinent alcohol-dependent adults with ADHD. The usual dosage for atomoxetine is 80–100 mg/day, and it is prescribed once daily. Bupropion is an inhibitor of catecholamines re uptake. It has

antidepressive effects but it is also used in the treatment of ADHD. However, its use has hardly been studied in double-diagnosis patients with SUD and ADHD. Bupropion is dosed 300–450 mg/day, divided over 1 or 2 doses.

13.6.2 Cognitive Behavioural Therapy and Coaching

Only recently, research has focused on Cognitive Behavioural Therapy (CBT) as treatment option for adults with ADHD. Even if medication is effective in a patient, for example by improving attention, many patients have never been able to learn basic planning and organizing skills. Moreover, the accumulation of failure experiences in the past may still have an impact on patient's functioning. CBT addresses these issues, by training planning and organization skills on one hand, and teaching the patient to tackle automatic negative thoughts on the other hand. Several randomized trials have studied the effect of CBT in adult ADHD patients, and found a remarkable effect, which also lasted at follow-up (e.g. Safren et al. 2010). Unfortunately, CBT for ADHD has not yet been studied in SUD patients with ADHD. At the present an integrated CBT treatment, which addresses both SUD and ADHD, is being investigated in a randomized controlled design in the Netherlands (van Emmerik-van Oortmerssen et al. 2013). SUD and ADHD symptoms can exacerbate one another, for example substances are sometimes used to alleviate ADHD symptoms (e.g. of restlessness), and at the same time substance use can worsen ADHD symptoms (e.g. concentration problems or impulsivity). The authors hypothesize that treating SUD and ADHD at the same time may result in better treatment outcomes for both SUD and ADHD. The integrated treatment incorporates both protocolled addiction treatment and elements of the CBT protocol for ADHD treatment by Safren and colleagues (Safren et al. 2005). After initial stabilization of substance use, sessions on addiction treatment alternate with sessions on ADHD treatment. Basic planning skills are trained by instructing patients to use a calendar and task list, and ample attention is paid to prioritizing tasks and managing overwhelming tasks by cutting them into small parts. Reducing distractibility and coping with negative automatic thoughts are also part of the treatment protocol. Results of the study are not yet available at the moment of writing this chapter, but are expected in 2016.

13.6.3 Order of Treatments

In treating SUD patients with ADHD, it is important to start with ADHD treatment as soon as possible. Symptoms of ADHD and addiction exacerbate each other and treatment of both disorders is therefore required. After initial stabilization of substance use, ADHD treatment in the form of psycho education and CBT or coaching can be taken up. In case of medication treatment, treatment should only be started once the patient is abstinent from substances.

Investing in a stable work alliance between patient and therapist is of extra importance in order to prevent patients from dropping out of treatment. Apart from this, extra efforts could be useful to help these, generally chaotic, patients to remember their treatment appointments. Scheduling appointments on a fixed day and time, and sending a reminder text message before the appointment for example, can be very helpful.

13.7 Prognosis

As stated earlier, SUD patients with ADHD represent a more severe subgroup of patients than patients with SUD only. They more often suffer from additional psychiatric comorbidities, and in general their SUD problems are more severe compared to SUD patients without ADHD. Furthermore, SUD patients with comorbid ADHD start abusing substances at a younger age, use more substances, and are hospitalized more often than SUD patients without ADHD (Arias et al. 2008). ADHD is also associated with higher relapse rates after SUD treatments (Ercan et al. 2003). On top of that, pharmacological treatment of ADHD symptoms has limited effect (Castells et al. 2011), and results of CBT approaches have not yet been described in this patient group.

All in all, treatment of these double diagnosis patients should include not only addiction care, but also diagnostic assessment and treatment for ADHD symptoms to optimize the prognosis. Still, treatment of SUD patients with ADHD is challenging because these patients are often struggling with many long-existing problems, and developing tailored treatment programs should be a focus of future research. A more extensive treatment is generally necessary in comparison to patients with uncomplicated SUD and can offer these patients a chance to overcome SUD problems and ADHD-related problems in their lives. Successful treatment may result in better quality of life and large health gains for these patients.

References

Arcos-Burgos M, Velez JI, Solomon BD et al (2012) A common genetic network underlies substance use disorders and disruptive or externalizing disorders. Hum Genet 131:917–929

Arias AJ, Gelernter J, Chan G et al (2008) Correlates of co-occurring ADHD in drug-dependent subjects: prevalence and features of substance dependence and psychiatric disorders. Addict Behav 33:1199–1207

Barkley RA (1997) Attention-deficit/hyperactivity disorder, self-regulation, and time: toward a more comprehensive theory. J Dev Behav Pediatr 18:271–279

Barkley RA, Brown TE (2008) Unrecognized attention-deficit/hyperactivity disorder in adults presenting with other psychiatric disorders. CNS Spectr 13:977–984

Biederman J, Faraone SV, Spencer TJ et al (2006) Functional impairments in adults with self-reports of diagnosed ADHD: A controlled study of 1001 adults in the community. J Clin Psychiatry 67:524–540

Bush G, Frazier JA, Rauch SL et al (1999) Anterior cingulate cortex dysfunction in attention-deficit/hyperactivity disorder revealed by fMRI and the Counting Stroop. Biol Psychiatry 45:1542–1552

Castellanos FX, Lee PP, Sharp W et al (2002) Developmental trajectories of brain volume abnormalities in children and adolescents with attention-deficit/hyperactivity disorder. JAMA 288:1740–1748

Castellanos FX, Proal E (2012) Large-scale brain systems in ADHD: beyond the prefrontal-striatal model. Trends Cogn Sci 16:17–26

Castells X, Ramos-Quiroga JA, Rigau D et al (2011) Efficacy of methylphenidate for adults with attention-deficit hyperactivity disorder: a meta-regression analysis. CNS Drugs 25:157–169

Charach A, Yeung E, Climans T et al (2011) Childhood attention-deficit/hyperactivity disorder and future substance use disorders: comparative meta-analyses. J Am Acad Child Adolesc Psychiatry 50:9–21

Cortese S, Castellanos FX (2012) Neuroimaging of attention-deficit/hyperactivity disorder: current neuroscience-informed perspectives for clinicians. Curr Psychiatry Rep 14:568–578

Crunelle CL, van den Brink W, Veltman DJ et al (2013) Low dopamine transporter occupancy by methylphenidate as a possible reason for reduced treatment effectiveness in ADHD patients with cocaine dependence. Eur Neuropsychopharmacol 23:1714–1723

Durston S, van Belle J, de Zeeuw P (2011) Differentiating frontostriatal and fronto-cerebellar circuits in attention-deficit/hyperactivity disorder. Biol Psychiatry 69:1178–1184

Epstein JE, Johnson DE, Conners CK (2001) Conners' adult ADHD diagnostic interview for DSM-IV (CAADID). Technical Manual. MHS, Toronto

Ercan ES, Coskunol H, Varan A et al (2003) Childhood attention deficit/hyperactivity disorder and alcohol dependence: a 1-year follow-up. Alcohol Alcohol 38:352–356

Faraone SV, Biederman J, Mick E (2006) The age-dependent decline of attention deficit hyperactivity disorder: a meta-analysis of follow-up studies. Psychol Med 36:159–165

Faraone SV, Perlis RH, Doyle AE et al (2005) Molecular genetics of attention-deficit/hyperactivity disorder. Biol Psychiatry 57:1313–1323

Faraone SV, Sergeant J, Gillberg C (2003) The worldwide prevalence of ADHD: is it an American condition? World Psychiatry 2:104–113

Franke B, Faraone SV, Asherson P et al (2012) The genetics of attention deficit/hyperactivity disorder in adults, a review. Mol Psychiatry 17:960–987

Kessler RC, Adler L, Barkley R et al (2006) The prevalence and correlates of adult ADHD in the United States: results from the National Comorbidity Survey Replication. Am J Psychiatry 163:716–723

Konstenius M, Jayaram-Lindstrom N, Beck O et al (2010) Sustained release methylphenidate for the treatment of ADHD in amphetamine abusers: a pilot study. Drug Alcohol Depend 108:130–133

Konstenius M, Jayaram-Lindström N, Guterstam J et al (2014) Methylphenidate for attention deficit hyperactivity disorder and drug relapse in criminal offenders with substance dependence: a 24-week randomized placebo-controlled trial. Addiction 109:440–449

Kooij SJ, Bejerot S, Blackwell A et al (2010) European consensus statement on diagnosis and treatment of adult ADHD: The European Network Adult ADHD. BMC Psychiatry 10:67

Kooij JJS, Francken MH (2010) DIVA. DIVA foundation, Den Haag

Levin FR, Evans SM, Brooks DJ et al (2007) Treatment of cocaine dependent treatment seekers with adult ADHD: double-blind comparison of methylphenidate and placebo. Drug Alcohol Depend 87:20–29

Mészáros A, Czobor P, Bálint S et al (2009) Pharmacotherapy of adult attention deficit hyperactivity disorder (ADHD): a meta-analysis. Int J Neuropsychopharmacol 12:1137–1147

Nigg J (2005) Neuropsychologic theory and findings in attention-deficit/hyperactivity disorder: The state of the field and salient challenges for the coming decade. Biol Psychiatry 57:1424–1435

Pennington BF, Ozonoff S (1996) Executive functions and developmental psychopathology. J Child Psychol Psychiatry 37:51–87
Plomp AS, Bergen AA, Florijn RJ et al (2009) Pseudoxanthoma elasticum: Wide phenotypic variation in homozygotes and no signs in heterozygotes for the c.3775delT mutation in ABCC6. Genet Med 11:852–858
Proal E, Reiss PT, Klein RG et al (2011) Brain gray matter deficits at 33-year follow-up in adults with attention-deficit/hyperactivity disorder established in childhood. Arch Gen Psychiatry 68:1122–1134
Safren SA, Perlman CA, Sprich S et al (2005) Mastering your adult ADHD: a cognitive-behavioral therapy approach. University Press, New York
Safren SA, Sprich S, Mimiaga MJ et al (2010) Cognitive behavioral therapy vs relaxation with educational support for medication-treated adults with ADHD and persistent symptoms: a randomized controlled trial. JAMA 304:875–880
Shaw M, Hodgkins P, Caci H et al (2012) A systematic review and analysis of long-term outcomes in attention deficit hyperactivity disorder: effects of treatment and non-treatment. BMC Med 10:99
Simon V, Czobor P, Balint S et al (2009) Prevalence and correlates of adult attention-deficit hyperactivity disorder: meta-analysis. Br J Psychiatry 194:204–211
Sonuga-Barke EJ (2003) The dual pathway model of AD/HD: an elaboration of neuro-developmental characteristics. Neurosci Biobehav Rev 27:593–604
Swanson J, Baler RD, Volkow ND (2011) Understanding the effects of stimulant medications on cognition in individuals with attention-deficit hyperactivity disorder: a decade of progress. Neuropsychopharmacology 36:207–226
van de Glind G, van den Brink W, Koeter MW et al (2013) Validity of the Adult ADHD Self-Report Scale (ASRS) as a screener for adult ADHD in treatment seeking substance use disorder patients. Drug Alcohol Depend 132:587–596
van de Glind G, Konstenius M, Koeter MW et al (2014) Variability in the prevalence of adult ADHD in treatment seeking substance use disorder patients; Results from an international multi-center study exploring DSM-IV and DSM-5 criteria. Drug Alcohol Depend 134:158–166
van Emmerik-van Oortmerssen K, van de Glind G, Koeter MWJ et al (2014) Psychiatric comorbidity in treatment-seeking substance use disorder patients with and without attention deficit hyperactivity disorder; results of the IASP study. Addiction 109:262–272
van Emmerik-van Oortmerssen K, van de Glind G, van den Brink W et al (2012) Prevalence of attention-deficit hyperactivity disorder in substance use disorder patients: a meta-analysis and meta-regression analysis. Drug Alcohol Depend 122:11–19
van Emmerik-van Oortmerssen K, Vedel E, Koeter MW et al (2013) Investigating the efficacy of integrated cognitive behavioral therapy for adult treatment seeking substance use disorder patients with comorbid ADHD: Study protocol of a randomized controlled trial. BMC Psychiatry 13:132
Volkow ND, Wang GJ, Fowler JS et al (2012) Addiction circuitry in the human brain. Annu Rev Pharmacol Toxicol 52:321–336
Wilens TE, Adler LA, Weiss MD et al (2008) Atomoxetine treatment of adults with ADHD and comorbid alcohol use disorders. Drug Alcohol Depend 96:145–154
Wilens TE, Biederman J, Faraone SV et al (2009) Presenting ADHD symptoms, subtypes, and comorbid disorders in clinically referred adults with ADHD. J Clin Psychiatry 70:1557–1562
Wilens T, Faraone SV, Biederman J (2004) Attention-deficit/hyperactivity disorder in adults. JAMA 292:619–623

Addiction and Autism Spectrum Disorder 14

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Abstract

At first glance, addictive and autism spectrum disorders (ASD) seem absolutely unrelated. However, in clinical practice this does not appear to be true at all. Many individuals with autism, neurobiological characterized by dopaminergic deregulations, are at high risk for developing addictive behaviors. A prime reason might be to alleviate the high levels of stress and anxiety that they experience in an environment with stimulus overload or in engaging in social

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situations. The use of substances or repetitive behaviors and bizarre habits may develop rapidly into substance use disorders or behavioral addictions. In some cases the diagnosis of ASD will have be made earlier in life, but parents and workers in the field of autism are often unaware of addiction as a comorbid condition to ASD. Conversely addicted individuals may have an autism spectrum condition that is not recognized, because both relatives and workers in the field of addiction and psychiatry are often unfamiliar with signs of ASD and unaware of the potential comorbidity. Thus the identification of both conditions is a core issue in managing comorbid ASD and addiction. Guidelines for ASD provide useful tools for assessment and guidance for treatment. In relapse prevention interventions, identifying those situations that cause stress and elicit addictive craving and behaviours is crucial. Training skills to learn how to cope, in another ways than by using substances, with these situations are essential within the treatment. In addition, rational pharmacotherapy may prove very helpful.

14.1 Introduction

Few people in the field of addiction and psychiatry are familiar with Autism Spectrum Disorders (ASD). Conversely most workers in the field of ASD are unaware of addiction and addictive behaviour in their patients. Yet in clinical populations prevalence of comorbid ASD and addiction is rather common (Singh et al. 2012; Sizoo et al. 2009; Van Wijngaarden-Cremers and Van der Gaag 2010). Due to a lack of awareness, knowledge and experience, both addictive behaviours in individuals with ASD as ASD in addicted individuals are often overlooked. This is detrimental for these patients and for their direct environment. Moreover, it leads to confusion and frustration in therapeutic teams that feel incapable of addressing these challenging behaviours that do not respond to the routine in their treatment plans and guidelines. Before entering into the theoretical overlaps between both disorders and the consequences for rational treatments, first two clinical cases two illustrate the point.

14.2 Case Histories

14.2.1 A late diagnosis: Peter, a case of marked autistic rigidity

Peter was 20 years of age when he was admitted to a detox unit with serious alcohol dependence and features of a cluster B personality disorder. He was pretty aggressive and would get extremely cross when hindered by his parents or others to consume alcohol. The detox did not pose any problems. These occurred when at the start of the rehabilitation he was assigned doing tasks within the group therapy. That day he had to do the shopping for the dinner. The therapeutic goal of such tasks is to learn how to perform tasks within a

certain time frame and take responsibility for oneself and others. He managed to get the shopping done in time but was tidying them at the time when he was expected to join a group therapy session. When one of the nurses confronted him, he went out of his mind, became very aggressive, and bashed doors and broke windows whilst threatening the nurse verbally. Due to this unacceptable behaviour he was dismissed from the program immediately. A week later he came back to our outpatient clinic and was asked what had happened and had caused his extreme reaction. He said that he became very angry because the nurse had interrupted him. It was for him inconceivable that he should have joined the group leaving his task unfinished. In the clinical interview it became clear that these rigid patterns of behaviour, his incapacity to communicate and an impaired social sensitivity had been characteristics during his whole development. Alcohol helped him to ease the path towards social encounters with others. A thorough assessment including interviews with his parents and the reading school reports confirmed a diagnosis of Asperger's within ASD. Once approached as such this difficult to handle young adult became compliant, cooperative, well willing, and managed to stop abusing alcohol.

Reflecting on this case one discovered that Peter's parents were utterly shocked when they realised that he had been consuming large quantities of alcohol. They had always known him as a strikingly honest lad. As from preschool he was extremely interested in archaeology. So were his "friends". These friends were very welcome, as he had none in his regular classes. He joined archaeological summer camps. In retrospect he may have started drinking at that point of time. Gradually his parents realized he was drinking before social events, possibly to reduce his "social" shyness (in retrospect anxiety). The explosions of anger such as they were seen in the detox, were also familiar to his parents. But they were surprised because up to then this only manifested in that way at home. He would have fierce anger tantrums whenever things did not go according to plan that is to say when he was not told on forehand. Parents were always worried about unexpected things beyond their control, such as spontaneous visitors, because they would have disastrous consequences. As a worker in the archive department at the town hall, he was valued for his accurate and precise way of working and his knowledge. Yet over the past months he was more stressed and a faint smell of alcohol during daytime had not gone unnoticed.

14.2.2 From ASD to Substance Abuse: Sarah, a preoccupation run out of hand

Sarah is a 14-year-old adolescent diagnosed with Asperger's. At the elementary school she was well accepted as a pedantic eloquent, clumsy girl with a special interest for all that was related to nature. She collected leaves and feathers and always had a tame rat under her pullover. She was left alone and no one dared to tease or bully her. She did well and went to the gymnasium the highest secondary school type in our country with Latin, Greek and sciences. Her interest shifted from nature to gaming. She would spend hours in a row, playing games and chatting with virtual friends. Once in a while these would organize meetings. There she met people who drank and smoked pot. She liked it because it helped her overcome her shyness. The group went on and experimented with speed. Her parents are amazed to witness a metamorphosis from socially aloof towards suddenly, spending time with "friends". One day they get a phone call from the police. Their daughter has been

arrested for dealing drugs. She has been used and (sexually) abused by dealers and used as a drugs courier. She confessed in a very naive manner, once in the detox, that she thought these were her first real friends and would do anything to be their friend. Once in detox she reappeared to be the socially isolated and clumsy intelligent young girl.

Reflecting on this case: Sarah is anxious and confused. She experiences flashback memories of being forced into sex by "boys" in her junk scene. Often she feels a complete outsider and a spectator of her own life. She feels filthy and betrayed when she finally thought she had found friends in the scene. It felt so much better than having only her tame rat as a companion. In secondary school her preoccupation was entirely out of tune with her peers who wanted to date and have fun. She was surprised when a boy showed interest in her rat. He asked her to join him and offered her a joint. When he insisted that they should have sex, she complied not daring to refuse, but feeling awfully miserable. She wanted to be part of the group and gave in. Finally people seemed interested in her. But as she was abused over and over again, things got out of hand and lead to her decompensation.

14.3 Epidemiology

Awareness to addictive behaviours in individuals with ASD has only been raised recently. There is a remarkable paucity of solid epidemiological data on the extend of the problem. Only recently have studies on comorbidity in ASD included substance use disorders in their listings on clinical samples in adults (Hofvander et al. 2009; Lugnegård et al. 2011). The prevalence of addiction in those ADS populations (19 %, respectively 16 % in both studies) is higher than that reported in the general population but lower than the reported prevalence of substance use disorders in other developmental psychiatric disorders such as ADHD and schizophrenia. Yet it could be hypothesized that one in five to six in individuals with ASD is only the top of an iceberg as in none of the studies thus far behavioural addictions such as (internet) gaming, Internet use, shopping, and stalking were taken into account.

14.4 Theoretical Underpinnings and Causal Pathways

At first glance addiction and autism seem very different disorders. In some respects they even seem to be each other's antipodes. The socially aloof naïve person with autism on one side, and the cunning, lying addicted individual on the other. But alongside these big differences some striking behavioural similarities can be found, e.g. both groups are extremely detail oriented and compulsive. Moreover both are developmental brain disorders with a strong dopaminergic component in their pathogenesis (Dichter et al. 2012). At the start preoccupations (e.g. with spinning objects) and stereotype movements (rocking, whirling, swinging: sometimes leading to trance-like state) in ASD are aimed at soothing over-arousal, stress, and anxiety. Likewise addiction often starts with taking substances or behaviours

(gambling) to feel better and regulate difficult to manage tensions. Stimulation of the dopaminergic reward system by substance use or habit behaviour might not only give a "good" feeling but also help to cope with scary, stressful situations.

So are there common neurobiological characteristics to both conditions? Recent studies provide some evidence for such neurobiological overlap in the dopaminergic deregulation of the cortico-striatal-limbic loop (leading to skewed and compulsive behaviours) both in addiction and autism (Langen et al. 2011). In this respect ASD is in terms of dopaminergic deregulation at the interface of ADHD on one side, addiction on the other along with obsessive–compulsive disorder (OCD). The motor stereotypies may point to a motor component related to motor neurological disorders such as Parkinson's disease. But this is yet small evidence in need of far more research to identify these relationships and the possible neurobiological links explaining the enhanced vulnerability to addictions in ASD.

In high functioning individuals with ASD a strong urge for social relationships emerges at puberty (Gerland 1996). But they have great difficulties in the social encounters due to their hampered empathy, lack of understanding of underlying intentions of others, and their relative incapacity to tune into other's needs. Alcohol and drugs prove helpful in overcoming their social awkwardness and shyness. They feel less uncomfortable and more at ease in engaging in social contacts. Yet their eagerness and naïve perception of others, makes them an easy prey for abusive individuals, e.g. the drugs scene. Of interest they often feel more at home in these substance using social groups that are, strangely, remarkable functional in the sense that the have strait forward rules of conduct and many visual cues.

14.5 Diagnosis

The screening and diagnosis of addictive disorders has been documented extensively in Chap. 17. Diagnosing Autism Spectrum disorders starts with screening and identifying of ASD in adults. The joint Anglo-Dutch guidelines (NICE 2012) urge to consider for possible autism when a person shows clinical features relating to the core symptoms of autism. These are, for example persistent difficulties in social interaction and social communication, stereotypic (rigid and repetitive) behaviours, and restricted interest and resistance to change. But also other features need to considered, i.e. when a person has difficulties in initiating and sustaining social relationships, problems in obtaining and sustaining education or employment, and or has a history of a neurodevelopmental condition (including learning disabilities and attention-deficit disorder) or mental disorders (especially anxiety, depression of borderline personality features in women). The further screening process can be facilitated by using the Autism-Spectrum Quotient—10 items (AQ-10), a short screening instrument for adults with suspected autism (Allison et al. 2012).

After a positive screening, a specialized multidisciplinary team should conduct a comprehensive assessment. They will look into the core signs and symptoms of autism, functioning at home, in education and employment, but also into social

flexibility such as participating in free-time activities and review carefully the developmental history. Part of the assessment will include enquiring about alcohol, drug use patterns, and repetitive and self-harming habits. It is also important to assess the perception style in the individual and ask for attention for detail. Important is to note that attention should be given to hyper- and hypo-sensory sensitivities as they can be a great source of discomfort and suffering that might lead to soothing habits as drugs- and medication abuse.

Different standardized assessment tools can be considered:

- The Autism Diagnostic Interview (ADI-R) (requires special training) (Lord et al. 1997)
- The Autism Diagnostic Observation Schedule—Generic Module 4 for Adults (Lord et al. 2000)
- The Adult Asperger Assessment (AAA) (Baron-Cohen et al. 2005)
- The Ritvo Autism Asperger Diagnostic Scale—Revised (RAARS-R) (Ritvo et al. 2011)

A neuropsychological assessment can prove very useful. It may help to underpin not only the weaknesses but also the strengths of the individual that need to be taken into account by those living or working with the person with ASD.

A detailed functional analysis of functioning is a welcome method to assess stress and arousal. This will help to identify situations in which the individual with ASD experiences high levels of stress and discomfort and may want to engage into addictive behaviour.

14.6 Treatment

14.6.1 Translating Into Clinical Practice

There is a variety of guidelines available on both ASD (e.g. NICE; ASD in children and adolescents revision 2011—first guideline for ASD in adults 2012; interestingly jointly developed with the Dutch Guideline in Autism in Adults) as on substance abuse drug disorders (e.g. NICE Drug misuse 2007 revised in 2011). Yet none of them includes the other condition as a possible co-morbid condition. The NICE guidance on ASD points attention for the need of always taking ASD into account when dealing with co-existing psychiatric conditions. This recommendation strengthens the intuitive clinical feeling that in treating individuals with ASD/SUD or SUD/ASD priming for ASD is important. One should tune into the communicative and structural needs of the person with ASD, in order to make treatment and guidance in this particular comorbidity possible. It is important also because in the causal pathway, as illustrated in both clinical vignettes, ASD is (even if not acknowledged for as such) present well before drugs misuse or addictive habits and behaviours occur. Therefore from a point of view of clinical experience (no comparative trials have been conducted thus far) it seems crucial to start with

treating the autistic condition, whilst addressing the addiction problem concurrently. Even in situations of acute detoxification approaching the patient with ASD in an appropriate, adapted way is very important. At the same time the treating physician/multidisciplinary team should perform a comprehensive diagnostic workout to get a profile of strengths and weaknesses and through functional analysis understand when and why the addictive component came in. This is essential. Because this precipitating factor will need close attention in order to adequately prevent relapse. Indeed, if the patient with ASD uses drugs to overcome social anxiety the treatment approach will be different in terms of skills training, than when the drugs and habits were first used to combat boredom and solitude or depression.

14.6.2 Characteristics Clinical Guidelines

In most clinical guidelines as summarized in the recent NICE guidelines, the essence of the treatment of ASD is that it requires specific knowledge and expertise and experience of the disorder. Professionals that are knowledgeable of ASD should perform the treatment and guidance for ASD and its coexisting conditions. In the case of the co-occurrence of ASD and substance misuse this asks for more than expertise in the field of ASD alone, as the combination of these skills is much more rare in professionals than the coexisting of ASD and addiction in patients. This needs specific attention in professional training and when considering the palette of competences required within multidisciplinary teams.

Adequate, adapted communication is primordial. Professionals dealing with patients with co-existing ASD and Addiction should know how to adequately communicate with people with ASD. And they should be trained in taking the ASD patient's point of view and his needs into account.

Professionals have to be prepared to team up with parents and relevant relatives and take a comprehensive approach ensuring quality of life in its entire facets. This requires coalitions with departments and services specialized in addiction (psychiatry).

The steps in the ASD schedule (NICE and Dutch Guidelines 2012 ASD in Adults) include:

1. (adapted) psycho-education: offering comprehensive information
2. Psychosocial Interventions aimed at the core symptoms of ASD
3. Psychosocial interventions focused on lifestyle skills
4. Adapted interventions aiming at reducing challenging behaviour
5. Biomedical treatments if additionally necessary

The schedule of management of substance use disorder is:

1. Detoxification
2. Psycho-education

3. Cognitive behaviour therapy: cue identification and relapse prevention—learning alternative skills to cope with craving.

14.6.3 Pharmacotherapy

There is no literature on addiction pharmacotherapy in individuals with ASD and in our perception rarely a need or indication for pharmaceutical substitution. In contrast, pharmacotherapy may play an important role in alleviating the pain and distress, associated with the high arousal, stress, and anxiety levels, when individuals with ASD engage in social situations. Pharmacotherapy aimed at stress reduction with none addictive agents (e.g. SSRIs or beta blockers) may be considered as well as low dosage antipsychotic drugs. Social isolation and a low self-esteem may induce depressive feelings and even a full-blown depression. These may necessitate a pharmacological intervention with SSRIs. Likewise pharmacotherapy may be considered in cases of comorbid ADHD with impulsive symptoms (methylphenidate) or in cases of challenging/conduct problems (low dosages of neuroleptic drugs).

It should be noted that individuals with ASD might respond differently to medication: high effect at low dosages and/or more side effects.

14.6.4 Case Conceptualization and Management Plan

Peter's ASD diagnosis was not known before he entered the department of addiction psychiatry. In retrospect he started drinking to help him break out of his social isolation. For him and his family the diagnosis was new. After detox the management plan focussed on

1. Psycho-education in which he and his parents were provided with general facts on ASD and specific information regarding his personal diagnostic profile
2. This diagnostic profile stemmed from a systematic assessment of his characteristics with his strengths and vulnerabilities. These are key features and the basis of a personalized management plan tailored to the individuals needs
3. Individual or group psychosocial skills training
4. Adapting the living and working environment to the needs of the individual with ASD. This might include providing information (together with the patient) to employers/co-workers—or teachers and fellow students on ASD, on how to approach, involve and help the individual with ASD in everyday life.

In cases of coexisting addiction an important addition to this therapeutic management scheme is *relapse prevention* (Roozen et al. 2007):

(a) Cue identification: learning to identify the moments and circumstances, which trigger the compulsive urge to start drinking
(b) Learning alternative behaviours and skills to cope with tensions and craving in a sound way. It helps to make lists of alternatives for using/abusing. Learning effective relaxation techniques proves helpful.
(c) Developing and training social skills to enlarge the behavioural repertoire in social circumstances in order to make ones point clear and communicate ones fears and needs.

All involved in the ASD/Addiction management schedule should be aware of the strong persistence of these problems: ASD and addiction are lifelong conditions. Of importance, in substance use disorder relapse is always an issue specifically when circumstances elicit tension and anxiety.

The second vignette has a different history that is of consequence for the management plan. Sarah had been in an ASD guidance plan as from the beginning of elementary school. Her parents were given support and trained in helping to activate Surah and stimulate her in social encounters and communicating. They had learnt how to explain Sarah's condition to others. But the support from the Autism Team ceased during middle school. She seemed to be doing well and to be more socially integrated. Her "better" functioning was misleading and formed a pitfall. The continuity of the support and guidance was not offered. In fact new impeding factors were overlooked. Suzan's case is far more complex. Alongside with the ASD features and emerging addiction problem, in her case traumatization played an important role in the dramatic course of her history. This has consequences for her management plan and based on her updated actual diagnostic status. It confronts us with lessons to be learnt in terms of continuity of support that will be discussed afterwards.

In the case of more complex comorbidity the management plan, based on the diagnostic appraisal will be more extensive.

1. The psycho-education should include besides information on the development of autism in adolescence, lessons to be learnt on boundaries between people and how to assert one's position in view of others in this case boys and men.
2. Relapse prevention should include learning to discriminate external and internal cues pointing to a transgression of boundaries and the potential re-enactment of (sexual) abuse and trauma.
3. Dealing with traumatization. This starts with psycho-education on post-traumatic stress disorder. This includes working through the various symptoms: flashbacks, dissociation, eroticized revenge actions. . .
4. Learning and training alternative skills to help her cope with discomfort in social encounters and situations and dealing with intimacy and avoiding no consented intercourse

The two vignettes show that in management of coexisting ASD and Addiction a proper assessment is crucial to understand why both conditions occur and how they

relate to each other. This functional analysis, which should consider even more coexisting problems (e.g. anxiety, depression, posttraumatic stress disorder among others), forms the basis for a comprehensive treatment plan that should take a broad perspective not only on treating psychopathology, but also considering social insertion in terms of housing, working/studying. The second lesson is that guidelines are of great help if they are applied in a sensible way. In the case of comorbid addiction in ASD cases, the approach of ASD should prime in order to facilitate communication and a better involvement and participation of the person with ASD the treatment plan and a better communication towards his/her environment.

14.6.5 Course of Treatment

Peter got back to work. Through the Adult Autism Society he has acquired some valuable chat-contacts. In the weekends he participates in a local autism "social" club. He got support from the department of occupational medicine who helped him explain to his colleagues at work both about his autism and his alcohol problem. The autism team helped him find his way to sheltered housing for adults with autism. During his holidays he experienced a big relapse. Neither Pieter nor his buddy had anticipated this fall-back. This made even clearer how important it is to take all aspects and situations into account that may cause stress with a craving for alcohol as a consequence. The relapse event was used in the treatment as a learning moment, to raise even more Pieter's awareness of his vulnerability for addiction. A consequence he had to face was that he is and will be unable to switch to "social drinking" and should be fully abstinent.

Sarah's treatment appeared to be much more difficult. Members of the Autism team found it difficult to reengage in contact and find new means of tuning into Sarah, as she had become no longer the aloof, rigid, preoccupied girl that needed training in structure and stimulation. Working with her challenging behaviour (anger, anxiety, and fragmented confusion on her depersonalization {estranging from herself}) was beyond their scope of competences. Her rapport with the junk scene and eroticizing behaviour were equally unfamiliar to them.

But on the other hand the addiction psychiatry couldn't cope with her either. The workers in that field were disconcerted by her tendency to take everything literally. Their confronting techniques and working through relationships and pushing her into group therapy were utterly unproductive. When she got referred to a dual-disorder setting with experienced professionals (psychiatrists/psychotherapists) things turned for the better.

Their approach was multimodal: first and most important was to perceive the world and her problems from her point of view. And take this as the starting point. From there on, she was encouraged to learn to discriminate thoughts and feelings and separate facts from (internal) beliefs. This cognitive-behavioural therapy adapted to her specific needs proved helpful. It enabled her to acknowledge feelings, the confusing experience of longing to belong to a social group versus

the anxiety emanating from (too intrusive) intimacy. This individual CBT was combined with education on relationships, sexuality, and boundaries. In these individual sessions she was educated and well informed on PTSD and on dissociation, in relation with the longing and craving for substances in order to sooth the internal pain. It took a long time before this approach turned into a success. Over and over again she teased out the therapists to check if she could trust them.

Now years later, she is still in contact with her psychiatrist, mainly through email. Her therapist works as a "Help-ego" to help her check her thoughts and feelings and reinforce the soundness of her ideas and decisions. She is now a successful university student and lives independently. She has a group of female friends as a warm support group. But intimacy is still a very sensitive issue. Her cravings and longings are the subject of her conversations with her doctor but no more drive her acting (out) in life. She uses sparsely and is in control.

Final Remarks and Recommendations

Coexisting ASD and addictive behaviours are far more common than often assumed. This finding strongly pleas for a better knowledge of developmental disorders and their interactions (e.g. addiction with ADHD and ASD both in men as in women). This should be implemented in medical education and clinical psychology and be part of postdoc training in medical specializations and clinical psychology. But theoretical background is not sufficient; professionals both in the field of ASD as in addiction should learn to work together. Clinical skills needed to make this mixture of expertise's, work, should be trained and supervised and tutored in those who feel still uncomfortable in dealing with this dual disorder. Motivating—confronting and relapse prevention on one hand, providing individual support and enhancing explicit communication and help in compensating for weak executive functions.

Finally and hopefully this chapter will have made a convincing point of continuous diagnostic evaluation as an important way of detecting underlying problems (such as trauma, anxiety, depression). Thus pleading for integrated clinical training schemes and cooperation between highly specialized services for the sake of good treatment for complex cases.

References

Allison C, Auyeung B, Baron-Cohen S (2012) J Am Acad Child Adolesc Psychiatry 51(2):202–212

Baron-Cohen S, Wheelwright S, Robinon J et al (2005) The Adult Asperger Assessment (AAA) a diagnostic method. J Autism Dev Disord 35:807–819

Dichter GS, Damiano CA, Allen JA (2012) Reward circuitry dysfunction in psychiatric and neurodevelopmental disorders and genetic syndromes: animal models and clinical findings. J Neurodev Disord 4(1):19. doi:10.1186/1866-1955-4-19

Gerland G (1996) A real person: life on the outside. Souvenir Press Limited, London

Hofvander B, Delorme R, Chaste P, Nydén A, Wentz E, Ståhlberg O, Herbrecht E, Stopin A, Anckarsäter H, Gillberg C, Råstam M, Leboyer M (2009) Psychiatric and psychosocial problems in adults with normal-intelligence autism spectrum disorders. BMC Psychiatry 10:9–35

Langen M, Durston S, Kas MJ, van Engeland H, Staal WG (2011) The neurobiology of repetitive behavior: . . .and men. Neurosci Biobehav Rev 35:356–365

Lord C, Pickles A, McLennan J et al (1997) Diagnsosing autism: analyses of data from the Autism Diagnostic Inverview (ADI). J Autism Dev Disord 27:501–517

Lord C, Risi S, Lambrecht L et al (2000) The Autism Diagnostic Observation Schedule—Generic: a standard measure of social and communicative deficits associated with the spectrum of autism. J Autism Dev Disord 30:205–223

Lugnegård T, Hallerbäck MU, Gillberg C (2011) Psychiatric comorbidity in young adults with a clinical diagnosis of Asperger syndrome. Res Dev Disabil 32(5):1910–1917

NICE Guideline on Autism in Adults (2012) ASD in Adults http://guidance.nice.org.uk/CG142

Ritvo RA, Ritvo ER, Githrue D et al (2011) The Ritvo Autism Asperger Diagnostic Scale—Revised (RAADS-R): a scale used to assist the diagnosis of autism spectrum disorders in adults: an international validation study. J Autism Dev Disord 41:1076–1089

Roozen HG, Van De Wetering BJM (2007) Neuropsychiatric insights in clinical practice: from relapse prevention toward relapse management. Am J Addict 16(6):530–531

Singh SK, Hellemans H, Dom G (2012) Autism spectrum disorder and substance use disorder: an unknown comorbidity? Tijdschr Psychiatr 54(10):893–897

Sizoo B, van den Brink W, Koeter M, van Gorissen EM, van Wijngaarden-Cremers P, van der Gaag RJ (2009) Treatment seeking adults with autism or ADHD and co-morbid substance use disorder: prevalence, risk factors and functional disability. Drug Alcohol Depend 107(1):44–50

Wijngaarden-Cremers PJM, van der Gaag RJ (2010) Verslaving als ontwikkelings-stoornis. Een andere kijk op neurobiologie en Comorbiditeit. Kind Adolescent 31(4):174–187, Themanummer Verslaving onder Jongeren (Red Malous Kleinjan, Rutger C.M.E. Engels & Rutger Jan van der Gaag)

Dual Disorders: Mild Intellectual Disability and Substance Abuse

15

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Abstract

In European countries, there is an increasing awareness that substance abuse also occurs among people with a mild intellectual disability (MID). Individuals with MID often do not fit within the traditional (addiction) treatment systems and subsequently treatment outcomes can be poor. To improve outcome and treatment retention, programmes should be adapted to the specific needs and competences of these patients. This chapter describes substance abuse among people with MID from a European perspective. It aims at providing information and practical tools for both screening and treatment interventions.

15.1 Mild Intellectual Disability

An intellectual disability (ID) is defined by three aspects: significant cognitive deficits; a significant impairment in adaptive behaviour; and onset before the age of 18 (APA 2013). Adaptive behaviour can be impaired in different areas, such as communication, personal hygiene, independent living, social and relational skills, participation in society, autonomy, health and safety, applied knowledge, leisure, and work. An IQ between 50/55 and 70 is generally considered a mild intellectual disability (MID), an IQ between 70/75 and 85 is considered a borderline intellectual disability (BID) (APA 2013). Since persons with both mild ID and borderline ID encounter similar problems regarding substance use and substance use treatment, in this chapter, the term "mild intellectual disability" (MID) will be used for both MID and BID.

As can be concluded from the definition of MID, the difficulties of persons with MID are not limited to the cognitive domain and their academic performance. Some problems that are often seen in persons with MID are (VanDerNagel et al. 2013b):

- Cognitive deficits, which can be evidenced in a less structured way of information processing, difficulties with abstract thinking, a less well-functioning memory, a limited attention span, a limited insight in causality of behaviour, and less mental flexibility
- Delayed social and/or emotional development and psychological maturation
- Limitations in social adaptation. People with MID are more vulnerable in their social-emotional development, may experience difficulties in overseeing complex social situations and are less able to cope with the practical aspects of daily life
- Lack of self-control and a greater degree of impulsivity
- Low socio economic status (SES). Many persons with MID live in underprivileged neighbourhoods, have low incomes and limited access to (paid) work
- Co morbid psychiatric disorders. Apart from other developmental disabilities such as ADHD and ASS, examples are psychosis and mood disorders (see Sect. 15.2.2)
- Co-occurring behavioural disorders. Examples of problem behaviour are oppositional behaviour; aggressive or violent behaviour, suicidal behaviour and auto mutilation
- Somatic co morbidity, such as hearing and vision deficiencies, motor problems, and epilepsy

These examples illustrate the numerous and complex challenges that people with MID face. Many of their difficulties, and even their MID itself often go unrecognized (both by themselves and by professionals). The discrepancy between chronological age, level of cognitive development and level of social emotional development evidenced by these individuals poses additional difficulties, both for themselves, their families and those who care for them, as the case-example of Peter (see below) illustrates. People with MID therefore often need specific care and treatment services, including both long term and intensive counselling.

15.1.1 Case 1: Peter

Peter (51 years old, married with 2 teenage daughters) started working at the age of 14. He was "not fit for school, more of a practical guy", worked as a hired help at a transportation company, and at age 21 got a commercial driver's licence. Since then, he has been employed as a truck driver. He enjoyed his work on long haul projects, driving bulk-goods from Rotterdam harbour to all parts of Europe. Being a truck driver, he stuck to his bosses rule of "a beer or two max a day", during his long weeks from home. During the occasional week off at home, he tended to drink somewhat more. During this time he could increasingly more often be found in the pub. At one point his company underwent reorganization and Peter was assigned to parcel delivery service. To plan his deliveries all over the Netherlands, Peter had to work with an electronic route manager. In the new situation he had to work a tight schedule. This was too much for Peter: he encountered numerous problems with the device, ran late and got more, and more frustrated and annoyed (as did his customers). After 2 weeks of trying to fulfil his new assignment, he went on sick leave. Bored at home, he spent more and more time in the pub, drinking until the point of obliviousness. When he had to visit the doctor to get a sick note, he was referred to a counsellor because of his drinking. During the intake, it became clear that Peter struggled to adapt not only to his new working conditions, but also to his role in his family, now that he spent more time at home. Drinking seemed Peters "solution" to ease his anxiety and stress. Peter was referred for psychological evaluation, during which it became clear that Peter could neither read nor write. He tested in the mild to borderline IQ range, with a verbal IQ of 74, and a performance IQ of 69. Only after this test did Peter reveal that as a child, he attended a "school for retarded children".

As the case of Peter illustrates, it may not immediately become clear during treatment that a person has MID. Though many persons with MID can benefit from social services for those with ID (such as sheltered living, sheltered working, or community-based services), a large majority (especially those with borderline ID) does not receive specialized help. In fact, many individuals with MID do not see themselves as being "handicapped" and may therefore refuse specialized services themselves. Others may have had some specialized care in the past, but then terminated the service, often because of a need of more autonomy and independence. Most countries currently have policies that encourage more inclusive

societal or community-based care. This allows many people with MID to live a "normal" life, albeit with a little help. Thus, the fact that a patient holds a job or lives with a family of his own, does not preclude him from having an MID.

15.2 Prevalence and Determinants of Substance Abuse Among People with Mild Intellectual Disability

MID is a common disability in all European countries, but no prevalence rates on a European level are available. In the Netherlands (a population of almost 17 million people) for example, it is estimated that 120,000 people have an intellectual disability (IQ lower than 70), of which 60,000 people have a mild intellectual disability (IQ between 50 and 70). Approximately two million people have a borderline intellectual disability (IQ between 70 and 85) (Ras et al. 2010). In the last decade, it has become clear that substance use is prevalent among those with MID, and that this concerns all types of substances including illicit drugs (To et al. 2014; VanDerNagel et al. 2011a).

Prevalence estimates for MID substance abusers in Europe suggest lower rates of alcohol and drug use and similar rates of smoking when compared to corresponding rates for the general population. In general, it is estimated that 3 % of all people with ID have problems with alcohol or drug use. However, several methodological issues limit the generalizability of international study findings regarding prevalence rates to a large MID population. Methodological reasons also complicate comparisons across countries, and between studies and subgroups. For instance, substance abuse is more common among people with MID and especially BID than among those with a moderate and severe intellectual disability (McGillicuddy 2006).

Well known risk factors of substance abuse, such as low socioeconomic status, problems with social contacts, behavioural and psychiatric problems, coping skill deficiencies, work-related problems, and financial problems are more often seen among people with MID than among their peers without MID (Hammink and Schrijvers 2012). Substance abuse among MID is also associated with co-occurring severe behavioural problems and/or psychiatric problems (Caroll Chapman and Wu 2012; Didden et al. 2009). Additional determinants of increased substance abuse are inadequate coping skills, struggling with feelings of loneliness, stigmatization, and limited social skills. Furthermore, the desire to fit in and be socially include is an important reason for using substances and could therefore be seen as a risk factor of substance abuse (Caroll Chapman and Wu 2012). Substance abuse in any population is associated with severe physiological, psychological, and social problems. The consequences of substance use among people with MID may be more severe because of higher levels of somatic and psychiatric co-morbidity (McGillicuddy 2006), prescribed medication and social factors including difficulty accessing appropriate treatment (Slayter 2010), work-related problems and social interaction problems.

15.2.1 Substance Use and Substance Abuse in Intellectual Disability Settings

In many European countries, changes in health-care systems have led to a greater degree of deinstitutionalisation and integration of people with MID in the community. It could be that these changes lead to an increased vulnerability of substance abuse among people with MID. However, substance use and abuse is common in all subgroups of MID, including those in residential care (VanDerNagel et al. 2011a). The use of psychoactive substances (other than prescribed drugs) may in itself be a problem for ID settings, as some institutions have regulations against using substances. Other settings allow use of (some) substances, mostly limited to alcohol and tobacco, provided that staff members and other patients are not confronted with excessive use or negative consequences. Although these rules may provide support for some patients to stay clear of substance use, others might not be deterred. In ID services that ban (all or some) substance use, the substance use may go underground, or clients might use within their own quarters or outside the facility, and refrain from asking help when substance use poses problems. Several ID-facilities across Europe recognize this risk, and have started programmes to promote early identification and—if needed—adequate referral to substance treatment facilities. For instance, several ID facilities in the Netherlands and Flanders have implemented the use of the SUMID-Q, a Dutch instrument used to screen for and assess substance use (risk) among patients with ID (see Sect. 15.4). Unfortunately, such programmes are not widely implemented yet.

15.2.2 Triple Diagnosis: Mild Intellectual Disability, Substance Abuse, and Psychiatric Problems

Co-occurring psychiatric problems are an additional risk factor for substance abuse among people with MID. At the European level, little is known about prevalence rates of MID substance users with co-morbid psychiatric problems. In a Dutch sample of 185 MID individuals admitted to substance abuse treatment facilities, 42 % had a co-occurring behavioural or emotional problem (Didden et al. 2009). In a sample of 115 MID adults seeking mental health services in London, 8 % were current substance abusers and 15 % had a history of substance abuse (Chaplin et al. 2011). These numbers suggest a need to incorporate the comprehensive assessment of substance abuse and psychiatric disorders into treatment plans for people with MID in mental health or psychiatric settings. Not in the least because triple diagnosis is often combined with problems in other areas such as housing, work, and social relationships.

The assessment of co-occurring psychiatric problems in those with MID and substance use disorder poses additional challenges to mental health care professionals for a variety of reasons. First, it requires knowledge of three fields of (mental) health care (addiction, general psychiatry and ID care). Though several countries (e.g. the UK) have excellent mental health services for those with MID, these services often do not include addiction services. Second, there is a lack of appropriate diagnostic

instruments and assessment methods for psychiatric conditions among those with MID. Third, psychiatric conditions may present differently among those with MID, and especially when there is co-occurring substance abuse.

15.2.3 Case 2: Claire

Claire is a 21 years young woman with trisomy 21 (Down's syndrome). At the age of 18 she moved to a community-based training house, to learn skills needed to live on her own. Shortly after this move, she experienced a depressive episode. This was attributed to the changes in lifestyle and demands associated with these changes and successfully treated with cognitive behavioural therapy in combination with temazepam prescribed by her GP because of her sleeping problems. After this major episode, Claire has generally been doing well. With some help of the ID service staff, she started working as an aid at a food court. Here she enjoyed serving customers and meeting new people. In the last year or so, she started to "hang out" with some of the local youth after work. After a while, she even joined this group on Friday night outings. At first the staff members applauded this, since making friends had always been difficult for Claire. However, after six months, there were some concerns. Claire was late in returning to the house several times and disregarded house rules regarding alcohol use and smoking. She also started talking rudely to the staff, claiming that she "was entitled to make her own choices". Even more concerns arose when Claire asked her older sister if she had ever tried ecstasy pills or speed. Fortunately, Claire also remained interested in improving her adaptive skills. Although she was always a bit anxious about living on her own, she seemed to consider this to be a serious option in the last few months. She even planned to get her drivers' licence, which appeared impossible, as Claire has difficulties negotiating busy traffic even when on foot. One Saturday, things went wrong. Claire, who had been partying the night before, was irritated by the sounds of her housemates and picked a fight. She ended up assaulting a staff member who tried to intervene, and kept yelling that she was to make her own choices. Even her parents were unable to calm her down. Even though the yelling stopped, Claire stayed restless, very talkative, and full of plans of how she wanted to change her life by moving out instantaneously, getting a better paid job and finding someone to start a family of her own. Nobody slept well that night, including Claire, who kept packing and unpacking her suitcase. The next day, Claire agreed to talk to a person of specialized mental health services, and eventually was admitted with a tentative diagnosis of "drug induced psychosis or mood disorder". Only when her irritability, grandiose and racing thoughts, sleeplessness, and restlessness did not subside after several weeks, did she receive the diagnosis of Bipolar I disorder.

The case of Claire illustrates how symptoms can be interpreted as being signs of psychological development, a struggle with discrepancy between abilities and social demands, a part of substance (induced) disorder, psychiatric illness, or a combination of these. This diagnostic puzzle can be further complicated by prolonged and progressed psychiatric illness, severe social problems (marginalization), forensic issues, medical conditions, etc. Therefore, a full assessment needs to be made, preferably by (a team of) clinicians with specific skills in working with

this group. In order to diagnose psychiatric disorders in people with MID, a healthcare professional can use the Diagnostic Manual-Intellectual Disability (DM-ID, Fletcher et al. 2007), an adapted version of the DSM-IV. The DM-IDII is currently being developed as an adapted version of the DSM-5.

As for the treatment of triple diagnosis, strategies for integrated treatment of dual diagnosis generally apply, as long as adaptations are made to better suit the needs of those with MID (see Sect. 15.5.2). Pharmacotherapy can often be necessary, but attention has to be paid to severe or unexpected side effects, as these seem to be more common among those with MID. For instance, benzodiazepines may lead to paradoxical agitation, or conversely, to severe drowsiness. Patients with MID may benefit from psychological treatment, including CBT and EMDR as well. In addition to the treatment of the patient's symptoms, psychoeducation of family and professional caregivers is essential, as is developing a relapse prevention plan in collaboration with these parties.

15.2.4 Substance Abusers with Mild Intellectual Disability in Forensic Settings

Substance abuse and forensic problems seem to be associated for MID substance abusers as well. However, little is known about the prevalence of MID substance abusers in forensic settings on a European level. In a Belgian sample of detained substance abusers, 50 % had MID (Vandevelde et al. 2005). These patients had more additional problems than detained substance abusers without MID, such as family issues and psychological problems. Another comparison, in this case between Dutch delinquent adolescents with and without MID showed that 56 % of the delinquent adolescents with MID used alcohol and 46 % used drugs compared to 27 % and 4 % among non-delinquent adolescents with MID (VanDerNagel and Kea 2013). Professionals in forensic settings may find it difficult to identify MID, substance abuse, or both. This makes providing sufficient care and preventing recidivism a challenging task.

In the Netherlands, an intervention called "Stay-away Plus" (Den Ouden et al. 2011) was developed specifically for adolescents with MID and substance abuse problems in the juvenile system. Characteristics of this intervention are a slower work pace than the regular Stay-away intervention, more room for explanation and repetition, more use of visual tools and less writing assignments. Increasing social control and avoiding risk situations are important goals, alongside increasing self-control. Another important characteristic is the involvement of an elder or counsellor to ensure generalisation towards external situations and external control or boundaries.

15.3 Screening for Mild Intellectual Disability in (Addiction) Care

For professionals in addiction care, mental health care and forensic care, it can be difficult to recognize MID. Screening for MID in these settings is important, but in most European countries validated screening instruments are lacking. An example

of a valid screening instrument, developed in the UK, is the Child and Adolescent Intellectual Disability Screening Questionnaire (CAIDS-Q). Another screening instrument, that can be used among people aged 13 and older, is the Hayes Ability Screening Index (HASI, Hayes 2000). This instrument has been translated into several languages, including Dutch and Norwegian. If available screening instruments are not (yet) in use, professionals must be alert for signs that might indicate MID, such as (Didden et al. 2013):

- Unfinished primary school, grade retention, history of special education
- Limited or absent social network
- Use of simple language, incorrect use of more complex expressions, or prototypical use of standard phrases ("parroting" others expressions)
- Difficulties with comprehending language, as can become apparent when asked to summarize the conversation
- Reading and calculating difficulties (especially multiplying)
- Difficulties in remembering what was being said
- Uncomfortable attitude towards difficult questions

An IQ-test can be used to determine MID, but psychiatric co-morbidity, cognitive damage due to frequent substance use, acquired brain injury or intoxication during performance of the test need to be taken into consideration during interpreting the results of this test. It is recommended to perform the IQ-test when a patient with MID and substance abuse is stable and sober for several (at least two) weeks, and if necessary repeat the test after a year. A full IQ-test is preferred over a shortened version or a screener.

The life course of a patient can further clarify whether cognitive or learning disabilities were present before the age of 18, before substance use, or can show that there was trauma that led to acquired brain injury. Neuropsychological tests could indicate whether there is damage due to substance abuse, such as attention deficits, disordered executive functioning (for example the ability to plan things ahead and impulse control), short-term memory, and orientation problems. Furthermore, verbal IQ seems to be less easily affected by substance abuse than does performance IQ.

15.4 Recognition and Screening of Substance Abuse in People with Mild Intellectual Disability

It is important to detect substance use in patients with MID in an early stage to estimate the risks and prevent development of problematic use. Most MID substance abusers start using substances in early to late adolescence. This means that professionals in special education schools or related settings need to be alert for signs of early substance use to prevent the development of problematic use (Caroll Chapman and Wu 2012). Many signs of substance use can also occur in people with MID that do not use substances. However, often signs of (problematic) use are behavioural changes or deterioration of physical functioning compared to the

period prior to (the increase of) substance use. Signs and signals of substance abuse can be divided into the following categories (VanDerNagel et al. 2013b):

- Physical signs (e.g. weight changes, increase in falls, poor physical condition)
- Psychological signs (e.g. mood swings, difficulty concentrating, deviant behaviour (aggression, disinhibition, peculiar behaviour, and fluctuating behaviour) without a clear cause
- Social signs (e.g. leaving school early, truancy, negligence of appointments, changing social environment, social isolation, police contacts)

No single symptom is "proof" of substance use and the signs and potential signals of substance use should be interpreted in the light of the general behavioural pattern of the person of interest.

In the MID population, signs and symptoms of substance use are often not recognized at all, or are misattributed to other factors such as physical or psychiatric conditions. It is only after the substance use problems have progressed, that (with benefit of hindsight), earlier symptoms are recognized as symptoms of substance (ab)use (Sturmey et al. 2003). Hence, there is a need for tools for screening and early identification. Unfortunately, screening and assessment of substance use in people with MID is hindered by a lack of suitable questionnaires (McGillicuddy 2006; VanDerNagel et al. 2011a). Widely used instruments that are validated for the general population (e.g. CAGE, MAST, AUDIT/DUDIT) require a basic level of knowledge, conceptual understanding, the ability to reflect on one's own behaviour, or an adequate memory that people with MID may lack. For instance, some patients use slang for the substances they use, and not recognize alternative terminology, or the fact that the term "drugs" applies to their use as well. Also, questions such as "how often do you drink to remediate symptoms of withdrawal" requires adequate memory and skills to relate causes and effects that persons with MID may lack. The fact that some questions may be too complex may not become clear during interviewing, as some persons with MID are (highly) suggestible, and may say "yes" or "no" according to their interpretation of what the interviewer wants to hear. To add to these problems related to structured questionnaires, some patients may tend to be secretive about their use, even when this is not in their best interest. All of these issues may lead to invalid responses when persons with MID are interviewed with unsuitable instruments (VanDerNagel et al. 2013a).

For this reason, VanDerNagel et al. (2011) developed a Dutch screening instrument, the Substance Use in Individuals with Mild Intellectual Disability-Questionnaire (SUMID-Q, Box 15.1) (VanDerNagel et al. 2011b). As far as we know, this is the only screening instrument as of yet available in Europe, which was specifically designed for the MID population.

Box 15.1. Steps of SUMID-Q

The SUMID-Q consists of several steps (VanDerNagel et al. 2011b):

Before step 1: Establish a good working relationship and be willing to discuss substance use in an open, empathetic way. Maintain this neutral stance and an inquisitive attitude during the whole interview.

Step 1: Talk about psychoactive substances in general

- Assess patient's familiarity with substances and his terminology (use pictures, starting with more common substances such as smoking and alcohol). Use the patient's terminology in the remainder of the interview, do not further enquire about substances the patient does not seem to be familiar with.
- Assess patient's further knowledge of and attitude towards each type of substance.

During this phase, remain interested in the patients opinion, do not correct or confront him/her unless you are asked for your opinion (if so, briefly present your point of view without elaborating or starting a discussion).

Step 2: Talk about other persons substance use in general

- For instance, discuss other person's substance use (substance use among peers, staff, family members: "Does your father/mother/sister/friend/caregiver use. . .")

Step 3: Enquire about patient's own experiences with substance use

- Ask about life time use ("Did you ever use . . . yourself?", if so: "How old were you?")

During this step, remain neutral. Try to be interested without being inquisitive. Accept whatever answer was given, without questioning its validity.

Step 4: Further inquire about the use of this type of substance to assess

- Patterns of use (frequency, quantity)
- Circumstances (alone/with others, at home or somewhere else)
- Effects (positive and negative)

In this phase it remains important to keep a genuine interest in the client's story. Focusing on the "how" "what" "when" "with whom" "to what effect" helps to do so. Try to avoid "why" questions.

Repeat steps 2–4 for other types of substances.

15.5 Treatment of Substance Abuse in People with Mild Intellectual Disability

Ideally, addiction care, intellectual disability services, and—when applicable—psychiatric and/or forensic services work closely together in the treatment of MID substance abusers with or without co-occurring psychiatric or behavioural problems. Unfortunately, this is far from reality. In daily practice, care and treatment for those with dual (MID and addiction), triple (MID, addiction; and psychiatric, behavioural or forensic problems) is scattered across services. Apart from collaboration issues, knowledge regarding intellectual disability (in addiction care or forensic settings) or substance abuse (in intellectual disability settings) is lacking. Therefore, those with MID (whether it is identified as MID or not) who are referred for addiction care often receive "standard care".

15.5.1 Problems in Standard Care

Unfortunately, addiction treatment protocols are often not suited to the needs of persons with MID. Problems may arrive as early as the referral; many persons with MID will not seek help, do not know where to go or a letter with scheduled appointment may remain unopened. During the initial assessment, similar problems may arise as during screening (see Sect. 15.4). Further, many persons with MID cannot voice their needs and problems, which can be mistaken for lack of motivation or no need for help. Treatment protocols, in addiction are often quite verbal, require reading skills and the capacity to do exercises at home. Many persons with MID lack skills needed for these actions.

Furthermore, many patients with MID have previous experiences with addiction treatment in which they have failed (for instance, because the programme was too difficult for them) and are not confident that a new attempt will succeed. Existing treatment programmes are not designed for people with MID, they often make a great appeal to the self-sufficiency of patients with MID. In general, it is important to embed treatment of substance use within the environment of the patient with MID. A patient can successfully complete a treatment in an institutional setting, but then be unable to apply the achieved skills in their own home environment (generalisation).

15.5.2 Ways to Adapt Treatment to the Needs of Those with Mild Intellectual Disability

To better suit the needs of those with MID, several adaptations can be made to standard treatment protocols and procedures. These adaptations concern treatment content, but even more so treatment length and the way that the content is presented and communicated (VanDerNagel et al. 2013b). Ideally, information about the cognitive level, communication skills, developmental level and co-morbidity is

collected before treatment starts. Developmental level in particular, rather than biological age or first impression needs to be taken into account when interviewing the patient. Treatment sessions must be planned according to the patient's needs. Most patients with MID benefit more from multiple shorter sessions, than from one single lengthy session. It is also preferable to keep waiting times in crowded waiting rooms as short as possible. Confrontation with other substance abusers may induce anxiety or lead to undesirable social interactions (VanDerNagel et al. 2013b).

The first step to successful treatment is establishing a good working relationship. This requires more effort from the therapist than with patients without MID (Sturmey et al. 2003). Many persons with MID are tense when confronted with a new therapist and will need some time before they feel at ease. It is often helpful when a mentor (from ID services) or a trusted family member can be present during sessions. Offering a cup of coffee, explaining the goals of the session, engaging in some "small talk" and taking a more supportive, positive stance may help the patient to feel comfortable with the new situation. During communication with the patient, it is preferable to use short sentences, avoid difficult wording, abstract concepts and complex phrases. It may be helpful to use pictures and (fake) props (e.g. beer bottles, washing soap as fake cocaine, herbs for cannabis) to (literally) show which substances are discussed. Communication with a patient with MID should be as precise and concrete as possible, asking one question at a time and not presenting too much information at once (Sturmey et al. 2003).

To check understanding and promote retention, it may be helpful to ask the patient to summarize what was discussed. When collateral information is needed, permission needs to be asked to address the person who accompanies the patient (this is generally granted). Main focus of the therapy should be to help the patient find solutions instead of emphasizing (or denying) problems. Further, positive feedback rather than confronting techniques or lectures should be used. With some help, most patients are able to fill out a (simplified) registration form, provided that filling out is practised during sessions. An analysis of the function of substance use as well as strong points, interests and social support factors of a patient generally helps to find new perspectives. Talking about the fact that relapse is not failure in and of itself often reduces both pressure and fear of trying to change (VanDerNagel et al. 2013b).

A number of existing treatment models and methods can be used for patients with MID, in some cases with several adjustments. First, motivational interviewing shows promising results in some small-N studies among those with MID (Mendel and Hipkins 2002; Trentelman et al. 2013) and can easily be modified to the needs of patients with MID (Frielink and Embregts 2013). Second, cognitive–behavioural therapy (CBT) is widely used in ID care, and as preliminary studies show, CBT-based interventions for substance use can be adapted to persons with ID (De Haan et al. 2012; VanDerNagel and Kiewik nd). A CBT based group intervention was successfully piloted in the Netherlands (Den Ouden et al. 2012). In both individual and group CBT interventions for MID, there is more focus on practising skills, rather than understanding behaviour. Also, these interventions were markedly longer, since people with MID generally require more time to learn new skills.

Third, self-help groups can be very supportive for persons with MID (Sturmey et al. 2003). In self-help groups, people with similar problems meet each other. Participants benefit from each other's experiences in solving problems or making them manageable. A well-known self-help group around the world is *Alcoholics Anonymous (AA)*. Many of these self-help groups use the Twelve Steps Programme, which is aimed at abstinence. This programme was developed for alcoholics, but is used for other addictions as well. In Germany, there are some AA-meetings for people with special needs (e.g. MID). Focusing in other ways on the betterment of the MID patient's personal relations is also worthwhile, as a supportive environment often is prerequisite to staying clear from substances. Third parties can also play an essential role in implementing new skills in daily situations.

Regarding pharmacological treatment of people with MID, similar criteria apply as for people without MID. However, some people with MID are more sensitive to side effects, so careful monitoring is necessary. Clear instructions—both to patient and caregiver—accompanied by a clear written instruction of dosage, usage and risks are necessary. Use of aversive drugs can be risky in those with limited understanding of the consequences of combining these drugs with alcohol.

Unfortunately, there are also some pitfalls in working with persons with both MID and substance use problems. Commonly made errors are i.e. mistaking the incapacity to adhere to treatment requirements (e.g. to do certain exercises) for lack of motivation, assuming the patient will tell the therapist when something is unclear, focussing on big (often abstract or seemingly unreachable) goals rather than short time successes, and assuming the patient can apply newly learnt skills in other situations (this generally takes a lot of practice) (VanDerNagel et al. 2013b). Furthermore, based on experience in clinical practice, follow up after reaching goals is often too short.

15.5.3 Inpatient Addiction Treatment

Though some clinics seem to be reluctant to admit patients with MID, indications for inpatient treatment are basically similar to those without MID. People with MID may benefit from a therapeutic setting, with 24/7 support, medical attention etc. Often, in acute clinical care (e.g. detoxification or short term admittance) advantages outweigh disadvantages (for those with a proper indication). In these short-term inpatient wards, focus often is on medical care and stabilization, rather than on psychological or group treatment. Prolonged clinical care, especially when group therapy is a major part of the therapy plan, generally needs more adaptations for those with MID (VanDerNagel et al. 2013b). However, downsides of admission to inpatient treatment are that leaving the home environment can be stressful and in some cases traumatizing for a patient with MID. Furthermore, because the treatment programme is not adjusted to the patient's needs or his MID is not acknowledged by the care professionals, the chance of overburdening a patient is present during inpatient treatment.

15.5.4 Case 3: Sandra

The first time Sandra (23 years, IQ about 60, ADD and cannabis use disorder) was admitted, she was reluctant to go. Though she agreed that "back home things did not work out", she was scared to meet other people (of course, when asked, she would deny this) and was convinced she could not be helped in reducing her cannabis intake. Unfortunately, her expectations became true. It was only upon admittance that it became clear that she was to share a room with another patient. Janet seemed nice enough, but she was much older and could not stop talking and asking Sandra questions. Then it became clear that Sandra had to quit smoking cannabis instantly, without any medication to reduce withdrawal symptoms, or to remediate the sleeping problems she had since early childhood. And finally, to her horror, Sandra had to participate in group therapy, and participate in cleaning the ward, setting the table etcetera. Sandra's shy and aloof attitude was addressed in a group meeting by one of the staff members. This was too much: Sandra ran out and discharged herself only days after admittance.

A year later, Sandra's problems had only gotten worse, despite prolonged outpatient treatment. Her parents (with whom she was still living) were getting desperate, and pushed for another attempt of inpatient detoxification. Sandra of course, was even more reluctant than before. This time however, Sandra and her case manager visited the clinic before admittance, and met with one of the senior nurses. She showed Sandra the ward, and asked her what she remembered from the last time. Sandra proudly showed that she still knew were the kitchen, bathrooms, and recreation area were. Only during this tour Sandra found out that there were also private rooms. With a little help from her case manager, she could explain why such a room would help her to get the rest she needed. When hearing about Sandra's sleeping problems, the nurse proposed that Sandra would sleep close to the nurses' quarters, so that she would not feel alone at night. During group sessions and meals, Sandra could be seated next to the staff as well, if she would like that. Finally, the nurse reassured Sandra that medication for withdrawal symptoms and sleeping problems need not be a problem. Eventually, Sandra decided to give it a go, and a 2 week inpatient detoxification was agreed upon. Sandra was admitted Friday afternoon, after several patients had left for a weekend at home. This allowed her a few quiet days to get used to being in the clinic. Two weeks later, Sandra was proud to have completed her inpatient treatment as planned.

15.5.5 Specialized Inpatient Treatment

In the Netherlands, a small number of addiction treatment services or ID treatment services offer specialised treatment programmes for patients with MID and substance abuse programmes. Similar programmes may exist in other European countries. These programmes are characterised by an integrated approach that focuses on the treatment of substance abuse and functioning of the patient in different areas, such as leisure time, guiding patients to daily activities or work,

keeping an appropriate day- and night rhythm, strengthening adaptive skills and building a social network. Another part of this type of treatment is restoring contact with family members. Admission in an inpatient treatment centre starts off with detoxification. In most cases, detoxification of patients with MID and addictive behaviour can be done in a regular detoxification unit, because clinical programmes during detoxification generally are not primarily aimed at changing behaviour and gaining insight. Also, there are few group activities during detoxification and mainly individual counselling is provided. First observations can be made during this phase, which can provide a basis for future diagnostics. In mainstream addiction treatment, group therapy is one of the main types of treatment. This group therapy has a tendency to overburden a patient with MID because of the assumed high level of social and emotional skills. Be this as it may, some patients with MID are able to function successfully in group therapy.

15.6 Future Directions

On a European level, attention towards substance abuse (and co-occurring psychiatric disorders) among people with MID is increasing. This chapter has shown that the screening on substance abuse in ID services or of MID in forensic or psychiatric services remains important. Further, more research is needed on treatment of dual and triple diagnosis in people with MID. Commonly used treatments methods, such as motivational interviewing, cognitive behavioural therapy and pharmacotherapy, can be used with people with MID, as long as the methods are modified towards the needs of people with MID. To offer a successful treatment, it is necessary to collaborate with all relevant services that are involved with the patient with MID (e.g. ID services, mental health services, forensic services, addiction care). Further, treatment needs to be embedded in a trajectory that focuses on the daily routine of people with MID, such as daily activities, job, social network, and skills to cope with adverse events. Because of the gaps and shortcomings in current research, collaboration on a European level regarding substance abuse among people with MID is desirable.

References

APA (2013) DSM-5. Washington DC/London, England, American Psychiatric Publishing

Caroll Chapman S, Wu L-T (2012) Substance abuse among individuals with intellectual disabilities. Res Dev Disabil 33(4):1147–1156

Chaplin E, Gilvarry C, Tsakanikos E (2011) Recreational substance use patterns and co-morbid psychopathology in adults with intellectual disability. Res Dev Disabil 32(6):2981–2986. doi:10.1016/j.ridd.2011.05.002

De Haan K, Wielenga F, Van Meijel B (2012) Leefstijltraining-PLUS. Handleiding voor de trainers. Hogeschool InHolland, Alkmaar

Den Ouden R, Ganpat SM, Boonstra J, Wits E (2011) Gedragsinterventie voor jeugdige delinquenten met risicovol middelengebruik. Tactus/IVO, Deventer/Rotterdam

Den Ouden R, Kiewik M, VanDerNagel J (2012) Handleiding minder drank of drugs, behandelmodule voor LVB patiënten met verslavingsproblemen. Tactus, Deventer

Didden R, Embregts P, van der Toorn M, Laarhoven N (2009) Substance abuse, coping strategies, adaptive skills and behavioral and emotional problems in clients with mild to borderline intellectual disability admitted to a treatment facility: a pilot study. Res Dev Disabil 30(5):927–932

Didden R, VanDerNagel J, Trentelman M, Stolker JJ (2013) Verstandelijke beperkingen en comorbiditeit. In: Dom G, Dijkhuizen A, Van der Hoorn B, Kroon H, Muusse C, Van Rooijen S et al (eds) Handboek dubbele diagnose. Utrecht, De Tijdstroom

Fletcher R, Loschen E, Stavrakaki C, First M (2007) Diagnostic manual—intellectual disability: a clinical guide for diagnosis of mental disorders in persons with intellectual disability. NADD, Kingston, New York

Frielink N, Embregts P (2013) Modification of motivational interviewing for use with people with mild intellectual disability and challenging behaviour. J Intellect Dev Disabil 38(4):279–291. doi:10.3109/13668250.2013.809707

Hammink A, Schrijvers C (2012) Middelengebruik en gokken onder jongeren en volwassenen met een licht verstandelijke beperking in de regio Rotterdam. Aard, omvang, zorgbehoeften en huidig zorgaanbod. Rotterdam

Hayes S (2000) Hayes Ability Screening Index (HASI) manual. Sydney

McGillicuddy NB (2006) A review of substance use research among those with mental retardation. Ment Retard Dev Disabil Res Rev 12(1):41–47. doi:10.1002/mrdd.20092

Mendel E, Hipkins J (2002) Motivating learning disabled offenders with alcohol-related problems: a pilot study. Br J Learn Disabil 30(153–158)

Ras M, Woittiez I, Van Kempen H, Sadiraj K (2010) Steeds meer verstandelijk gehandicapten? Ontwikkelingen in vraag en gebruik van zorg voor verstandelijk gehandicapten 1998–2008. Zorg en Financiering 9. Den Haag. doi:10.1007/BF03095370

Slayter EM (2010) Disparities in access to substance abuse treatment among people with intellectual disabilities and serious mental illness. Health Soc Work 35(1):49–59

Sturmey P, Reyer H, Lee R, Robek A (2003) Substance related disorders in persons with mental retardation. NADD, Kingston, New York

To WT, Neirynck S, Vanderplasschen W, Vanheule S, Vandevelde S (2014) Substance use and misuse in persons with intellectual disabilities (ID): results of a survey in ID and addiction services in Flanders. Res Dev Disabil 35(1):1–9. doi:10.1016/j.ridd.2013.10.015

Trentelman M, Nieuwold M, Didden R (2013) Motiverende gespreksvoering voor begeleiders. In: Didden R, Moonen X (eds) Met het oog op behandeling—III. LKC & De Borg, Amersfoort, pp 47–54

VanDerNagel J, Kiewik M (nd) CGT-plus, cognitieve gedragstherapie voor verslaving bij mensen met een licht verstandelijke beperking. Amersfoort

VanDerNagel J, Kea R (2013) Jonge delinquenten van 16-23 jaar met een lichte verstandelijke beperking en problematisch middelengebruik. Een verkenning op basis van literatuur en ervaringen van experts van de (jeugd)reclassering. Deventer, Amsterdam

VanDerNagel J, Kiewik M, Buitelaar J, De Jong C (2011a) Staff perspectives of substance use and misuse among adults with intellectual disabilities enrolled in Dutch disability services. J Pol Pract Intellect Disabil 8(3):143–149

VanDerNagel J, Kiewik M, Van Dijk M, De Jong C, Didden R (2011b) Handleiding SumID-Q. Meetinstrument voor het in kaart brengen van middelengebruik bij mensen met een lichte verstandelijke beperking. Tactus, Deventer

VanDerNagel J, Kemna L, Didden R (2013a) Substance use among persons with mild intellectual disability: approaches to screening and interviewing. The NADD Bulletin 16(5)

VanDerNagel J, Kiewik M, Didden R (2013b) Iedereen gebruikt toch? Boom, Amsterdam

Vandevelde S, Broekaert E, Schuyten G, Van Hove G (2005) Intellectual abilities and motivation toward substance abuse treatment in drug-involved offenders: a pilot study in the Belgian criminal justice system. Int J Offender Ther Comp Criminol 49(3):277–297. doi:10.1177/0306624X04270779

Non-Substance-Related Disorders: Gambling Disorder and Internet Addiction

16

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Abstract

Behavioural addictions are highly prevalent in specific subgroups and have a major individual and societal impact. Moreover, given the availability and increase of potentially addictive activities in our societal development (e.g. internet, gaming, online pornography) an increase in these types of behavioural disorders is very likely. Gambling Disorders are best studied among the non-chemical addictions. However, effective treatment interventions need to be further developed, in particular for Internet Addiction. Most of the available evidence supports behavioural interventions as first-line treatment. Specifically for Gambling Disorder, pharmacotherapy can be a useful augmentation. Psychiatric comorbidities are frequent in patients with behavioural addictions and negatively affect the course of non-substance-related disorders. Concurrent treatment of these comorbid disorders is advised, although there is a clear need of conducting studies evaluating the effectiveness of integrated treatment approaches.

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16.1 Introduction

Besides substance-related disorders, several behavioural patterns are suggested to lead to addictions such as eating, working, loving, gaming, having sex, taking exercises, and buying (Sussman et al. 2011; Report on the WHO Collaborative Study on Strategies for Extending Mental Health Care 1984). Nevertheless, for several of these "non-chemical addictions" evidence is limited to speak of an addiction that is comparable to chemical addictions, in terms of genetics, diagnostic criteria, impairment, epidemiology, and treatment. In this chapter, we will focus on Gambling Disorder which is now included in the DSM-5 chapter on Substance-Related and Addictive Disorders (American Psychiatric Association 2013a) and on Internet Addiction which is a rather new phenomenon covering a broad spectrum of Internet activities. Gaming is the most prominent one and is considered as a condition for further study in DSM-5. For both addictions, we will give a definition featuring diagnostic criteria, prevalence estimates, comorbidity rates, and an outline on treatment options.

16.2 Diagnostic Criteria

Both Internet Addiction and Gambling Disorder include criteria that are similar to diagnostic aspects of substance-related disorders such as tolerance, withdrawal, or loss of control but cover as well specific symptoms such as to escape or relieve a negative mood.

16.2.1 Diagnosis of Gambling Disorder

In the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV; American Psychiatric Association 1995), Pathological Gambling was subsumed under impulse-control disorders and described as a "persistent and recurrent maladaptive gambling behaviour". Five of ten criteria had to be fulfilled for diagnosis. Due to the number of similarities between substance-related addictions and Pathological Gambling found in recent research, Pathological Gambling was reclassified in the 5th revision of the DSM as an addictive behaviour in the section "Substance-Related and Addictive Disorders" (DSM-5; American Psychiatric Association 2013b). Changes pertained the reduction to nine criteria due to the elimination of DSM-IV criterion 8 (commitment of illegal acts) and the classification of the severity of the disorder in "mild" (4–5 criteria), "moderate" (6–7 criteria), and "severe" (8–9 criteria) (Table 16.1).

Table 16.1 DSM-5 criteria for gambling disorder (American Psychiatric Association 2013a, b)

Criterion A. The person concerned:
1. Needs to gamble with increasing amounts of money in order to achieve the desired excitement
2. Is restless or irritable when attempting to cut down or stop gambling
3. Has repeated unsuccessful efforts to control, cut back, or stop gambling
4. Is preoccupied with gambling
5. Gambles when feeling distressed
6. After losing money gambling, often returns another day to get even ("chasing")
7. Lies to family members, therapist, or others to conceal the extent of involvement with gambling
8. Has jeopardized or lost a significant relationship, job, or educational or career opportunity because of gambling
9. Relies on others to provide money to relieve a desperate financial situation caused by gambling

Additionally, the gambling disorder has to be distinguished from gambling behaviour in a manic episode (criterion B)

16.2.2 Diagnosis of Internet Gaming Disorder/Internet Addiction

Diagnostic approaches to specify Internet Addiction have used criteria from Substance-Related Disorders as well as from Pathological Gambling. While first approaches were not much evidence-driven, meanwhile some empirical studies have proposed specific criteria. The most promising have been from Tao and colleagues (Tao et al. 2010) who proposed eight criteria and Ko et al. (2009b) suggesting nine criteria with both approaches overlapping in several characteristics. While these suggestions cover the broad concept of Internet Addiction which is related to different activities in the Internet such as gaming, watching pornography, using social networks and chats or compulsively downloading or searching specific material or topics, the DSM-5 has focused only on gaming because the evidence is best in this area. Hence, a new category is proposed called Internet Gaming Disorder (IGD), which is part of the chapter on conditions for further study. Criteria are described in more detail with suggestions for items to assess them in Petry et al. (2014). In view of the various approaches in the past and the lack of a consensus, the DSM-5 criteria can be regarded as an important milestone stipulating and streamlining future research. Within DSM-5, it is suggested that five or more criteria indicate IGD (Table 16.2). In a first study coming from Taiwan, this threshold could be confirmed (Ko et al. 2014).

With respect to the broader concept of Internet Addiction, no generally accepted diagnostic criteria exist; however, suggestions that have been made are quite similar to IGD or have been precursors for the respective criteria in DSM-5. Unpublished data on a follow-up sample of excessive Internet users recruited through a large general population study indicate that the IGD-criteria can be applied to other Internet activities such as using Social Networks (Rumpf et al. 2014a).

Table 16.2 Criteria Internet gaming disorder, section III, DSM-5 (American Psychiatric Association 2013a, b)

1. Preoccupation with Internet games as can be manifested by persistent thoughts about previous gaming activity or anticipations of playing the next game. Internet activity evolves to be the dominant activity in daily life.
2. Withdrawal symptoms such as irritability, anxiety, or sadness when playing is not possible.
3. Tolerance as manifested by the need to spend increasing amounts of time engaged in Internet games.
4. Unsuccessful attempts to control gaming.
5. Loss of interest in previous hobbies and entertainment in favour of Internet gaming.
6. Continued excessive Internet gaming despite knowledge of psychosocial problems.
7. Deception of family members, therapists, or others with respect to the amount of Internet Gaming.
8. Internet Gaming to escape or relieve a negative mood such as feelings of helplessness, guilt, or anxiety.
9. Jeopardizing or loosing a significant relationship, job, educational or career opportunity due to excessive use of Internet games.

16.3 Prevalence Estimates

16.3.1 Prevalence of Pathological Gambling

To date, a number of epidemiological studies estimated the prevalence rates of Pathological Gambling. Estimates are varying according to methodological and regional characteristics. Stucki and Rihs-Middel summarized 33 prevalence studies in a review (Stucki and Rihs-Middel 2007). Restricted to 12-month prevalence, the review presented weighted mean prevalence rates from 0.8 % to 1.8 %, depending on measuring tools. Prevalence estimates in Europe were lower (0.2–0.8 %) than in US-American studies (0.5–3.5 %). This is in the same range as a recent epidemiological survey in Germany, the "Pathological Gambling and Epidemiology"-study (PAGE) with 15,023 respondents which found 12-month prevalence rates of 0.3 % and lifetime prevalence to be 0.6 % with increased rates among males, younger age groups, and individuals with migration background (Meyer et al. 2014).

16.3.2 Prevalence of Internet Addiction

Estimates on Internet Addiction or IGD have to be regarded with caution because of various diagnostic assessment instruments and diagnostic thresholds. As a consequence, prevalence estimations differ widely. One paper found prevalence rates between 1 and 14 % (Tao et al. 2010). A systematic review of problematic Internet use of studies on US-youth ranged from 0 to 26 % (Moreno et al. 2011). Sample selection bias is very likely to be a major cause of divergent prevalence estimates. One pitfall is that most studies come from convenience samples recruited via online

solicitations or in sub-populations such as students. In these studies, probability of study inclusion was obviously likely to be confounded with the problem behaviour to be measured and such approaches tend to lead to overestimation. Few studies are representative for the population under study and few data are general population based. Studies focusing on excessive computer gaming found lower rates compared to those on the broader diagnosis of Internet Addiction. In addition, prevalence rates are higher in younger cohorts and as well in Asian countries. With respect to the general population, four studies on Internet Addiction have been published and finding rates ranging from 0.3 % (Aboujaoude et al. 2006) to 2.1 % (Müller et al. 2013).

In the absence of a consensus concerning criteria to define and tools to assess Internet Addiction, one study used a statistical approach by performing a latent class analysis in a large general population sample (Rumpf et al. 2014b). In the entire sample aged 14–64, 1 % was classified as having Internet Addiction. Percentages were higher in younger age groups with up to 4 % in participants aged 14–16. There were no overall gender differences while males reported Internet Gaming as main activity and females Social Networks. Unemployment and migration background were related to Internet Addiction.

16.4 Psychiatric Comorbidity

16.4.1 Psychiatric Comorbidity of Pathological Gambling

Pathological gamblers are known to show high rates of co-morbid psychiatric disorders, similarly to individuals with substance use disorders (Crockford and el-Guebaly 1998). The worldwide largest representative study with data for Pathological Gambling, the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) also assessed Alcohol and Drug Use, Mood and Anxiety Disorders, and Personality Disorders (Petry et al. 2005). Of the participants with Pathological Gambling during lifetime, 73.2 % had also a lifetime Alcohol Use Disorder. Additionally, 49.6 % suffered from a Mood Disorder during lifetime, and 41.3 % had an Anxiety Disorder. An Antisocial Personality Disorder was diagnosed in 23.3 % of the participants. Furthermore, an Obsessive–Compulsive Personality disorder was diagnosed in 28.5 % of the pathological gamblers. In a 3-year-follow-up, 53.8 % of the population with Gambling Disorders had developed an incident Axis I disorder (Chou and Afifi 2011).

In another US study, the National Comorbidity Survey (NCS-R), Kessler and colleagues showed that 96.3 % of the pathological gamblers had also suffered of at least one Axis-I disorder during their lifetime (Kessler et al. 2008). The Odds Ratios (OR) were 3.7 for any Mood Disorder, 3.1 for any Anxiety Disorder, and 5.5 for any Substance Disorder.

The German PAGE-study also assessed co-morbid psychiatric disorders. Of the pathological gamblers, 85.1 % had any co-morbid psychiatric disorder (without tobacco dependence) during lifetime with the highest rates for Alcohol Use

Disorders (61.7 %) and Mood Disorders (46.8 %), followed by Anxiety Disorders (38.3 %) (Bischof et al. 2013). Compared to a general population sample, pathological gamblers showed a 3.7 times higher risk for Alcohol Use Disorders, a 3.1 times higher risk for a Mood Disorder, and an OR of 3.8 for Anxiety Disorders.

Taken together and as confirmed by a systematic review by Lorains and colleagues, there is a significant psychiatric comorbidity in pathological gambling, with Substance Use Disorders to be the most prevalent, followed by Mood Disorders and Anxiety Disorders (Lorains et al. 2011).

16.4.2 Psychiatric Comorbidity of Internet Addiction

Quite a number of studies have analysed psychiatric comorbidity of Internet Addiction/Internet Gaming Disorder. A systematic review identified 20 studies most of them coming from Asian countries. Of all studies, 75 % reported significant correlations of problematic Internet use with Depression, 57 % with Anxiety, 100 % of the studies with symptoms of ADHD, 60 % with obsessive-compulsive symptoms, and 66 % with hostility or aggression. None of the studies included in this review reported associations between problematic Internet use and Social Phobia (Carli et al. 2013). The weakest association was found for hostility/aggression and the strongest for depression while associations were higher among males.

Of special interest are studies with longitudinal study designs to analyse if specific characteristics in terms of comorbidity are risk factors for the development of Internet Addiction or other outcomes. One study conducted follow-ups of a sample of adolescents from ten junior high schools in Taiwan over a period of 2 years (Ko et al. 2009a). Aim was to evaluate if psychiatric comorbidities or personality characteristics predict the onset of Internet Addiction. Among those without this disorder at the baseline assessment but with Internet Addiction at follow-up, Depression, ADHD, Social Phobia, and hostility were found as predictors. Regardless of gender, ADHD and hostility were the strongest predictors. As a shortcoming it has to be mentioned that the assessment of the comorbid disorders were based on rather brief questionnaires instead of in-depth diagnostic interviews. Another study focused on gaming and followed-up school children in Singapore over a period of 24 months (Gentile et al. 2011). This study used a longitudinal latent class approach to identify distinct groups of participants who started, continued or stopped to be pathological Internet gamers within the follow-up period or who never had problematic gaming. Predictors of pathological gaming were lower social competence and empathy, poorer emotional regulation skills and greater impulsivity. Important to notice is that depression, anxiety, social phobia (as well as lower school performance) were found to be sequelae of the pathological gaming not precursors. This is very important because Internet Addiction or Internet Gaming Disorder is often regarded as a symptom of another (underlying) disorder. These data speak against this hypothesis. Although studies are rare, to date it can be summarized that psychiatric comorbidity may as well play a role in the development of Internet Addiction as well as being a consequence.

One German study has followed-up individuals from a large general population sample (Rumpf et al. 2014b) exploring signs of excessive internet use and psychiatric comorbidity. In those who fulfilled at least 5 DSM-5 criteria for Internet Gaming Disorder and who reported that gaming was their main activity in the Internet, high proportions of comorbid disorders were found: Substance Dependence 46.7 %, Mood Disorders 46.7 %, Anxiety Disorders 23.3 %, Cluster A personality disorder 4.%, Cluster B personality disorder 12.0 %, Cluster C personality disorder 24.0. Findings were comparable for other Internet activities showing that between 28 % and 33 % (depending on main activity) had at least one personality disorder.

16.5 Therapeutic Approaches for Pathological Gambling and Internet Addiction

Similar to substance-related disorders, behavioural addictions are regarded as repetitive, excessive behavioural patterns that increasingly turn into an automatized action, which is difficult to control intentionally and causes harm to the afflicted individual. Learning processes reinforces this automatic behaviour. Treatment aims at finding alternatives for gambling/gaming activities and to re-establish social contacts. This subchapter provides an overview of studies assessing the effects of different psychotherapeutic—as well as pharmacological interventions and gives a more detailed description of psychotherapeutic treatment options.

16.5.1 Psychosocial Interventions for Pathological Gambling

A recently published Cochrane Collaboration meta-analysis assessing the efficacy of psychological interventions in the treatment of pathological gamblers (PG) reported a superiority of cognitive behavioural therapy over other psychological treatments (Cowlishaw et al. 2012). This is very similar to the treatment of chemical addictions (Magill and Ray 2009). However, in the case of PG given the small samples and the high variation of therapeutic procedures within the interventions, the reported therapy effects should be interpreted with caution.

Overall, patients with PG can be treated safely and effectively either within a psychiatric clinic (i.e. inpatient and day patient treatment) or on an outpatient basis. The treatment choice depends on the symptom severity and other comorbidities. The overall aim of the intervention is to motivate and support patients in the achievement of gambling abstinence as well as to help them in taking responsibility in managing their problems. The treatment of pathological gamblers generally involves group as well as individual settings. The key elements in the treatment of PG are:

– To inform the patient about the PG disorder (psychoeducation) and to involve him/her in the development of an individualized explanatory model

- The identification of dysfunctional and harmful cognitions (e.g. the belief of not being good enough at home or at work) as well as the restructuring of these negative core beliefs that otherwise lead to the weakening of self-esteem and the reduction of self-efficacy in staying abstinent
- Identification and analysis of high-risk situations for gambling relapses
- Restructuring of gambling-related cognitive distortions (e.g. "The winnings when gambling depend on my skills" or "If I had concentrated more, I would have won")
- Training on money management
- Skills training for dealing with emotional instability and stress.

The process of working on an individual explanatory model together with the patient improves the person's understanding of his/her dysfunctional gambling behaviour. Furthermore, in doing so helps the patient to learn about neurobiological, genetic as well as social factors influencing and maintaining PG.

Often, patients exhibit a negative self-concept that becomes apparent in negative core beliefs such as being terrible and worthless. These beliefs in turn induce negative feelings and physical tension that maintain the vicious circle to use gambling as a coping strategy. Thus, gambling-associated triggers (situations, feelings, or gambling stimuli) activate the dopaminergic reward system in the brain and entail hedonistic feelings. This in turn leads to the ignorance of negative long-term consequences.

The issue that most patients are not aware of the variety of triggers inducing craving for gambling leads to a relapse in many cases. Therefore, the therapist assesses these underlying situational processes together with the patient, trying to underline the connections between the triggers (e.g. an interpersonal conflict with the spouse), the cognitive, emotional and behavioural reactions as well as the short-term and long-term consequences. This behavioural assessment, as the SORC model differentiates between S—Stimulus or antecedent conditions that trigger gambling (e.g. an interpersonal conflict with the spouse), O—Organismic variables related to the problematic behaviour (e.g. the patient is harm avoidant), R—(Responses): physical (e.g. tension in shoulders, increased heart frequency), emotional (e.g. feelings of anxiety, anger, sadness, anxiety to loose someone, craving), cognitive (e.g. thoughts of wanting to go out of this conflict) and behavioural (gambling) as well as C—Consequences of the problematic behaviour.

Studies assessing PG-influencing personality traits indicate that patients show a high degree of impulsivity (O-variable), which in turn impacts and impairs the behavioural control over gambling (Blaszczynski et al. 1997). Inhibitory control deficits are one of the main etiological factors increasing the risk for both substance-related and non-substance-related addictive behaviour (Goldstein and Volkow 2002; Goudriaan et al. 2008; Blanco et al. 2009; Blaszczynski et al. 1997). Individuals exhibiting a high degree of impulsivity often show deficits in the perception and management of feelings. These persons have to deal with tension felt in their body and nervousness without being able to identify the main underlying feelings or to localize the cause of their problem. The tension is often

induced by distorted perceptions and emotions arising through negative past experiences.

Exercises to reduce this emotional dysregulation are specifically described in the techniques of Dialectic behavioural therapy (DBT; Linehan 1993). DBT can be regarded as a sub-form of cognitive-behavioural therapy and includes the training in which the patients learn skills enabling them to deal consciously with feelings and interpersonal conflicts. One exercise is the specific use of mindfulness techniques, described as a mental training to learn self-awareness and self-regulation in order to manage own negative reactions and impulses.

A further relevant basis for therapy, especially in the outpatient treatment, is writing a diary. Every day, the patient is asked to describe his/her degree of craving for gambling, previous negative or positive situations together with the related feelings, the gambling duration, and monetary loss as well as the skills that enabled the patient to avoid gambling. This overview gives a treatment-update for both patient and therapist and helps summarizing learned skills as well as identifying high-risk situations still difficult to handle for the patient.

Another aspect of PG-therapy is the work on a patient's attitude towards money. Most pathological gamblers report that money itself lost its high value for them. For example coins are just thrown into a slot machine until none are left. This appraisal is also underlined by neurobiological studies indicating that it is not the monetary win per se that activates the dopaminergic limbic reward system in the brain. Rather, continued gambling despite negative consequences is thought to be driven by strong feelings of uncertainty to win or lose money, which trigger the striatum of the dopaminergic limbic reward system (Chase and Clark 2010; Linnet et al. 2012) and influences the development of addictive, habitual gambling behaviour.

Additionally, gambling-related cognitive distortions also reinforce the maintenance of problematic gambling (Ladouceur 1996). For instance, the cognitive distortion termed "G*amblers Fallacy*" involving the belief that a frequent loss in a game increases the likelihood of a win in the next (Ladouceur 1996) can be regarded a strong predictor for continuing gambling (Goodie and Fortune 2013).

Another relevant aspect in PG-therapy is a possible involvement of relatives, who are helpless and exhausted in many cases. Often, they develop serious health problems such as affective disorders, suicidal tendencies and addictions to medication or alcohol (Grüsser and Albrecht 2007). Relatives often do not know how to handle PG patients, who might betray trust by promising to quit gambling to the point of stealing money. Furthermore, relatives might be overwhelmed by the financial and social problems caused by a patient's excessive gambling. The therapist informs the relatives about the PG-etiology and maintaining factors.

Relatives are encouraged to seek additional help if necessary which may include psychotherapy. Additionally, advice on self-help groups for relatives and further clinical possibilities in the case of psychological and physical problems is provided.

In conclusion, the severity of the PG disorder, psychosocial factors as well as comorbidities should be considered in the choice of treatment for a patient with pathological gambling.

The focus of psychotherapeutic interventions lies on characteristics underlying emotional regulation, the (re-) configuration of relationships as well as on a reduction of the often occurring negative self-evaluation of PG patients.

16.5.2 Psychosocial Interventions for Internet Addiction (Gaming)

The treatment of Internet addictive behaviours is still in its infancy and only a limited number of studies have been conducted so far. Moreover, comparison and interpretation of these studies is difficult due to the many methodological differences and shortcomings (King et al. 2011).

Most of the studies come from Asian countries and explore different types of behavioural interventions. However, although positive treatment effects have been found, these results are not overall consistent (Su et al. 2011; Du et al. 2010). In the USA, Young (2007) studied the effect of a (group) cognitive behavioural intervention. An overall increment of symptoms associated with computer as well as Internet addiction was reported. However, the reported findings lack validated measures for psychosocial symptoms.

Currently, a multicentre trial, STICA (Short-term Treatment for Internet and Computer game Addiction) is running in Austria and Germany (Jager et al. 2012). Main goals of the treatment are (1) abstinence of the problematic behaviour/reduction of online time to normal use, (2) relearning of alternative behaviours that might have been reduced like former hobbies. Additionally social contacts should be reactivated. (3) Treatment of psychiatric comorbidities, (4) individual problem understanding.

The therapy is based on eight single and fifteen group sessions in an outpatient setting. Thus the social life and the embedding in the original social environment as well as relapse can directly be integrated in the psychotherapeutic process and treatment. Especially the group setting provides the chance to learn on the model of others by observing relapse or therapy success and related emotional and personal reactions. The decision to consume the internet ongoing leads to psychosocial, emotional and cognitive behavioural patterns that are not necessarily conscious to the patient, but effect their behaviour and life significantly. During an individual observation of play the processes that are leading to an ongoing play are identified and further understanding of this process is elaborated. Exposure training with the treatment seekers' avatars is common part of the treatment. A paper print of the avatar is used to transfer the digital avatar to physical presence in the therapy setting. The patients evaluate these avatars. The evaluation of the own avatar by other patients is a highly emotional moment for the patients. Patients' task is to describe positive and negative aspects of the—over years—developed avatar. The culmination of this situation finds patients themselves choosing parts of the avatar that would stay online (negative ones) and positive aspects that might be transferred to the patients' everyday offline life. A clear distance to the online game is highly supporting the abstinence from online games. It is often hard for the patients to bid farewell to their—second life—avatar. The reason is that the avatar represents so

many time, online experience, endurance, thoughts, and wishes. Patients describe the group setting and its support as well as reactivate or newly created social contacts as most effective in the therapy process. The chance of stabilization of the therapy success beyond the psychotherapeutic treatment is increased by rediscovery of self-reflection, rediscovered corporeality, direct emotional as well as social feedback and newly implemented coping mechanisms. The delineated multicentre STICA RCT is currently evaluating the outcomes of the described CBT modules (Jager et al. 2012).

16.5.3 Psychopharmacological Treatment of Pathological Gambling

Given the similarities between substance use disorders and pathological gambling, not surprisingly, efforts have been made over the past two decades to investigate the potential benefits of pharmacological treatments in pathological gambling. Recently, Grant et al. (2014) presented a systematic review of the 18 double-blind placebo-controlled pharmacotherapy studies conducted for the treatment of pathological gambling. The trials reviewed include studies on antidepressants, opioid antagonists, mood stabilizers, atypical antipsychotics, glutamatergic agents, and atypical stimulants. Among substances influencing the glutamatergic system N-acetyl cysteine, a glutamate-modulating agent, seems promising with 83 % responders compared with 28.6 % of those assigned to placebo. Especially the opioid antagonists Naltrexone and Nalmefene have demonstrated their efficacy in treating symptoms associated with pathological gambling. In contrast antidepressant, mood stabilizers and atypical antipsychotics have shown inconsistent results. Among the limitations of the published study are relatively small sample sizes, short duration, and often the exclusion of psychiatric comorbidities. Further shortcomings are the use of different response measures, the heterogeneity of samples, atypical gender distribution, and the missing use of a validated instrument among others.

In summary, Grant et al. (2014) conclude that opioid antagonists and glutamatergic agents seem promising for individuals with PG suffering for intense urges. Considering the fact that several studies consistently demonstrated the efficacy of opioid antagonists they should currently be considered the first-line treatment for PG.

16.5.4 Psychopharmacological Treatment of Internet and Computer Game Addiction

Pharmacological studies on Internet Addiction are very limited and small sample sized (King et al. 2011). Han and colleagues conducted a clinical trial on 62 children aged between 8 and 12 years with ADHD and comorbid Internet addiction (Han et al. 2009). The primary endpoint regarded to efficacy of Methylphenidate (18 mg/d) on symptoms of Internet Addiction. After 8 weeks of medication, significant

reduction of symptoms of Internet Addiction was observable. Additionally, improvements in visual attention became evident.

In a second study by the same authors (Han et al. 2010), 19 patients (aged between 17 und 29 years) with internet addiction were included in a trial, with Bupropion (a dopamine–norepinephrine reuptake inhibitor). A comparison between the treatment group and a wait list control was conducted with a self-report score and cue-induced cortical reactivity (assessed by fMRI) as primary endpoints. After 6 weeks of treatment there was a significant decrease regarding craving for online games and daily use of online games. Additionally, a decrease of cue-induced dorsolateral prefrontal activity was found among the treatment group.

However, given the paucity of studies, currently no recommendations on the use of pharmacological treatments for Internet Addiction can be given.

16.5.5 Treatment of Comorbid Behavioural Addictions and Psychiatric Disorders

Although studies show a high prevalence of psychiatric comorbidity within individuals suffering from PG or Internet Addiction, very few studies have been conducted on the treatment of these dual disorder patients. This is specifically pitiful given the negative impact of these comorbidities on patients' disease course. Indeed, psychiatric comorbidity is common among pathological gamblers and is associated with greater severity of clinical problems (Ibanez et al. 2001). As indicated earlier in this chapter, substance use disorder, mood and anxiety disorders are respectively the most frequent psychiatric disorders to be dealt with in PG patients. Less is known for Internet Addiction, where among children and adolescents also ADHD are a frequently found.

Although no studies currently are available providing evidence for integrated treatment interventions, it is in our view warranted to state that concurrent treatment for both the addictive and the other psychiatric disorder needs to be available for and actively offered to the comorbid patient.

Conclusions and Recommendations

Behavioural additions are highly prevalent having major individual and societal consequences. Given the availability and increase of potentially addictive activities such as gambling, gaming, and online pornography, an increase of these types of behavioural disorders is very likely. Although there are promising psychosocial treatments for pathological gambling and specifically for gaming, effective treatments need to be further developed and established in the health care. Most of the available evidence support behavioural interventions very similar to addiction treatment such as behavioural assessment, cognitive restructuring, emotion management and involvement of relatives as first line treatment. Specifically in gambling disorders, pharmacotherapy can be a useful augmentation. Psychiatric comorbidities are frequently found in patients with behavioural addictions and negatively affect the course of the disorders.

Concurrent treatment of comorbid disorders is advised. However, there is a clear need of studies that evaluate the efficacy and effectiveness of integrated treatment approaches.

References

Aboujaoude E, Koran LM, Gamel N, Large MD, Serpe RT (2006) Potential markers for problematic Internet use: A telephone survey of 2,513 adults. CNS Spectr 11(10):750–755

American Psychiatric Association (1995) Diagnostic and statistical manual of mental disorders, international version, 4th edn. American Psychiatric Association, Washington, DC

American Psychiatric Association (2013a) Diagnostic and statistical manual of mental disorders, 5th edn. American Psychiatric Association, Washington, DC

American Psychiatric Association (2013b) Diagnostic and statistical manual of mental disorders, international version, 5th edn. American Psychiatric Association, Arlington, VA

Bischof A, Meyer C, Bischof G, Kastirke N, John U, Rumpf HJ (2013) Comorbid Axis I-disorders among subjects with pathological, problem, or at-risk gambling recruited from the general population in Germany: results of the PAGE study. Psychiatry Res 210(3):1065–1070. doi:10.1016/j.psychres.2013.07.026

Blanco C, Potenza MN, Kim SW, Ibanez A, Zaninelli R, Saiz-Ruiz J, Grant JE (2009) A pilot study of impulsivity and compulsivity in pathological gambling. Psychiatry Res 167(1–2):161–168. doi:10.1016/j.psychres.2008.04.023

Blaszczynski A, Steel Z, McConaghy N (1997) Impulsivity in pathological gambling: the antisocial impulsivist. Addiction (Abingdon, England) 92(1):75–87

Carli V, Durkee T, Wasserman D, Hadlaczky G, Despalins R, Kramarz E, Wasserman C, Sarchiapone M, Hoven CW, Brunner R, Kaess M (2013) The association between pathological internet use and comorbid psychopathology: a systematic review. Psychopathology 46(1):1–13. doi:10.1159/000337971

Chase HW, Clark L (2010) Gambling severity predicts midbrain response to near-miss outcomes. J Neurosci 30(18):6180–6187. doi:10.1523/jneurosci.5758-09.2010

Chou KL, Afifi TO (2011) Disordered (pathologic or problem) gambling and axis I psychiatric disorders: results from the National Epidemiologic Survey on Alcohol and Related Conditions. Am J Epidemiol 173(11):1289–1297. doi:10.1093/aje/kwr017

Cowlishaw S, Merkouris S, Dowling N, Anderson C, Jackson A, Thomas S (2012) Psychological therapies for pathological and problem gambling. The Cochrane database of systematic reviews 11:Cd008937. doi:10.1002/14651858.CD008937.pub2

Crockford DN, el-Guebaly N (1998) Psychiatric comorbidity in pathological gambling: a critical review. Can J Psychiatry 43(1):43–50

Du YS, Jiang W, Vance A (2010) Longer term effect of randomized, controlled group cognitive behavioural therapy for Internet addiction in adolescent students in Shanghai. Aust N Z J Psychiatry 44(2):129–134. doi:10.3109/00048670903282725

Gentile DA, Choo H, Liau A, Sim T, Li D, Fung D, Khoo A (2011) Pathological video game use among youths: a two-year longitudinal study. Pediatrics 127(2):e319–e329. doi:10.1542/peds.2010-1353

Goldstein RZ, Volkow ND (2002) Drug addiction and its underlying neurobiological basis: neuroimaging evidence for the involvement of the frontal cortex. Am J Psychiatry 159(10):1642–1652

Goodie AS, Fortune EE (2013) Measuring cognitive distortions in pathological gambling: review and meta-analyses. Psychol Addict Behav 27(3):730–743. doi:10.1037/a0031892

Goudriaan AE, Oosterlaan J, De Beurs E, Van Den Brink W (2008) The role of self-reported impulsivity and reward sensitivity versus neurocognitive measures of disinhibition and

decision-making in the prediction of relapse in pathological gamblers. Psychol Med 38(1):41–50. doi:10.1017/s0033291707000694

Grant JE, Odlaug BL, Schreiber LR (2014) Pharmacological treatments in pathological gambling. Br J Clin Pharmacol 77(2):375–381. doi:10.1111/j.1365-2125.2012.04457.x

Grüsser SM, Albrecht U (2007) Rien ne va plus—wenn Glücksspiele Leiden schaffen. Hans Huber

Han DH, Hwang JW, Renshaw PF (2010) Bupropion sustained release treatment decreases craving for video games and cue-induced brain activity in patients with Internet video game addiction. Exp Clin Psychopharmacol 18(4):297–304. doi:10.1037/a0020023

Han DH, Lee YS, Na C, Ahn JY, Chung US, Daniels MA, Haws CA, Renshaw PF (2009) The effect of methylphenidate on Internet video game play in children with attention-deficit/hyperactivity disorder. Compr Psychiatry 50(3):251–256. doi:10.1016/j.comppsych.2008.08.011

Ibanez A, Blanco C, Donahue E, Lesieur HR, Perez de Castro I, Fernandez-Piqueras J, Saiz-Ruiz J (2001) Psychiatric comorbidity in pathological gamblers seeking treatment. Am J Psychiatry 158(10):1733–1735

Jager S, Muller KW, Ruckes C, Wittig T, Batra A, Musalek M, Mann K, Wolfling K, Beutel ME (2012) Effects of a manualized short-term treatment of internet and computer game addiction (STICA): study protocol for a randomized controlled trial. Trials 13:43. doi:10.1186/1745-6215-13-43

Kessler RC, Hwang I, LaBrie R, Petukhova M, Sampson NA, Winters KC, Shaffer HJ (2008) DSM-IV pathological gambling in the National Comorbidity Survey Replication. Psychol Med 38(9):1351–1360. doi:10.1017/S0033291708002900

King DL, Delfabbro PH, Griffiths MD, Gradisar M (2011) Assessing clinical trials of Internet addiction treatment: a systematic review and CONSORT evaluation. Clin Psychol Rev 31(7):1110–1116. doi:10.1016/j.cpr.2011.06.009

Ko CH, Yen JY, Chen CS, Yeh YC, Yen CF (2009a) Predictive values of psychiatric symptoms for Internet addiction in adolescents A 2-year prospective study. Arch Pediatr Adolesc Med 163(10):937–943

Ko CH, Yen JY, Chen SH, Wang PW, Chen CS, Yen CF (2014) Evaluation of the diagnostic criteria of Internet gaming disorder in the DSM-5 among young adults in Taiwan. J Psychiatr Res 53:103–110. doi:10.1016/j.jpsychires.2014.02.008

Ko CH, Yen JY, Chen SH, Yang MJ, Lin HC, Yen CF (2009b) Proposed diagnostic criteria and the screening and diagnosing tool of Internet addiction in college students. Compr Psychiatry 50(4):378–384. doi:10.1016/j.comppsych.2007.05.019

Ladouceur R (1996) A cognitive perspective on gambling. Trends in cognitive and behavioural therapies. Wiley, New York

Linehan M (1993) Skills training manual for treating borderline personality disorder. Guilford, New York, 180

Linnet J, Mouridsen K, Peterson E, Moller A, Doudet DJ, Gjedde A (2012) Striatal dopamine release codes uncertainty in pathological gambling. Psychiatry Res 204(1):55–60. doi:10.1016/j.pscychresns.2012.04.012

Lorains FK, Cowlishaw S, Thomas SA (2011) Prevalence of comorbid disorders in problem and pathological gambling: systematic review and meta-analysis of population surveys. Addiction 106(3):490–498. doi:10.1111/j.1360-0443.2010.03300.x

Magill M, Ray LA (2009) Cognitive-behavioral treatment with adult alcohol and illicit drug users: a meta-analysis of randomized controlled trials. J Stud Alcohol Drugs 70(4):516–527

Mellody P (1991) Verstrickt in die Probleme anderer: über Entstehung und Auswirkung von Co-Abhängigkeit, 2nd edn. Kösel, München

Moreno MA, Jelenchick L, Cox E, Young H, Christakis DA (2011) Problematic internet use among US youth: a systematic review. Arch Pediatr Adolesc Med 165(9):797–805. doi:10.1001/archpediatrics.2011.58

Meyer C, Bischof A, Westram A, Jeske C, deBrito S, Glorius S, Schön D, Porz S, Gürtler D, Kastirke N, Hayer T, Jacobi F, Lucht M, Premper V, Gilberg R, Hess D, Bischof G, John U,

Rumpf HJ (2014) The "Pathological Gambling and Epidemiology" (PAGE) study program: design and fieldwork. Int J Methods Psychiatr Res (in press)
Müller KW, Glaesmer H, Brähler E, Wölfling K, Beutel ME (2013) Prevalence of internet addiction in the general population: results from a German population-based survey. Behav Inform Technol 33:757–766. doi:10.1080/0144929X.2013.810778
Petry NM, Rehbein F, Gentile DA, Lemmens JS, Rumpf HJ, Mossle T, Bischof G, Tao R, Fung DS, Borges G, Auriacombe M, Gonzalez Ibanez A, Tam P, O'Brien CP (2014) An international consensus for assessing internet gaming disorder using the new DSM-5 approach. Addiction. doi:10.1111/add.12457
Petry NM, Stinson FS, Grant BF (2005) Comorbidity of DSM-IV pathological gambling and other psychiatric disorders: results from the National Epidemiologic Survey on Alcohol and Related Conditions. J Clin Psychiatry 66(5):564–574
Report on the WHO Collaborative Study on Strategies for Extending Mental Health Care (1984) World Health Organ Tech Rep Ser 698:35–59
Rumpf HJ, Bischof G, Bischof A, Besser B, Glorius S, deBrito S, Rehbein F, Mößle T, Gürtler D, John U, Meyer C, Petry NM (2014a) Applying DSM-5 criteria for Internet gaming disorder to different Internet activities, Manuscript Draft. University of Lübeck, Germany
Rumpf HJ, Vermulst AA, Bischof A, Kastirke N, Gürtler N, Bischof G, Meerkerk GJ, John U, Meyer C (2014b) Occurence of internet addiction in a general population sample: a latent class analysis. Eur Addict Res 20:159–166
Stucki S, Rihs-Middel M (2007) Prevalence of adult problem and pathological gambling between 2000 and 2005: an update. J Gambl Stud 23(3):245–257. doi:10.1007/s10899-006-9031-7
Su W, Fang X, Miller JK, Wang Y (2011) Internet-based intervention for the treatment of online addiction for college students in China: a pilot study of the Healthy Online Self-helping Center. Cyberpsychol Behav Soc Netw 14(9):497–503. doi:10.1089/cyber.2010.0167
Sussman S, Lisha N, Griffiths M (2011) Prevalence of the addictions: a problem of the majority or the minority? Eval Health Prof 34(1):3–56. doi:10.1177/0163278710380124
Tao R, Huang XQ, Wang JN, Zhang HM, Zhang Y, Li MC (2010) Proposed diagnostic criteria for internet addiction. Addiction 105(3):556–564. doi:10.1111/j.1360-0443.2009.02828.x
Young KS (2007) Cognitive behavior therapy with Internet addicts: treatment outcomes and implications. Cyberpsychol Behav 10(5):671–679. doi:10.1089/cpb.2007.9971

Part III

Topics of Interest

Assessment Strategies and Instruments in DD

17

Rolf-Dieter Stieglitz and Veerle Raes

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Abstract

The aim of this chapter is to provide the reader of a strategy to decide which instruments to use in case of dual disorder. Depending on the level in the diagnostic process, distinction should be made between the need for screening and than further assessment. Then, several instruments are presented for the screening of substance use or abuse in general psychiatric context and for the screening of comorbidity in treatment context of substance use disorders. Instruments should cover a number of criteria such as reliability and validity,

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relative easy training and—in a European context—availability in several languages.

Once the screening is able to confirm a suspected diagnosis, rating scales and structured interviews are recommended. In case of substance use disorder, the instruments should be multidimensional and sometimes substance specific. To assess comorbidity, comprehensive clinical experience is basic, beside the use of structured and standardized instruments and rating scales, in order to reduce sources of error. It is concluded that more standardization of the diagnostic process needs to be taken for the future of empirical research in psychiatry to advantage consistency and comparability of data across studies. Next to the need of more standardization of the diagnostic process, standard use of instruments in clinical practice could also enhance communication and alliance between patient and therapist. By incorporating patient and therapist ratings in the assessment process, clinical usefulness, personal relevance, and meaningfulness to the patient could be enhanced.

17.1 Introduction

17.1.1 Goals for Screening and Assessment

A psychiatric assessment or psychological screening is a process of gathering information about a person within a (mental) health service. Mostly, the purpose of assessment is to make a diagnosis within a clinical context. It is commonly carried out as a first step in the treatment process with clinical or therapeutic purposes. Although assessment can be carried out with other purposes, the focus of this article will be on clinical assessment.

Depending on the specificity of the health service the person is presenting at (mental health or addiction care) as well as the acuteness of the treatment demand, a distinction should be made between screening and assessment in order to make a diagnosis.

The main *goal or purpose* of screening is to detect the frequency of a certain condition in a wide range of people. Co-occurring alcohol, other drug, and mental health conditions seem to be common among people in addiction care, although a number of them display only some or milder symptoms while not meeting the ICD or DSM criteria for the diagnosis of a mental health disorder (Mills et al. 2009). Vice versa, prevalence of substance abuse in psychiatric populations is high (Kerkmeer et al. 2003). So, in case of suspicion of co-occurring addictive and psychiatric disorders, screening for both addiction and mental health symptoms/disorder is indicated.

The original *goal or purpose* of more in-depth assessment is to diagnose the existence of a mental health and/or addiction disorder in order to build a treatment plan. In medicine, a diagnosis frequently refers to the ability to identify the origin/cause of a medical condition, based on symptoms and complaints. In mental health care, a diagnosis provides more gradual information about the type/category/class

and severity of symptoms/a disorder, including the broad (bio-psycho-social-moral) perspective of personal, medical and family history, trauma history, risk assessment, and strengths and weaknesses to current mental state and presenting issues.

17.1.2 Relevance and Function

Screening could have several functions. Within the context of this article, we would like to focus on two of them. In the first place, screening allows measuring the *prevalence* of either addiction or mental health disorder in populations that present in mental health or addiction care, respectively. The relevance of screening is associated with our knowledge that comorbidity can produce negative consequences on treatment outcome. Apart from that knowledge and although comorbid mental health conditions are more complex, those populations could benefit as much from traditional alcohol and drug treatment as people without comorbid profiles (Mills et al. 2009). Therefore, early recognition and assessment of both conditions is crucial, as early detection and treatment of psychiatric and substance use disorders and problems enhance the probability of better outcomes (Tiet et al. 2008).

Another important function of screening is to be able to determine those persons for whom further, more in-depth assessment on their mental health and/or addictive condition is needed. Only in the case of dual disorder, one could argue that screening is not relevant anymore (de Weert-Van Oene et al. 2013). However, screening is often a first step in any assessment strategy. Therefore, screening instruments that can be used in broader practice are also presented.

Also more in-depth assessment within the treatment process can have multiple functions and relevance. While looking at the instruments our focus will mainly be on the following characteristics: Firstly, the instrument should be able to classify a person within the diagnostic system of mental disorders. As an even more important second step, we will look at the existence of connecting factors in order to build a treatment plan, to monitor the response to treatment, and to enhance communication and patient involvement.

17.1.3 Characteristics for Measurement

Screening and assessment should occur as transparent and objective as possible. Therefore, the use of standardized instruments or tools by trained people is preferable. Of course, the instruments and tools themselves should meet several conditions.

While screening instruments mostly focus on only one mental health and/or addiction condition, assessment should cover several life areas that are relevant in case of comorbidity. Because of the *multidimensionality* of substance use and mental health disorders, several areas can be relevant. Traditionally there are six areas in addiction treatment to consider: physical health, education—work-income, substance

use, judicial status, family and/or social relations, and mental health. Since a couple of areas seem to fail in this listing, the International Classification of Functioning, Disability and Health (ICF) can serve as a guideline for relevance check.

A valuable tool should be *reliable and valid*. In case of screening, the tool should be able to identify the existence of a disorder, and do so without any coincidences (reliability). It should be able to distinguish people that need further assessment on a certain condition from those who do not (validity) referring to the sensitivity and specificity of the tool. In order to avoid false positives and/or negatives, the tool must be sufficiently sensitive (ability to recognize the disorder) and specific (ability to exclude people without the disorder). According to the Dutch guideline for screening, for example, sensitivity seems more important (Kerkmeer et al. 2003). Yet, in case of high sensitivity more false-positive cases will be found, which could in turn compensate for the lower proportions in case of high prevalence. However, when high prevalence is expected, the need for screening disappears, as in this case full assessment should be provided for all people directly. The best way to control for reliability and validity of instruments is a search for publications on the psychometric characteristics (e.g. meta-analysis).

Within the European context, the availability of an instrument in *several languages* is advantageous.

As generally *routine outcome monitoring* is required, tools should also be suitable for repeated use. They should be sensitive for the measurement of change/outcome. The monitoring of an individual patient's progress is perceived as one-way to improve treatment outcome. Actually, the social context is claiming the necessity of a monitoring perspective as an aspect of quality assurance. Since assessment with feedback evidentially leads to positive effects on retention in treatment (Raes et al. 2011), the possibility of integrating the instrument within the clinician–patient encounter in order to provide double-sided feedback on the results will also be rated.

This means that the burden for clinical workers and the patient should be taken into account. The instruments themselves should be as short as possible, and easy to interpret**.** Hence, time to complete and ***training aspects*** will be considered in the overview. It is important that the training for the use of the instrument should be short and feasible without (eventually a minimum of) advanced specialization in mental health disorders and/or substance abuse disorders, respectively.

Last but not least, a **good balance between *costs* and *benefits*** should be found. Especially for screening tools, that are to be conducted in larger groups, the conduct/administration-price of the tool should be evaluated and free availability is preferable.

17.2 Multimodal Assessment

It is generally agreed upon that human behaviour and experience have to be measured in a multimodal way (other terms occasionally used: multi-method, multi-methodically). Thus, distinctions are made between the following aspects (Baumann et al. 1985): databases (e.g. psychological), eventually partial aspects

Table 17.1 Multimodal assessment

Databases	Basic units of consideration (perspectives: e.g. biochemical, physiological, psychological, social, ecological)
Sources of data	Data provider (e.g. patient, therapist, nursing staff, reference person, neutral observer)
Functional ranges	Partial aspects/constructs within a database (e.g. psychological databases: experiences, behaviour, feeling, working capacity)

within a relevant area (constructs) and sources of the information/data (see Table 17.1) as well as the type of instruments which are used to assess the relevant aspects of interest.

Multimodal assessment can be understood as a *general framework* which has to be specified for the concrete assessment of individual persons or groups of persons, making it necessary to select specific instruments. The choice should be made according to specific criteria (see Sect. 17.1.3).

A multimodal approach is generally required for evaluation, e.g. of psychotherapy and psychotropic drugs research in order to cope with the complexity of the phenomena studied. Multimodal assessment in this area is increasingly gaining importance because of the range of competing psychotherapeutic methods, the development of disorder-specific treatment approaches as well as manualized/standardized therapy approaches. Furthermore, a multimodal approach is essential in order to account for the varying degrees of exactness in databases and data providers as well as their functional ranges.

Last but not least, the necessity of a multimodal approach arises from the need to reduce investigator dependent rating bias and results in the inclusion of different perspectives. With regard to self-rating scales, bias may include acquiescence, central tendency, or social desirability; on the level of observer-rating scales it may come from insufficient experience with the scale, or response biases such as generosity error or error of leniency.

In the field of multimodal assessment the relation between self- and observer-rating scales is of special relevance. Both self- and observer-rating scales (with the patient and the therapist as the most important sources) are characterized in relation to other assessment methods in that they are applicable in a vast range of areas and that they are easy to administer (e.g. time-saving).

There is extensive literature available since several years comparing the results of self- and observer rating scales (e.g. Baumann et al. 1985; Smolka and Stieglitz 1999), especially in the area of psychotherapy and psycho-pharmacotherapy. Independent of the analysed groups of disorders the results of the studies coincide. The following conclusions can be drawn in relation to self- and observer rating scales:

- Both groups of instruments only correlate to a medium degree.
- Observer-rating scales often provide a better differentiation between groups of patients than self-rating scales.

Table 17.2 Multimodal assessment of anxiety disorders (examples)

Databases	Psychological, physiological, social
Sources of data	Patient, therapist, independent/trained rater, relevant others (e.g. family members)
Functional ranges	• Psychological database: cognitions, emotional reactions, behaviour • Physiological database: physiological reactions • Social database: impairments and handicaps, social support
Assessment instruments	Self- and observer-rating scales, structured or standardized interviews, diaries, behaviour observations, behavioural tests, self-monitoring, physiological assessment instruments.

- Observer-rating scales are more sensitive in detecting differences between groups of patients than self-rating scales.
- Great discrepancies are often observed on the level of individual patients.
- Various factors may account for these discrepancies: The instruments cover different aspects of the construct of interest (e.g. the different instruments used to assess the depressive syndrome).
- The perspective of the patient him-/herself and of other data sources are different.

In summary, one should not conclude that observer-rating scales are generally preferable to self-rating scales. They should rather be seen as complementary, as not all phenomena of interest (e.g. mood, feelings, complaints) can be assessed with observer-rating scales.

For most psychiatric disorders, a multimodal approach is necessary for an adequate description, as a gold standard is missing. An example is present in Table 17.2. Addictive disorders are particularly characterized as multidimensional with different aspects to consider such as subjective experiences, specific behavioural reactions, and social interactional consequences, as well as a broad spectrum of somatic dysfunctions.

Depending on the specific aim of the assessment (e.g. the natural course, efficacy of a therapeutic intervention), a broad range of aspects has to be taken into account.

17.3 Assessment Instruments

Before presenting and discussing the instruments, some general remarks concerning differences between the US and European approach in the diagnosis could be made. The main difference consists in focusing on ICD-10 in Europe and DSM in the USA. In addition, in the USA more rating scales are used, e.g. to quantify the symptomatology. Also, the use of diagnostic interviews in the USA is more important, while in Europe the assessment of classical psychopathology plays a bigger role.

17.3.1 Screening of Substance Use/Abuse

Properly trained mental health and addiction workers understand the role, function, and difference between screening tools and clinical measures, and of course no screening tool or clinical measure suffices on its own. In fact, their most important function is to assist practitioners and patients in clinical decision making. In case of screening, the goal is to discover potential risk areas. They are not designed to make a clinical diagnosis.

In an early study from 2004, three instruments were discussed for the screening of substance use disorders (Dom et al. 2004): *CAGE* (Cut down, Annoyed, Guilty, Eye-opener), the Alcohol Use Disorders Identification Test (AUDIT-10q) or short version *AUDIT-C* (3 q), the Munich Alcoholism Test (MALT) or short version (MALT-3), and the Dartmouth Assessment of Lifestyle Instrument (*DALI*). In the UNODC-Treatment program (UCLA 2006), some of these instruments were also suggested besides the availability of similar instruments: the *ASSIST* (Alcohol, Smoking, and Substance Involvement Screening Test), the Drug Use and Cannabis Disorders Identification Test (*DUDIT* and *CUDIT*) (Adamson and Sellman 2003), the *DAST-10* (Drug Abuse Screening Test), the CRAFFT (6 q) (Car, Relax, Alone, Forget, Family or friends, Trouble), and the TWEAK (Tolerance, Worried, Eye-opener, Amnesia, Cut down). The Dutch guideline for dual disorder (Kerkmeer et al. 2003) added to that list the Alcohol Dependence Scale (ADS), the CAGE Adapted to Include Drugs (*CAGE-AID*), the Short Drug Abuse Screening Test (*S-DAST*), the Mac Andrew Alcoholism Scale (*MAC*), the Michigan Alcoholism Screening (*MAST*) and Short MAST (*S-MAST*), the Reason's for Drug Use Screening (RDU), and the Severity of Dependence Scale (*SDS*).

Based on the discussion and commonalities in the conclusions of the three guidelines, we inserted the CAGE, CAGE-AID, AUDIT, AUDIT-C, DUDIT, CUDIT, DAST, and the ASSIST into Table 17.3.

CAGE and CAGE-AID are screening tools for alcohol and drugs, respectively, by means of four items: Cutting Down, Annoyance resulting from criticism, Guilt feeling, and Eye-opener. AUDIT is a brief structured interview, which can also be used as a self-rating list with ten questions. CUDIT and DUDIT were developed for the screening of cannabis and drug use disorder, respectively. Within psychiatric samples, they were all found suitable for use in first episode psychosis (Adamson and Sellman 2003). ASSIST has been developed to detect substance use disorder in primary health care. It screens for all levels of problem or risky substance use in adults. It consists of eight questions covering the main substance categories. DAST, consisting of 28 or 10 (short version) items measuring drug-related problems in the last 12 months has good psychometric qualities and is the only screener that has been validated within a psychiatric sample (Maisto et al. 2000).

CAGE and CAGE-AID are most widely used (Aertgeerts et al. 2000), although AUDIT had better psychometric properties. It is the length of the AUDIT that hampers its use. Drug screens for routine use should be brief. However, for the determination whether further assessment for substance use disorder ought to be implemented, the brief version of AUDIT (AUDIT-C), and their derived

Table 17.3 Instruments for the screening of substance use/abuse

Name of instrument	Type	Available languages	Sensitivity for change/ therapeutic use and feedback properties	Time to complete	Need for training	Cost
ASSIST (alcohol and drugs)	Structured interview	English French German Spanish Portuguese Russian . . .	− (for primary health care) + (feedback properties) + (repeatable)	5–10 min	Self-training is possible	free (WHO)
AUDIT/ AUDIT-C (alcohol) CUDIT (cannabis) DUDIT (drugs)	Structured interview	AUDIT: English and numerous languages including Dutch French German Italian Spanish and Slovenian DUDIT: English Dutch German Spanish Portuguese Danish Norwegian Swedish Finnish Hungarian and Turkish CUDIT: English French German Italian	+	1–3 min	Minimal	Free

CAGE (alcohol)/ CAGE-AID (drugs)	Self-rating scale	English Dutch	+	1–2 min	Minimal	?
DAST/S-DAST (alcohol)	Self-report or structured interview	English Finnish	+	5 min	Careful reading and adherence to the instructions in the "DAST Guidelines"	Without or at nominal cost

instruments DUDIT and CUDIT are advised. Validity of the abbreviated versions has been confirmed as well as the efficiency of the language adapted versions (de Meneses-Gaya et al. 2009). For epidemiologic and/or research purposes, it may be advisable to choose the WHO-screening instrument ASSIST, which has been validated with the MINI-Plus (Tiet et al. 2008). ASSIST and AUDIT are available in different European languages, as well (WHO 2013).

17.3.2 Problem Identification, Diagnosis, and Monitoring

The instruments for problem identification and diagnosis proposed in Dom and colleagues (2004) are the EuropASI: European Addiction Severity Index, the CIWA-AR: Clinical Institute Withdrawal Assessment for Alcohol—revised, the OCDS: Obsessive Compulsive Drinking Scale, the FTND: Fagerström Test for Nicotine Dependence and the RCQ: Readiness to Change Questionnaire, which is more suitable for the assessment of motivational factors related to change in substance abuse.

In the UNODC Treatment program (UCLA 2006), only the Addiction Severity Index (ASI) is suggested for the assessment of substance abuse. Other instruments discussed in the Dutch Guideline for dual disorder (Kerkmeer et al. 2003) are the Alcohol Use Disorder and Associated Disabilities Interview Schedule (DIS), the Composite International Diagnostic Interview (CIDI) (WHO 1997; Andrews and Peters 1998), the Maudsley Addiction Profile (MAP) (Marsden et al. 1998), the Opiate Treatment Index (OTI), the Self-Administered Alcoholism Screening Test (SAAST), the Structured Clinical Interview for DSM Disorders (SCID), the Semi-Structured Assessment for the Genetics of Alcohol (SSAGA).

A more recent Dutch publication (De Weert-Van Oene et al. 2013) promotes the use of a new instrument, combining on the one hand an international classification system of functioning and on the other hand parts of different separate instruments that each time focus on an important aspect to be assessed in case of dual disorder: the Measurement in Addiction for Triage and Evaluation (MATE) (Schippers et al. 2010). The MATE includes the Composite International Diagnostic Interview (CIDI), the Maudsley Addiction Profile—Health Symptoms Scale (MAP—HSS), the Standardized Assessment of Personality Abbreviated Scale (SAPAS), the International Classification of Functioning, disability and health (ICF) (Baron and Linden 2008), the Obsessive Compulsive Drinking (and drug use) Scale (OCDS), and the Depression Anxiety Distress Scales (DASS 21) (De Beurs et al. 2001).

From the instruments mentioned above, EuropASI is the European standardised version of the original American ASI. Primarily, DIS was preceding the CIDI. CIDI and SCID will be discussed in the context of the assessment of comorbidity. Therefore, solely the following are kept in Table 17.4: the EuropASI and all instruments that are fully or partly taken in the MATE, as there are OCDS, MAP-HSS, SAPAS, ICF, and DASS.

OCDS, SAPAS, and DASS could be seen as relevant screeners for strongly prevalent (mental health) comorbidity in populations with substance abuse.

Table 17.4 Instruments for multi-dimensional assessment in patients with substance use disorder

Name of instrument	Description	Available languages	Sensitivity for change/therapeutic use and feedback properties	Time to complete	Need for training	Cost
ASI/ EuropASI	Semi-structured interview, covering 7 potential problem areas	English Dutch German Greek French Spanish . . .	+(follow-up version available)	30–45 min	1,5 day training	Free
OCDS[MATE]	16-items self-rating scale	English		5 min	Minimal	
CIDI[MATE]	Structured diagnostic interview conforming DSM or ICD Max 376 items in 14 diagnostic categories	English Dutch	+ − in case of cognitive limitation	Time spending	Intensive training needed Risk of over-diagnosing	WHO
MAP/MAP-HSS[MATE]	Short structured interview. 56 items in four areas Problem-identification at intake and outcome measure	English Italian Spanish Portuguese		12 min	Moderate	?
SAPAS[MATE]	Brief screening test for personality disorder					
ICF[MATE]	Classification system					WHO
DASS 21[MATE]						
MATE	Multimodal	Dutch English German				

EuropASI has been a gold standard for years, considering treatment demanding people in substance related and/or mental health facilities. Recently a new instrument, elaborated in the Netherlands is gaining attention: the Measurement in the Addictions for Triage and Evaluation (MATE) Table 17.5. The instrument is composed of ten modules, constructed according to the World Health Organisation (WHO) classification systems International Classification of Diseases (ICD), and International Classification of Functioning, Disabilities and Health (ICF). It was decided to arrange the instruments in Table 17.4 in order of priority: firstly, those that refer to WHO classifications and/or instruments (CIDI, ICF); secondly, the common ones in the three guidelines; and thirdly, the MATE. Since not all of the instruments exist in several European languages, preferences could depend on the language issue. There are only poor arguments to prefer one instrument to another due to psychometric characteristics. Preference should be based upon measurement purpose (research, treatment plan, supporting therapeutic alliance, monitoring. . .), most adapted modality in practice (interview, self-rating scale, screening test or classification system), realism to implement (time to complete, need for training, cost). Instruments combining several of these characteristics are most promising in a decade where outcome measurement and monitoring are upcoming issues. The importance of assessment with feedback to support clinical meetings is essential for implementation (Raes 2012).

The MATE itself can be considered a multimodal assessment tool, since it includes several main areas, specific subareas, self-rating scales as well as interview schedules, observation items and health symptoms. An overview has been given in Schippers et al. (2010). MATE consists of ten modules, each of them referring to a specific tool within a specific domain.

17.3.3 Instruments to Assess Comorbidity

The process of diagnosis of comorbid disorders is a complex one. The investigator must have comprehensive clinical experiences and extensive knowledge of current classification systems, as well as specific knowledge with regard to individual disorders and their defining symptoms. Since comorbidity also may occur in different stages of life, the sequence must be observed. A clinical interview is problematic and prone to failure with respect to these aspects. Here structured and standardized interviews can help to reduce these sources of error. Since such interviews are usually very time-consuming, screening instruments should be used before a comprehensive assessment. Recently Mestre-Pintó and colleagues (2014) developed the short screening interview "Dual Diagnosis Screening Interview" (DDSI; application time about 20 min). Even check lists can be very helpful here (e.g. SCL; Table 17.6).

For the screening of personality disorders, SAPAS is brief and suitable for addictive populations. In case of substance abuse, an indication of obsessive compulsive behaviour can be elicited by the OCDS. The instrument measures alcohol (or drugs) craving, while it conceptualizes craving as similar to obsessive

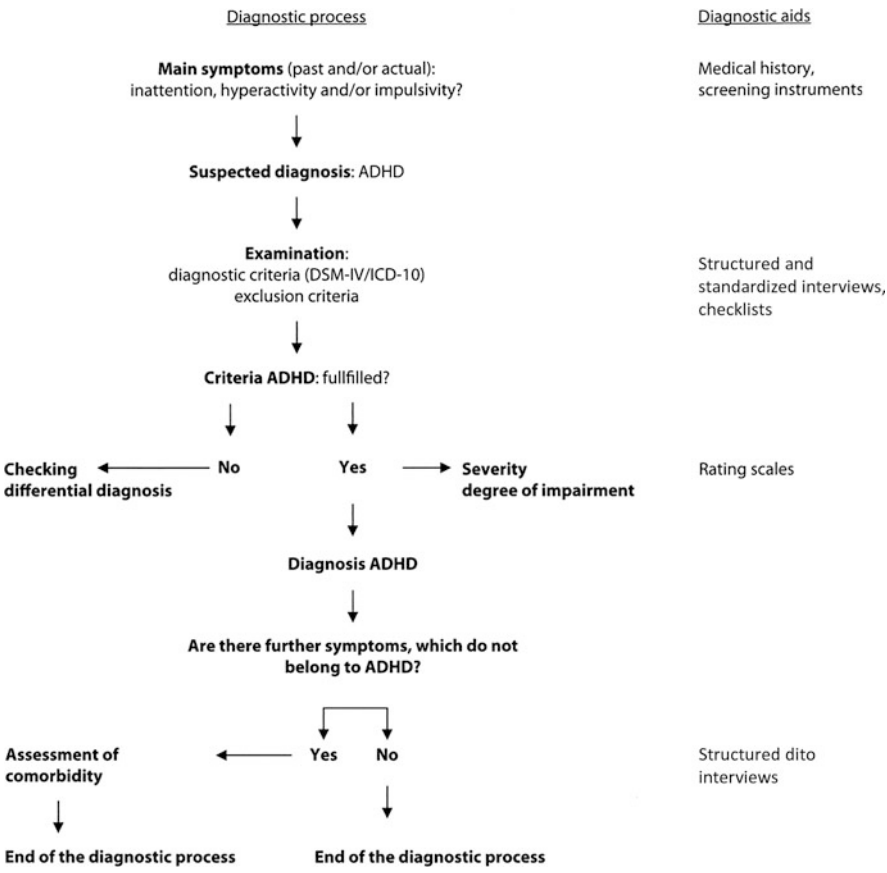

Fig. 17.1 Steps in the diagnostic process

compulsive disorder. To detect depression and/or anxiety, the Depression and Anxiety Scale DASS is a good screening tool. The Obsessive Compulsive Drinking Scale and the Depression and Anxiety Scale are both self-rating scales with 16 or 21 items, respectively, while SAPAS is a screening test/interview for personality disorders done by the clinician.

In clinical routine the diagnostic process to find one or more diagnoses is a complex process (see Fig. 17.1). Several issues should be considered, for example the problems of a clinical interview to assess all information, the differentiation between different disorders and the evaluation of comorbid diagnosis. The process is exemplified by ADHD diagnostics.

To support this process specific instruments are valuable tools. Especially the enormous increase in the use of psychoactive substances and related problems in public health emphasizes the great need for diagnostic instruments, which could be used for different purposes in different settings. Üstün and Wittchen (1992)

Table 17.5 Framework of the MATE

Domain	Module	Classification system	Original tool
Substance related disorders	M1: Substance Use: quantity, frequency and variability	Use grid	
	M4: Substance dependence and abuse	ICD/DSM dependence criteria/abuse criteria	
	Q1: Craving	Self-report quest	OCDS adapted
Psychiatric comorbidity	Q2: Depression, anxiety, stress	Self-report quest	DASS
	M2: Indications for psychiatric or medical consult (psychotic symptoms, suicidality and current psychiatric treatment)	Interview	
	M6: Personality	Interview	SAPAS
Physical comorbidity	M5: Physical complaints; and M2	Interview	MAP-HSS
Personal and social functioning	M7: Activities and participation: care and support	ICF coreset and need for care	
	M8: Environmental factors influencing recovery		
No system	M3: Treatment history	Interview	

discussed the relevance of diagnostic instruments, especially structured and standardized interviews (see Table 17.6): (1) epidemiological methods in general population surveys are necessary to assess on-going changes and trends on the basis of instruments which produce comparable data; (2) screening or case-finding instruments are essential for the early detection of potential cases or actual cases and related prevention and intervention programs; (3) the reliable and valid assessment of diagnostic features such as comorbidity, abuse patterns and substance-related problems is necessary for systematic treatment, rehabilitation and social reintegration of patients; (4) standardized instruments are the basis for evaluation of symptom patterns across substances delineating the course and natural history of disorders; (5) diagnostic instruments are essential for the evaluation of intervention programs in terms of their process, outcome, cost effectiveness, impact and acceptability.

17.3.3.1 Standardized Interviews, Structured Interviews and Checklists

Composite International Diagnostic Interview

The CIDI is a standardized diagnostic interview developed on the basis of the Diagnostic Interview Schedule (DIS) by WHO and associated working groups. The

Table 17.6 Instruments for the assessment of substance use and comorbid disorders according to DSM-IV and/or ICD-10

Instruments	Format	System	Application	User
CIDI	StandI	ICD-10 DSM-IV	Training	Lay interviewer Psychiatrist Psychologist
CIDI–SAM	StandI	ICD-10 DSM-IV	Training	Lay interviewer Psychiatrist Psychologist
M.I.N.I.	StandI	ICD-10 DSM-IV	Training	ICD-10 DSM-IV
SCID	StrucI	DSM-IV	Training Knowledge of the system	Psychiatrist Psychologist
SCAN	StrucI	ICD-10 DSM-IV	Training Knowledge of the system	Psychiatrist Psychologist
IDCL	CL	ICD-10 DSM-IV	Training Knowledge of the system	Psychiatrist Psychologist

StandI Standardized Interview, *StrucI* Structured Interview, *CL* Checklist

CIDI was designed primarily for epidemiological studies. Content and structure of the interview follow a high level of standardization of diagnostic questions and coding procedures to ensure that the instrument could be used for clinical or research purposes in a wide range of settings. The use of the interview has to be trained over a period of at least 1 week and could be conducted by trained clinicians as well as non-clinicians. The duration of the assessment encompasses a range between 1 and 3 h. The core version has an alcohol and other drug use section within 15 general sections in a modular format. Using a related computer program, CIDI could produce most important ICD-10 and DSM-IV diagnoses. A computer-assisted version (CIDI-A) and a training package is available. Feasibility and reliability of the instrument were tested in different field trials (Wittchen et al. 1991). Sufficient inter-rater reliability coefficients (kappa >0.60) were usually found for substance use disorders.

Composite International Diagnostic Interview: Substance Abuse Module (CIDI–SAM)

The CIDI–SAM is a standardized interview, which was designed as an optional module to expand the substance use sections of the CIDI core version. In contrast to CIDI, CIDI–SAM includes substance-specific questions on medical, psychological, and social consequences as well as onset, recency, quantity, and frequency for each substance used. Diagnoses following DSM-III, DSM-III-R, DSM-IV, Feighner, Research Diagnostic criteria, and ICD-10 could be produced covering alcohol- and drug-related disorders. The diagnostic and item reliability of the interview was tested sufficiently (Cottler et al. 1991). Using the CIDI–SAM, several authors found a high degree of concordance with respect to harmful use (Cottler 1993; Rapaport et al. 1993).

Mini-International Neuropsychiatric Interview (M.I.N.I.)

The M.I.N.I. is a short structured diagnostic interview for DSM-IV and ICD-10 psychiatric disorders (Sheehan et al. 1998). With an administration time of approximately 15 min, it was designed to meet the need for a short but accurate structured psychiatric interview for multi-centre clinical trials and epidemiologic studies and to be used as a first step in non-research clinical settings. The interview was validated in relation to the Structured Clinical Interview for DSM-III-R and the Composite International Diagnostic Interview (CIDI).

Structured Clinical Interview for DSM-IV (SCID)

The SCID is the most important DSM-related instrument, which is largely used in the USA (Kosten et al. 1990) and in other countries. It was developed by Spitzer and Williams (1980), which demonstrated high reliability coefficients. Additionally, a more detailed version of alcohol and drug use disorders was developed. Using this approach, Bryant et al. (1992) have shown that the coexistence of psychiatric and substance dependence disorders has an adverse effect on accurate diagnosis.

Schedules for Clinical Assessment in Neuropsychiatry (SCAN)

SCAN is a comprehensive structured psychiatric interview, which was developed by WHO (1995) on the basis of the Present State Examination. The SCAN system has a modular format covering the most important DSM-IV and ICD-10 diagnoses, a syndrome checklist, and a clinical history schedule. The system includes a diagnostic computer program, a computer-assisted interview, and a training package (Wing et al. 1992).

Symptom Checklists (SCL)

A more economic and simple method of registering diagnostic criteria are symptom checklists. The International Diagnostic Checklists (IDCL) for ICD-10 and DSM-IV (Hiller et al. 1993) provide lists with the relevant criteria and diagnostic decision rules for each group of disorders. The criteria are assessed by an interviewer on the basis of free clinical interviews and other sources of information.

The ICD-10 Symptom Checklist for Mental Disorders (ICD-10 SCL) (Janca et al. 1994) is another checklist intended for clinicians' assessment of psychiatric symptoms in the F1 category of ICD-10. The lists are accompanied by instructions intended to help the user in considering differential diagnoses. Data concerning inter-rater reliability have not been available so far.

17.3.3.2 Conclusion

During the last few years a number of instruments (interviews and checklists) have been developed to improve the reliability of clinical judgement, whose aim was to reduce specific sources of error (information, observation and/or interpretation variance) (Spitzer and Williams 1980).

This standardization of the diagnostic process is important for the future of empirical research in psychiatry, as cumulative impact of research was often considerably reduced by the fact that results of different studies were not

comparable due to differences in diagnoses and especially amongst diagnostic instruments on which the diagnoses were based. In most studies, however, no instrument was used. According to Helzer (1983), the advantages of using interviews for research are consistency and comparability of data across studies, uniformity and reliability of data within studies, and a reduction of examiner bias in the collection and interpretation of data. Although sufficient or high reliability is achieved with most instruments, we have to consider that validity will always be limited to the validity inherent in the diagnostic criteria on which the instruments are based and the exactness with which the instruments elicit the behaviour, thoughts, and feelings described by these diagnostic criteria.

17.3.4 Other Areas

In case of dual disorder, a multimodal approach requires the consideration of areas beyond substance abuse alone and beyond solely psychiatric diagnosis and classification (see Sect. 17.2). EuropASI is covering the severity of problems in seven relevant life areas, including physical health, education, work and income, alcohol abuse and drug abuse, judicial status, family and social relations, and mental health. Each of the areas can be further explored by more specific tools after an area has been found problematic. MATE is covering ten domains, referring to WHO instruments and classification systems (DSM, ICD and ICF), as there are substance related disorders (use, abuse, dependence, craving), psychiatric comorbidity (depression and anxiety symptoms, personality disorders, suicidality, psychotic symptoms), physical comorbidity (complaints and symptoms) and personal and social functioning (problems, support, and participation). Table 17.6 lists different areas and related instruments valuable for assessment. We can use them at the beginning of treatment (e.g. evaluation of the general level of psychopathology with the SCL-90-R), during treatment (e.g. evaluation of progress or specific problems) and at the end of treatment (e.g. evaluation of success).

To summarize, we have to make assessments on different levels (see Table 17.7). On the first level we have to make a diagnosis. On the second level, a categorical view ought to be implemented by adding more information concerning the general level of symptomatology as well as the patient's personality profile. On the third level, aspects such as impairment or quality of life should be taken into account. Here, the assessment has to focus on therapy-related aspects in regards to the intervention chosen (Table 17.8).

Table 17.7 Relevant fields in the context of addictive behavior

Area	Examples
General psychopathology	Symptom Checklist—90-Revised (SCL-90-R)
Personality	NEO—Personality Inventory—Revised (NEO-PI-R)
Interpersonal problems	The Inventory of Interpersonal Problems (IIP)
Relationship analysis	Structural Analysis of Social Behaviour (SASB)
Social adjustment	Social Adjustment Scale (SAS), by Weisman
Impairments	Sheehan Disability Scale (SDS)
Quality of life	SF-36 Health Survey (SF-36)

More details to assessment instruments see APA (2000)

Table 17.8 Diagnostic levels and related instruments

Level 1	Categorical diagnostics of addictive behavior and comorbid disorders according to ICD-10 or DSM-IV (e.g. by means of structured interviews)		
Level 2	Global assessment (e.g. by means of CGI or GAF)	General psychopathology (e.g. by means of SCL-90-R)	General aspects of personality (e.g. by means of NEO-PI-R)
Level 3	*Impairments* (e.g. by means of Sheehan-Scale)	*Quality of Life* (e.g. by means of SF-36)	
Level 4	*Diagnostics related to disorder and therapy* (e.g. cognitive-behavioural)		

Summary and Perspectives

Multimodal assessment is not only a must in the area of psychotherapy research and evaluation, but it is of even greater importance in daily clinical practice. For both the researcher and the practitioner, it requires the adoption of a bio-psycho-social and ethical model. Furthermore, clinicians should take into account multiple perspectives (patient, therapist, context. . .) in order to enhance communication. Therefore, several types of validated and preferably standardised instruments are available. Actually, decisions about where to start screening and where to go further into assessment often depend on the focus of the treatment facility and the first treatment demand of the patient. In substance abuse treatment facilities, the adoption of a bio-psycho-social and ethical model is already obvious, but the way psychiatric comorbidity is assessed and recognized is not always clear. The use of a screening instrument for comorbidity is advised in that situation. In general psychiatric facilities, the first treatment demand is not always substance related. In such cases, the use of a screening tool for substance abuse is recommended. In a specific facility exclusively specialized on psychiatric patients or substance abusing patients, respectively, it may be relevant to go further into one particular area, based on a positive quick screen.

Several screening instruments are available to screen for substance abuse in psychiatric populations, but only a few can be used in substance abuse populations to screen for comorbidity. Screening instruments are often self-

rating scales, which are usually preferred by clinical workers due to their brevity and feasibility to use in daily practice. Although discrepancies in ratings between the patient perspective and the one of the therapist can be a problem in the field of research, they are important and useful issues in clinical practice. There, the discrepancies in the measurement between patient and therapist can be used as a mean to enhance communication between patient and therapist, and so enhance alliance. Moreover, in psychotherapy, patients benefit from psychological assessment through active engagement and the provision of ongoing feedback (Clair and Prendergast 1994). By incorporating patient and therapist ratings in the assessment process, clinical usefulness, personal relevance, and meaningfulness to the patient could be enhanced. The information of the therapist is not the sole goal of clinical assessment anymore; it became just as important to develop alliance, to provide collaborative feedback and to come to a shared decision making about treatment options (Pope 1992; Joosten 2009). It would be ideal if in clinical practice the following strategy could be implemented: assess—treat—reassess—adjust treatment (Hunsley and Mash 2005).

References

Adamson SJ, Sellman DJ (2003) A prototype screening instrument for cannabis use disorder: the cannabis use disorders identification test (CUDIT) in an alcohol-dependence clinical sample. Drug Alcohol Rev 22:309–315

Aertgeerts B, Buntinx F, Bande-Knops J et al (2000) The value of CAGE, CUGE and AUDIT in screening for alcohol abuse and dependence among college freshmen. Alcohol Clin Exp Res 24:53–57

Andrews G, Peters L (1998) The psychometric properties of the Composite International Diagnostic Interview. Soc Psychiatry Psychiatr Epidemiol 33:80–88

Baron S, Linden M (2008) The role of the "International Classification of Functioning, Disability and Health, ICF" in the description and classification of mental disorders. Eur Arch Psychiatry Clin Neurosci 258(5):81–85

Baumann U, Eckmann F, Stieglitz RD (1985) Self-rating data as selecting factor in clinical trials of psychotropic drugs. Eur Arch Psychiatry Clin Neurosci 235:65–70

Bryant KJ, Rounsaville B, Spitzer RL et al (1992) Reliability of dual diagnosis. Substance dependence and psychiatric disorders. J Nerv Ment Dis 180:251–257

Clair D, Prendergast D (1994) Brief psychotherapy and psychological assessments: Entering a relationship, establishing focus, and providing feedback. Prof Psychol-Res Pract 25:46–49

Cottler LB (1993) Comparing DSM-III-R and ICD-10 substance use disorders. Addiction 88:689–696

Cottler LB, Robins LN, Grant BF et al (1991) The CIDI-Core substance abuse and dependence questions: cross-cultural and nosological issues. Br J Psychiatry 159:653–658

De Beurs E, Van Dyck R, Marquenie LA et al (2001) DASS: A questionnaire for the measurement of depression, anxiety and stress (De DASS: een vragenlijst voor het meten van depressie, angst en stress). Gedragstherapie 34:35–53

De Meneses-Gaya C, Zuardi AW, Loureiro SR et al (2009) Alcohol Use Disorders Identification Test (AUDIT): an updated systematic review of psychometric properties. Psychol Neurosci 2:83–97

De Weert-Van Oene G, de Jong C, Raes V et al (2013) Problem identification, diagnostic and monitoring in case of double diagnosis (Probleemidentificatie, diagnostiek en monitoring bij dubbele diagnose). In: Dom G, Dijkhuizen A et al (eds) Handbook double diagnosis (Handboek Dubbele Diagnose). De Tijdstroom, Utrecht, pp 41–53

Dom G, Raes V, van den Brink W (2004) Instruments for measuring addictive disorders [Meetinstrumenten bij stoornissen in het gebruik van middelen. Tijdschr Psychiatr 46:671–674

Helzer JE (1983) Standardized instruments in psychiatry. Psychiat Dev 1:161–178

Hiller W, Zaudig M, Mombour W et al (1993) Routine psychiatric examinations guided by ICD-10 diagnostic checklists (International Diagnostic Checklists). Eur Arch Psychiatry Clin Neurosci 242:218–223

Hunsley J, Mash EJ (2005) Introduction to the special section on developing guidelines for the Evidence-Based Assessment (EBA) of adult disorders. Psychol Assess 17:251–255

Janca A, Ustun TB, van Drimmelen J et al (1994) ICD-10 Symptom Checklist for Mental Disorders (ICD-10 SCL, Version 2.0). WHO, Geneva

Joosten E (2009) Let's decide together. Shared decision-making in addiction health care. Dissertation, Radboud University Nijmegen

Kerkmeer M, Blanken P, de Klerk C (2003) Double diagnosis, double aid. Diagnostic guidelines and treatment (Dubbele Diagnose, dubbele hulp. Richtlijnen voor diagnostiek en behandeling). Parnassia, Den Haag

Kosten TR, Bryant K, Rounsaville BJ (1990) The SCID: a clinical instrument for assessing psychiatric disorders. NIDA Res Monogr 105:213–219

Maisto SA, Carey MP, Carey KB et al (2000) Use of the AUDIT and the DAST-10 to identify alcohol and drug use disorders among adults with a severe and persistent mental illness. Psychol Assess 12:186–192

Marsden J, Gossop M, Stewart D, Best D, Farrell M, Lehman P et al (1998) The Maudsley Addiction Profile (MAP): a brief instrument for assessing treatment outcome. Addiction 93:1857–1867

Mestre-Pintó JI, Domingo-Salvany A, Martin-Santos R, Torrens M et al (2014) Dual diagnosis screening interview to identify psychiatric comorbidity in substance users: development and validation of a brief instrument. Eur Addict Res 20:41–48

Mills LK, Deady M, Proudford H et al (2009) Guidelines on the management of co-occurring alcohol and other drug and mental health conditions in alcohol and other drug treatment settings. National Drug and Alcohol Research Center, Sydney

Pope K (1992) Responsibilities in providing psychological test feedback to clients. Psychol Assess 4:268–271

Raes V (2012) Assess and give feedback! The effect of using assessment instruments on substance-abuse outpatients' adherence to treatment. Dissertation, Ghent University

Raes V, De Jong CAJ, De Bacquer D et al (2011) The effect of using assessment instruments on substance-abuse outpatient adherence to treatment: a multicenter randomized controlled trial. BMC Health Serv Res 11:123–132

Rapaport MH, Tipp JE, Schuckit MA (1993) A comparison of ICD-10 and DSM-III-R criteria for substance abuse and dependence. Am J Drug Alcohol Abuse 19:143–151

Schippers GM, Broekman TG, Buchholz A et al (2010) Measurement in the addictions for triage and evaluation (MATE): an instrument based on the World Health Organisation family of international classifications. Addiction 105:862–871

Sheehan DV, Lecrubier Y, Sheehan KH et al (1998) The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. J Clin Psychiatry 59:22–33

Smolka M, Stieglitz RD (1999) On the validity of the Bech-Rafaelsen Melancholia Scale (BRMS). J Affect Disord 54:119–128

Spitzer RL, Williams JBW (1980) Classification in psychiatry. In: Kaplan HI, Freeman AM, Sadock BJ (eds) Comprehensive textbook of Psychiatry, 4th edn. Williams & Williams, Baltimore, pp 591–613

Tiet QQ, Finney JW, Moos RH (2008) Screening psychiatric patients for illicit drug use disorders and problems. Clin Psychol Rev 28:578–591

UCLA Integrated Substance Abuse Programs (2006) Drug dependence treatment: training package Volume A: Screening, assessment, and treatment planning. UNODC-Office on Drugs and Crime. http://www.unodc.org/ddt-training/treatment/a.html

Üstün TB, Wittchen HU (1992) Instruments for the assessment of substance use disorders. Curr Opin Psychiatry 5:412–419

Wing JK, Sartorius N, Üstün TB (1992) Diagnosis and clinical measurement in psychiatry: a reference manual for SCAN. University Press, London

Wittchen HU, Robins LN, Gottler LB et al (1991) Cross-cultural feasibility, reliability and sources of variance of the Composite International Diagnostic Interview (CIDI). The Multicentre WHO/ADAMHA Field Trials. Br J Psychiatry 159:645–653

World Health Organization (1995) Schedules for clinical assessment in neuropsychiatry (SCAN). WHO, Geneva

World Health Organization (1997) Composite International Diagnostic Interview (CIDI) Version 2.1. WHO, Geneva

World Health Organization (2013) Alcohol, smoking and substance involvement screening test (ASSIST). http://www.who.int/substance_abuse/activities/assist_test/en. Accessed 14 Aug 2013

Evidence-Supported Psychosocial Treatment for Dual Disorder Patients

18

Franz Moggi and Agneta Öjehagen

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Abstract

Results on the effectiveness of psychosocial treatments for patients with comorbid psychiatric and substance use disorders (dual disorders) will be discussed based on relevant meta-analyses and comprehensive reviews. Findings pertaining to severe (e.g., schizophrenia) and mild to moderate (e.g., anxiety disorders) dual disorders will be presented. The heterogeneity in patient characteristics, treatments, settings, and measured outcomes within the studies hinders the extraction of simple conclusions regarding how to effectively integrate psychiatric and addiction-

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oriented services into one psychosocial treatment. However, promising treatment strategies and interventions include integrative programs that comprise motivational interviewing; disorder-specific cognitive-behavioral interventions; substance use reduction interventions such as relapse prevention or contingency management; and/or family interventions. Such programs are generally superior to control groups (e.g., waiting list, treatment as usual) and are sometimes superior to other active treatments (e.g., skills training) in outcomes of substance use, psychiatric disorders, and social functioning.

18.1 Introduction

When systematic research on the efficacy and effectiveness of psychosocial therapy in dual disorder patients (DDPs) began some 20 years ago, the rehabilitation of patients with both substance use disorders (SUDs) and one or more other psychiatric disorders (PDs) was assumed to be a *mission impossible* (Roberts et al. 1992). Today, enough controlled clinical trials have been conducted to allow for comprehensive reviews (Cleary et al. 2009; Drake et al. 2004, 2008; Hesse 2009; Horsfall et al. 2009; Kelly et al. 2012; Lubman et al. 2010; Murthy and Chand 2012; Tiet and Mausbach 2007; Pennay et al. 2011) and the performance of sound meta-analyses on the efficacy of psychosocial treatment in DDPs, particularly in patients with severe mental disorders such as schizophrenia, bipolar disorders, or severe depression (Jeffrey et al. 2007; Cleary et al. 2010; Chow et al. 2012; Hunt et al. 2013). However, effective psychosocial treatment for DDPs still is considered a mission impossible, as indicated by the title of Chow and colleagues' (2012) recently published meta-analysis: "Mission impossible: treating serious mental illness and substance use co-occurring disorder with integrated treatment: a meta-analysis." Further, in the latest Cochrane meta-analysis, Hunt and colleagues (2013) conclude that there is no compelling evidence to support any one psychosocial intervention over another (i.e., treatment as usual) for patients to remain in treatment, to reduce substance use, or to improve mental health state in patients with severe mental illness. However, methodological difficulties (e.g., lack of high quality trials) exist which hinder pooling and interpretation of the results.

The distressing verdict of the mission impossible might not result from the challenge of treating dual disorders, per se. Instead, the inconsistent findings may result primarily from the *heterogeneity* among the studies, which is extraordinarily great in terms of patient characteristics and the setting, length, and outcome of treatment; thus it appears almost impossible to find two comparable studies.

For example, De Witte and colleagues recently sought to determine which interventions or programs are effective in outpatient DDPs with comorbid schizophrenia and SUDs (De Witte et al. 2014). First, only eight out of fourteen eligible randomized controlled trials (RCTs) exclusively included patients with schizophrenia. To increase the sample size, the authors included all 14 RCTs for comorbid

SUD and severe mental disorders, which comprised patients with schizophrenia as well as other severe mental disorders (e.g., bipolar disorders). Second, the authors identified four different treatment types in the studies: (a) RCTs implementing a single intervention, mostly for SUD; (b) RCTs adding a standardized set of interventions for substance abuse; (c) RCTs implementing integrated assertive community treatment (ACT) teams; and (d) RCTs comparing *integrated treatment programs* (ITPs), defined as comprehensive programs in which mental health and addiction interventions are offered at the same time, in the same setting, and by the same health professionals. It varied whether a given intervention was a single element, part of a set of interventions, or part of a fully integrated program. Moreover, the interventions comprised one or more of the following: motivational interviewing (MI), cognitive-behavioral interventions (CBI), relapse prevention (RP), contingency management (CoM), case management (CM), ACT, and family interventions (FI).

Further, in the studies presented in De Witte and colleagues' review, the concept of *integrated treatment* (IT) refers to two different levels. The first level is often referred to as a coordination strategy for the delivery of treatment to DDP, which may sometimes include integration between different health care systems (i.e., psychiatric and addiction systems). For example, ACT, standard CM, or intensive CM could be named as *integrated treatment strategies* (ITS), even though these are sometimes labeled as ITP. ACT refers to a treatment team integrating interventions for substance use disorder into psychiatric teams, sometimes by use of a case manager, while case manager outside ACT often coordinates different treatments available in psychiatric and addiction systems. Certainly, both ACT and CM also are supporting interventions, but these strategies are not considered specific treatments. The second level is the integration of disorder-specific treatment interventions for SUDs or PDs, or both SUDs and PDs, into one single program. Unfortunately, it is not often clearly presented how these disorder-specific interventions are integrated (e.g., RP for SUD and FI for PD). Moreover, adding one or more disorder-specific interventions to treatment as usual (TAU) is sometimes also named an ITP and compared to TAU alone in studies, although it is not always clear how these additional interventions were integrated into TAU.

Finally, studies differ considerably in the measurement of SUDs, PDs, and functioning as outcomes, making it difficult to compare treatments. This is exacerbated by the fact that sufficient information for effect size computation is sometimes not provided. Given the great heterogeneity in patient, treatment, and outcome characteristics, it is not surprising that the effect sizes vary substantially within a broad range from $d = 0.14$ to 1.42. Nevertheless, most interventions and ITP showed some beneficial effect in some measures over TAU.

18.2 Heterogeneity of Studies and Its Consequences

There are additional problems that might contribute to the perspective that the treatment of DDPs is complicated or unlikely to be successful. First, it has been suggested that IT is a more effective therapy for DDPs than is the parallel (i.e., treatments at the same time but not coordinated) or serial (i.e., one treatment at a time) treatment of the two disorders by different health care providers. IT addresses two fundamental concerns: (a) improving access to mental health and addiction interventions by offering them at the same time, in the same setting, and by the same health professionals; and (b) improving individualization and clinical relevance by combining the two intervention types (Drake et al. 2008). There are many well-known barriers to integration, including organizational, financing, training, and professional turf issues, which lead to virtually two separate health care systems. The distance between the treatment systems for SUD and PD is even more evident in some Scandinavian countries, where social authority is responsible for SUD treatment and health care authority is responsible for PD, making it even more difficult to implement ITPs (Öjehagen 2006).

Second, efforts to define homogenous types of DDPs to promote research on treatment strategies were essentially unsuccessful because patients substantially differ with regard to social functioning, work conditions, and living situation. One example is Rosenthal and Westreich (1999), two researchers who proposed a quadrant model whereby diagnoses were assigned to one of four quadrants (Rosenthal and Westreich 1999). These were defined by the severity of two dichotomous dimensions: psychopathology (mild vs. severe) and addiction (mild vs. severe). For example, schizophrenia or bipolar disorder is regarded as severe, while mild depression or anxiety disorders are considered mild; substance abuse is deemed as mild, and substance dependence is considered severe. However, this model has not substantially increased knowledge about assessment, diagnosis, etiology, indication for intervention, or treatment. This model still creates problems, separating which persons belong to which treatment.

The vast majority of research has been conducted in severe DDPs, and there is a surprising paucity of studies on mild DDPs (Kelly et al. 2012; Tiet and Mausbach 2007). In recent years, clinicians and researchers began to reject the heterogeneous dual disorder concept in favor of specific treatment combinations for comorbidities, such as for example posttraumatic stress and substance abuse disorders (Schäfer and Najavits 2007), depression and alcohol abuse and dependence (Baker et al. 2010), or schizophrenia and SUD (Barrowclough et al. 2010). Thus, we might be on the way to developing specific treatments for specific comorbidities and abandoning the idea of a uniform treatment approach for all DDPs. Nevertheless, integration of treatments for both disorders is of importance, but the integration of disorder-specific interventions delivered by the same professional for both disorders is a step further.

Third, this focus on studies on patients with severe disorders, such as schizophrenia, bipolar disorders, severe depression, posttraumatic stress disorders, or personality disorders (e.g., borderline personality disorder), might influence

knowledge of treatment effects on DDPs in general. Only a few controlled studies have been carried out in DDPs with SUDs and anxiety disorders and mild or moderate depression (Hesse 2009); however, psychosocial treatments are more effective in patients with less severe PDs than in those with more severe PDs. In the latter, medication is typically necessary to elicit significant clinical improvement (Pfammatter et al. 2006). From this perspective, substantial differences in the efficacy of psychosocial treatments are unlikely to be observed. This is particularly true for research in the DDP field, where the studies generally have a small sample size (Cleary et al. 2009; Hunt et al. 2013).

Finally, too few RCTs have been conducted on the efficacy of treatment in DDPs to draw an evidence-based conclusion. For example, the meta-analyses by Chow and colleagues (2012) include a diversity of designs and comparisons; however, the results from these studies appear difficult to generalize. By expanding comprehensive reviews on sound clinical studies with less internal (i.e., non-RCT) but high external validity (i.e., statistical or matching procedures to control important variables), clinicians may develop hypotheses on how combinations of therapies may effectively treat comorbid PDs and SUDs (Drake et al. 2004, 2008; Horsfall et al. 2009; Kelly et al. 2012; Lubman et al. 2010; Tiet and Mausbach 2007; Cleary et al. 2009).

The authors of this chapter also believe this can be achieved through meta-analyses, reviews, and reporting the findings and conclusions of dual disorder treatment studies. However, there are only few published European studies; thus, it is necessary to rely on the results on our valuable colleagues in the USA, Canada, and Australia. This chapter will present evidence relating to different PDs; however, no distinctions will be made between different kinds of SUDs (e.g., alcohol use disorders (AUDs) vs. drug use disorders (DUDs)) because the number of studies is too low to establish appropriate categories.

18.3 Severe Mental Health and Substance Use Disorders

Severe mental health disorders are characterized by psychosis and include schizophrenia, schizophrenia spectrum disorders, schizoaffective disorder, and severe cases of bipolar and mood disorders; very rarely, personality disorders, such as borderline or antisocial disorders, are placed in this category (Rosenthal and Westreich 1999). In this chapter, discussion of comorbid SUDs and schizophrenia and other psychotic disorders as well as bipolar disorders is divided into two subchapters (see Sects. 18.3.1 and 18.3.2). Results of studies on comorbid depression and SUDs are presented in another subchapter (see Sect. 18.4).

18.3.1 Schizophrenia and Other Psychotic Disorders

In their multiple *systematic reviews* on the efficacy of treatment for severe DDPs, Drake and colleagues present evidence for integrated treatment that uses

motivational interviewing (MI) (Miller and Rollnick 2002) to engage patients in programs that are based on the Transtheoretical Model (TTM) (Osher and Kofoed 1989; Prochaska et al. 1992; Drake et al. 1998, 2004, 2008; Drake and Mueser 2000). In their comprehensive review, Drake et al. (2008) identified 45 controlled studies (22 experimental and 23 quasi-experimental studies) that assessed the capacity of group counseling, contingency management (CoM), and long-term residential treatment to reduce substance use and improve functioning (e.g., hospitalization rate, engagement in treatment, housing, employment, or quality of life). In addition, case management was consistently associated with improved function, but this and other interventions, such as individual counseling, intensive outpatient rehabilitation, and legal interventions, were seldom related to mental health improvement. Most of those studies had a short-term (i.e., 1–2 year) outcome perspective. However, Drake and colleagues published a 10-year follow-up of 130 patients and found a steady improvement in several areas such as psychiatric symptoms, substance abuse, institutionalization, functional status, and quality of life (Drake et al. 2006).

At that time, only one study from *Europe* had evaluated *ITP;* the ITP examined in this study comprised family intervention (FI) among MI and individual cognitive-behavioral therapy (CBT), and was associated with improvements in all three outcome areas (Barrowclough et al. 2001; Haddock et al. 2003). Recently, the effectiveness of that integrated MI and CBT was evaluated without FI and compared to TAU (ITP $n = 164$ vs. TAU $n = 163$) in a large British RCT. ITP did not improve outcomes in terms of hospitalization, psychiatric symptoms, or functioning, but increased patient readiness to reduce substance use and engagement in treatment; in addition, patients who completed the treatment reduced their substance use for at least 1 year (Barrowclough et al. 2010). In a study from Belgium, two groups of patients with schizophrenia and substance use disorders received either an ITP or TAU (Morrens et al. 2011). Patients in the ITP condition reduced their substance use, showed improvements in their psychiatric symptoms, and reported higher quality of life and social functioning. In contrast, patients' improvements in the TAU group were moderate and limited to only a few substance use and psychiatric outcomes. The TAU group had a significantly higher dropout rate at the 6- and 12-month follow-ups, suggesting that ITP is more successful in keeping patients in treatment.

Several nonexperimental outcome studies on *ITS* have been conducted in Europe. A naturalistic multicenter study in Sweden ($N = 358$) found that ITS, which was implemented to improve cooperation between psychiatric health units and social services responsible for SUD treatment, was associated with DDPs' improvement in alcohol and drug use; psychiatric symptoms; and family, physical, and legal situation at the 1½-year follow-up; however, it did not impact patients' employment status. At the 5-year follow-up, improvement was stable, and further improvements in legal issues and psychiatric symptoms were observed. However, the death rate had increased. Overall, the standardized mortality rate (SMR) was 7.9 (CI-95 %: 5.5–11.2) (women's SMR = 6.5 (CI-95 %: 2.1–15.2); men's SMR = 8.3 (CI-95 %: 3.3–8.3)) (Schaar and Öjehagen 2001, 2003; Öjehagen and Schaar 2003).

Cleary and colleagues found similar results as Drake and colleagues in a systematic review of 53 controlled studies (30 experimental and 23 quasi-experimental studies) (Cleary et al. 2009). Evidence suggested that MI was most effective in reducing short-term substance use and, when combined with CBT, improving mental health. Results also indicated that long-term residential treatment programs and CoM reduced substance use. The heterogeneous patient samples, treatment programs, and interventions may explain the inconsistent results regarding the efficacy of CBT alone. Furthermore, CBT is a psychotherapy model that comprises different interventions, and it has not often been well defined in terms of substance abuse in DDP studies. However, in contrast to Drake and colleagues' results (Drake et al. 2008), group counseling was inconsistently supported, which the authors state resulted from differences in the way studies were categorized (Cleary et al. 2009). In addition, some reviews identified RP as a promising intervention for severe DDPs; RP is often a part of CBT and has been associated with positive effects on SUDs, PDs, and functioning outcomes (De Witte et al. 2014; Kelly et al. 2012).

In their recent review on outpatient treatment for DDPs with schizophrenia and SUDs, De Witte and colleagues (2014) concluded that more elaborate, intensive, and long-term programs, such as combinations of several interventions (e.g., predominantly MI, CBT, RP, CoM, and FI), ITPs (e.g., Behavioral Treatment for Substance Abuse in Severe and Persistent Mental Illness (BTSAS) (Bellack et al. 2006)), or the Family Intervention for Dual Diagnosis Disorder (FIDD) (Mueser et al. 2013), are more likely related to a broader spectrum of improvement in several outcomes of SUDs, PDs, and functioning than are single or limited sets of interventions. Both BTSAS and FIDD comprise social skills training and psychoeducational programs, but BTSAS includes additional MI, RP, and CoM; FIDD emphasizes stage-wise intervention and single and multiple family groups.

However, when ITPs or single interventions are tested with the criteria of RCT, the results are unequivocal: there is no compelling evidence that ITPs reduce substance use, improve psychiatric symptoms, or increase treatment adherence relative to control groups that received TAU or other active treatments (Cleary et al. 2010; Jeffrey et al. 2007; Chow et al. 2012; Hunt et al. 2013). In addition, although often an essential part of treatment of DDPs, ACT showed mixed results and was not consistently associated with better outcomes (Cleary et al. 2009). Moreover, despite the caseload in favor of a lower ratio in ACT, no substantial differences between ACT or CM were found in content or effectiveness (De Witte et al. 2014).

Taken together, results of experimental and quasi-experimental studies assessing the effectiveness of psychosocial interventions for DDPs with psychoses and SUDs appear mixed but generally encouraging. Comparison between studies is hindered by small and heterogeneous patient samples; unclear descriptions of ITPs, sets of interventions, single interventions, and control conditions; outcome heterogeneity; high attrition rates; and short-term follow-up. Long-term retention in programs; residential treatment for severe or complex DDPs; and stage-wise treatments comprising components such as MI, CBT in combination with MI, CoM, RP,

CM, ACT, and FI are promising strategies for the treatment of patients with psychoses and SUDs, particularly when the components help reduce substance abuse. For those DDPs with very *complex disorders* (i.e., dysfunction in several areas such as cognitive impairment, treatment resistance, housing and vocational problems) comprehensive services should be made available to overcome therapy hindrances (Horsfall et al. 2009; Lubman et al. 2010).

18.3.2 Bipolar Disorders

Studies on the effectiveness of treatment for severe DDPs often include patients with bipolar disorders (Drake et al. 2008; Horsfall et al. 2009). There is weak evidence showing that ITP may be more effective than TAU for patients with comorbid bipolar disorders and SUDs, mainly because there are just two studies in which the sample consisted only of patients with bipolar disorders and SUDs (Kelly et al. 2012; Tiet and Mausbach 2007). In a pilot study by Weiss and colleagues, patients showed significant reductions in drug and alcohol use and improvement in mania symptoms, but no differences were observed in depression symptoms relative to controls following a manual-based integrated group therapy (Frank et al. 2000). Interpersonal and Social Rhythm Therapy (IPSRT) focuses on helping patients with bipolar disorders to gain insight into the relationship between mood changes and interpersonal events, stabilize their circadian rhythm by structuring daily routines, and control their symptoms (Weiss et al. 2000). IPSRT was more effective than medication alone in preventing relapse, improving functioning in relationships, and increasing life satisfaction (Kelly et al. 2012).

We found that studies on treatment for comorbid bipolar disorders and SUDs are seriously underrepresented in research on DDP treatment. More studies are needed to determine which programs and components are necessary to effectively treat these patients. Further, it is particularly necessary to explore the increased risk of suicide in patients with bipolar disorder and concomitant substance use disorders (Schneider 2009; Sher 2006).

18.4 Depression and Substance Use Disorders

As for bipolar disorders, studies examining the efficacy of treatment for comorbid depression and SUDs are lacking. Only five controlled studies have been published on this matter (Hesse 2009; Murthy and Chand 2012; Tiet and Mausbach 2007), and all have high attrition rates and small sample sizes at follow-up ($n < 40$). Overall, patients in the experimental groups showed some improvement in substance use and depression, increased motivation to change, and greater adherence to treatment. The heterogeneity of the experimental treatments is considerable, extending from IPTs for depression and SUDs to only CBT in conjunction with TAU for depression. Moreover, the control conditions also differ from TAU; employed treatments

have included Brief Supportive Psychotherapy, 12-Step Facilitating Therapy, and Relaxation Training.

A large ($n = 284$) RCT was recently published on manualized MI combined with CBT in patients with comorbid depression and AUDs that compared the efficacy of brief interventions, individually single-focused interventions, or individually integrated psychological interventions (Baker et al. 2010). Patients were randomly allocated to brief intervention only (90-min session) or a brief intervention followed by nine 1-h sessions, with either an alcohol or depression focus, or an integrated focus on both depression and alcohol. Compared to the brief intervention, the ten-session intervention was associated with a greater improvement in drinking outcomes at the 18-week follow-up. Compared to single-focused interventions, integrated treatment was associated with a greater reduction in depression and the number of days per week that patients consumed alcohol. For men, the alcohol-focused rather than the depression-focused intervention was associated with a greater reduction in average drinks per day and per week and an increased level of general functioning. Women showed greater improvements in each of these variables when they received depression-focused rather than alcohol-focused treatment. The authors concluded that individually integrated treatment was superior to single-focused treatments for comorbid depression and alcohol problems. Gender differences between single-focused depression and alcohol treatments warrant further study. This was the first RCT on comorbid depression and AUDs large enough to yield sound and promising results regarding differences in efficacy between an individually integrated treatment comprising MI and CBT and individually single-focused interventions, and to indicate gender differences in short-term treatment outcomes. However, these results were not observable at the 6-, 12-, 24-, and 36-month follow-ups (Baker et al. 2013). All patients improved in the three outcomes, and there were only a few significant differences between the treatment conditions. Compared to the brief interventions, the three longer interventions tended to be more effective in reducing depression and improving function. Single-focused treatment was as effective as integrated treatment, and alcohol-focused treatment was as effective as depression-focused treatment in reducing depression but more effective in reducing alcohol use. Baker and colleagues (2013) concluded that the best approach seems to be an initial focus on both alcohol use and depression followed by additional integrated or alcohol-focused treatment.

Finally, Riper and colleagues recently published a meta-analysis on the effectiveness of the specific combination of MI and CBT in the treatment of comorbid clinical or subclinical depression and AUD (Riper et al. 2013). They included 12 studies with an overall sample of 1,721 comorbid patients. With a small overall effect size, MI and CBT proved effective for these DDPs in treating both depressive symptoms and alcohol use.

18.5 Anxiety Disorders and Substance Use Disorders

In his review of studies on ITPs for anxiety disorders and SUDs, Hesse states that the programs generally increase days of abstinence, and may decrease symptoms and improve treatment adherence (Hesse 2009). He concluded that psychological interventions alone seem insufficient for the treatment of anxiety disorders and SUDs, and that there may be a need for ITPs with other sets of interventions for this kind of comorbidity than those evaluated in the studies. Very similar conclusions were drawn by authors of other comprehensive reviews (Tiet and Mausbach 2007; Kelly et al. 2012).

However, it should be noted that these reviews comprised studies of patients suffering from a broad range of anxiety disorders (i.e., panic disorder, social anxiety, obsessive–compulsive disorder, or posttraumatic stress disorder) and SUDs (i.e., AUD, DUD, or any kind of SUD) and very different treatment approaches in various settings (i.e., in- vs. outpatient, therapeutic community); thus, it was difficult to draw conclusions regarding the effective treatment of anxiety disorders and SUDs. Therefore, it is necessary to further do research on this topic.

18.5.1 Posttraumatic Stress Disorder and Substance Use Disorders

Treatment of posttraumatic stress disorder (PTSD) can be divided into three phases: stabilization, confrontation, and reintegration. Exposure treatment is considered the first line of treatment in the confrontation phase. While it was recommended for a long time to use exposure interventions only when SUDs are under control, today there are ITPs available that begin with exposure and addiction interventions at the same time at beginning of treatment (Schäfer et al. 2011).

In their review, Schäfer and colleagues differentiated between ITPs for the stabilization phase and ITPs for the confrontation phase (Schäfer et al. 2011). No studies appeared to have been conducted on the reintegration phase. For the *stabilization phase*, the only treatment model thus far established as effective for this comorbidity is the Seeking Safety manual (Najavits 2002; Najavits et al. 2008), which has been associated with positive outcomes relative to controls for both PTSD and SUDs in 16 studies, including RCTs and multisite studies (Schäfer and Najavits 2007). However, Seeking Safety was not superior to an RP program in long-term SUD outcomes (Kelly et al. 2012; Tiet and Mausbach 2007). The Trauma Recovery and Empowerment Model (TREM) (Harris 1998), a further treatment manual for the stabilization phase, yielded mixed results in the two controlled studies in which it was examined. In particular, SUD outcomes did not differ significantly between TREM and TAU (Kelly et al. 2012; Schäfer et al. 2011). In another meta-analysis combined with a systematic review, Trochalla and colleagues (2012) included 17 trials with ITP (nine controlled trials having a control group) with more than 4,000 patients (Torchalla et al. 2012). ITPs effectively reduced trauma symptoms and substance abuse from pretreatment to the follow-

ups; however, relative to the control group, which received a non-ITP treatment, there were no significant differences in effectiveness between ITP and the comparison condition (e.g., relapse prevention, 12-step treatment, or TAU for SUD).

Several treatment models have been introduced for the *confrontation phase*; however, most were evaluated only in uncontrolled or very small studies with low sample sizes (up to $n = 46$) and showed minimally encouraging results (Schäfer et al. 2011). The exception is a recently published randomized controlled trial from Australia (Sannibale et al. 2013). Sannibale and colleagues (Sannibale et al. 2013) compared 12 once-weekly individual sessions of either integrated CBT for AUD and PTSD, including exposure therapy (ITP, $n = 33$), or CBT for AUD combined with supportive counseling (ASC; $n = 29$), on outcomes such as alcohol use and related problems, severity of PTSD, and depression and anxiety symptoms at 5- and 9-months follow-up. Significant improvements were found in all outcomes for both ITP and ASC. However, patients in the ITP group exhibited a twofold greater rate of clinically significant change in PTSD severity at follow-up if they had received a sufficient dose of exposure therapy (i.e., one or more sessions), while ASC patients exhibited greater improvement in AUD outcomes. Sannibale and colleagues concluded that patients with comorbid PTSD and AUD could derive substantial benefit from CBT for AUD, with greater benefits associated with exposure therapy for PTSD. Earlier, Mills and colleagues (2012) published a randomized controlled trial on PTSD and SUD with 55 patients in the ITP group and 48 patients in the TAU-only group. They found results similar to those of Sannibale and colleagues, except that patients in both treatment conditions (ITP and TAU) showed improvement in the initial SUD outcome assessment; however, no group differences were found at the 6-week or 3- and 9-month follow-up (Mills et al. 2012). Further, a recent randomized controlled study by van Dam and colleagues of 34 patients suffering from PTSD and SUD found similar results using structured writing therapy as the treatment for PTSD (van Dam et al. 2013). In contrast, Foa and colleagues did not find any differences in PTSD symptoms between four treatment groups (a total of 165 patients) when comparing prolonged exposure versus supportive counseling combined with naltrexone or placebo at the 3- and 6-month follow-up (Foa et al. 2013). However, they did show that naltrexone may effectively treat AUD in patients with PTSD without exacerbating PTSD symptoms and that prolonged exposure therapy is protective against relapse in the 6 months following treatment.

In conclusion, the most promising treatment for the stabilization phase is the Seeking Safety manual; for the confrontation phase, the following therapies may be effective: ITP of CBT for AUD and PTSD including exposure therapy. Nevertheless, there is a surprising paucity of sound studies on comorbid PTSD and SUDs, making it hardly possible to recommend any specific program.

18.6 Personality Disorders and Substance Use Disorders

Psychosocial treatment, in particular psychotherapy, is the treatment of choice for personality disorders, for which disorder-specific psychotherapies should be used whenever possible. Disorder-specific psychotherapies are highly effective in the treatment of borderline personality disorder and other severe personality disorders. To date, there are very few RCTs on DDPs with personality disorders other than borderline personality disorder. As suggested in the systematic reviews by Pennay and colleagues (2011) and van den Bosch and Verheul (2007) on the interventions for comorbid borderline personality disorders and SUDs, three different types of psychotherapies are supported by randomized controlled trials: Dialectic Behavioral Therapy (DBT) and its extended version targeting substance abuse (DBT-S) (Dimeff and Linehan 2008), Dynamic Deconstructive Psychotherapy (DDPT) (Gregory and Remen 2008), and Dual-Focused Schema Therapy (DFST) (Ball 1998).

Overall, there were three studies on DBT and DBT-S showing mixed results for the improvement of SUDs, PDs, and functioning outcomes. While DBT or DBT-S was mostly superior to TAU in all outcomes (van den Bosch et al. 2005), the results for DBT were less promising when it was compared to acceptance-based strategies in combination with a 12-step abstinence program. DDPT showed better results on AUDs and PDs outcomes than TAU in a well-controlled trial and thus merits further research. Finally, DFST showed some promise in the treatment of comorbid personality disorders, including various kinds of personality disorders, in two preliminary trials; however, these trials had significant limitations (e.g., low sample sizes, low retention rates). All six studies showed high levels of polydrug use and comorbid Axis I disorders, such as depression and anxiety, so there is currently insufficient evidence to recommend any one treatment over another. It is evident that further research is urgently needed to develop effective treatment for comorbid personality disorders and SUDs (Pennay et al. 2011; van den Bosch and Verheul 2007).

18.7 Promising Dual Disorder Treatment Characteristics: Conclusions and Perspectives

In this chapter, we aimed to present a clearer picture of the effective treatments for DDPs by discussing published meta-analyses, comprehensive reviews on sound clinical studies, and several other important studies. Overall, the studies reveal great heterogeneity in characteristics of patient samples, treatment strategy (evaluation of ITS (i.e., coordination strategies such as ACT or CM) or ITP (e.g., integrating disorder-specific interventions such as MI, RP, CoM) compared to TAU), setting (e.g., residential vs. outpatient), intensity (i.e., long- vs. short-term treatment), and outcomes (i.e., SUD, PD, and functioning). This heterogeneity makes it difficult to compare results and draw conclusions about the psychosocial treatment for DDPs. The only consistent commonality between the studies is the

countries in which they were conducted: the USA (predominantly), Canada, Australia, and Great Britain. Indeed, there are several studies from countries in Europe (Barrowclough et al. 2001, 2010; Moggi et al. 1999, 2002; Morrens et al. 2011; Schaar and Öjehagen 2001, 2003; van den Bosch et al. 2005; van Dam et al. 2013), but most are laden with methodological problems and some of them are not published in English, rendering them inaccessible to English-speaking researchers performing meta-analyses or writing reviews about controlled studies. Nevertheless, there are some manuals of IPT programs in European languages that have been well received by at least some providers in the mental health or addiction care system (D'Amelio et al. 2007; Moggi and Donati 2004).

We may very cautiously conclude that ITS, the coordination of treatment strategies within and between different services, and ITP, the combination of disorder-specific interventions, are more effective than no treatment (e.g., waiting control group). Moreover, in some studies, both ITS and ITP are superior to TAU in some outcomes; at best, they are superior in all outcomes. A broader set of interventions is likely more effective than single interventions. Residential treatment is indicated if patients are suffering from severe PDs and SUDs with poor functioning; however, intensive outpatient treatment is sometimes sufficient. Parallel, but not sequential, treatment might be effective as well, particularly when addiction interventions to reduce substance use are successful. Stepped care programs based on the stages of change according to the TTM are likely more effective; while they may not be efficient, they are nonetheless promising, at least for severe DDP.

Several components of IPTs repeatedly showed *some* efficacy in SUDs, PD, and functioning; some components were effective in only one of these measures, while others were effective in two or even three. First, motivational interventions, in particular MI, help patients set treatment goals, decide to change behavior to reach those goals, and execute behavioral changes. Thus, MI helps both SUDs and PDs prepare for change. Second, in combination with MI, CBT can be successful if its disorder-specific interventions to change behavior are used. Third, RP and CoM are promising and sometimes have the same efficacy as ITPs in successfully reducing substance use to enable the treatment of the PDs (e.g., see results of PTSD and SUD). Fourth, FI appears valuable for patients who still have good relationships with their families. Finally, disorder-specific interventions for PD or SUD seem to also work for DDPs. Thus, it is not necessary to develop new treatments for DDPs but to integrate effective disorder-specific interventions (Tiet and Mausbach 2007). Some of the SUD-specific interventions also seem to have a positive effect on PDs (e.g., MI, RP, or CoM).

These conclusions are tentative, and there is a need for much more empirical support. Although research on treatment of DDPs began some 20 years ago, there is still a lack of methodologically sound studies, and those studies performed are highly heterogeneous in terms of sample, aim (coordination strategy or treatment interventions), setting, and outcome characteristics. Future studies should concentrate on ITS and ITPs that include MI in combination with CBT, particularly interventions for reducing substance use (e.g., RP, CoM), and involve patients'

social (e.g., FI) and professional (e.g., by ACT, CM) resources. Disorder-specific interventions also seem to be effective for DDPs, and some SUD-specific interventions have an effect on the other part of the dual disorder (e.g., MI, RP, CoM). Since most studies concern DDPs with severe or moderately severe conditions, future studies should include DDPs with less severe manifestations of SUD, PD, and overall dysfunction, since these individuals represent the largest proportion of DDPs. From the perspective of prevention, research is necessary on the identification of risk factors for hazardous substance use in patients with PDs in order to prevent the development of alcohol or drug use disorders

Clinical Recommendations

Overall, although no treatment was identified as efficacious for both PD and SUD, our findings allow us to provide several clinical recommendations. First, efficacious treatments for PD also tend to work in DDP. Second, efficacious treatments for reducing substance use also decrease substance use in DDP. Third, although the efficacy of integrating treatments and treatment systems is still unclear, programs that include motivational interviewing, simultaneous administration of disorder-specific cognitive-behavioral interventions for both PD and SUD, and family interventions (where necessary) are more likely to meet treatment goals for both PD and SUD. Finally, a reduction and/or stabilization in substance use appears necessary for clinically significant PD improvement and effective PD treatment for the purposes of further improving substance misuse.

References

Baker AL, Kavanagh DJ, Kay-Lambkin FJ, Hunt SA, Lewin TJ, Carr VJ, Connolly J (2010) Randomized controlled trial of cognitive-behavioural therapy for coexisting depression and alcohol problems: short-term outcome. Addiction 105(1):87–99. doi:10.1111/j.1360-0443.2009.02757.x

Baker AL, Kavanagh DJ, Kay-Lambkin FJ, Hunt SA, Lewin TJ, Carr VJ, McElduff P (2013) Randomized controlled trial of MICBT for co-existing alcohol misuse and depression: outcomes to 36-months. J Subst Abuse Treat. doi:10.1016/j.jsat.2013.10.001

Ball SA (1998) Manualized treatment for substance abusers with personality disorders: dual focus schema therapy. Addict Behav 23(6):883–891

Barrowclough C, Haddock G, Tarrier N, Lewis S, Moring J, O'Brien R, Schofield N, Jip MG (2001) Randomized controlled trial of motivational interviewing and cognitive behavioral intervention for schizophrenia patients with associated drug or alcohol misuse. Am J Psychiatry 158:1706–1713

Barrowclough C, Haddock G, Wykes T, Beardmore R, Conrod P, Craig T, Davies L, Dunn G, Eisner E, Lewis S, Moring J, Steel C, Tarrier N (2010) Integrated motivational interviewing and cognitive behavioural therapy for people with psychosis and comorbid substance misuse: randomised controlled trial. BMJ 341:c6325. doi:10.1136/bmj.c6325

Bellack AS, Bennett ME, Gearon JS, Brown CH, Yang Y (2006) A randomized clinical tral of a new behavioral treatment for drug abuse in people with severe and persistent mental illness. Arch Gen Psychiatry 63:426–432

Chow CM, Wieman D, Cichocki B, Qvicklund H, Hiersteiner D (2012) Mission impossible: treating serious mental illness and substance use co-occurring disorder with integrated treatment: a meta-analysis. Mental Health Subst Use 6:1–19

Cleary M, Hunt GE, Matheson S, Walter G (2009) Psychosocial treatments for people with co-occurring severe mental illness and substance misuse: systematic review. J Adv Nurs 65 (2):238–258. doi:10.1111/j.1365-2648.2008.04879.x

Cleary M, Hunt GE, Matheson SL, Siegfried N, Walter G (2010) Psychosocial interventions for people with both severe mental illness and substance misuse (Review). The Cochrane Library (3)

D'Amelio R, Behrendt B, Wobrock T (2007) Psychoedukation Schizophrenie und Sucht: Manual zur Leitung von Patienten- und Angehörigengruppen, 2nd edn. Urban and Fischer, Frankfurt

De Witte NAJ, Crunelle CL, Sabbe B, Moggi F, Dom G (2014) Treatment for outpatients with comorbid schizophrenia and substance use disorders: a review. Eur Addict Res 20(3):105–114

Dimeff LA, Linehan MM (2008) Dialectical behavior therapy for substance abusers. Addict Sci Clin Pract 4(2):39–47

Drake RE, McHugo GJ, Xie H, Fox M, Packard J, Helmstetter B (2006) Ten-year recovery outcomes for clients with co-occurring schizophrenia and substance use disorders. Schizophr Bull 32(3):464–473. doi:10.1093/schbul/sbj064

Drake RE, Mercer-McFadden C, Mueser KT, McHugo GJ, Bond GR (1998) Review of integrated mental health and substance abuse treatment for patients with dual disorders. Schizophr Bull 24:589–608

Drake RE, Mueser KT (2000) Psychosocial approaches to dual diagnosis. Schizophr Bull 26 (1):105–118

Drake RE, Mueser KT, Brunette MF, McHugo GJ (2004) A review of treatments for people with severe mental illnesses and co-occurring substance use disorders. Psychiatr Rehabil J 27 (4):360–374

Drake RE, O'Neal EL, Wallach MA (2008) A systematic review of psychosocial research on psychosocial interventions for people with co-occurring severe mental and substance use disorders. J Subst Abuse Treat 34(1):123–138. doi:10.1016/j.jsat.2007.01.011

Foa EB, Yusko DA, McLean CP, Suvak MK, Bux DA Jr, Oslin D, O'Brien CP, Imms P, Riggs DS, Volpicelli J (2013) Concurrent naltrexone and prolonged exposure therapy for patients with comorbid alcohol dependence and PTSD: a randomized clinical trial. JAMA 310(5):488–495. doi:10.1001/jama.2013.8268

Frank E, Swartz HA, Kupfer DJ (2000) Interpersonal and social rhythm therapy: managing the chaos of bipolar disorder. Biol Psychiatry 48(6):593–604

Gregory RJ, Remen AL (2008) A manual-based psychodynamic therapy for treatment-resistant borderline personality disorder. Psychotherapy (Chic) 45(1):15–27. doi:10.1037/0033-3204.45.1.15

Haddock G, Barrowclough C, Tarrier N, Moring J, O''Brien R, Schofield N, Quinn J, Palmer S, Davies L, Lowens I, McGovern J, Lewis S (2003) Cognitive-behavioral therapy and motivational intervention for schizophrenia and substance misuse. Br J Psychiatry 183:418–426

Harris M (1998) Trauma recovery and empowerment: a clinician's guide for working with women in groups. The Free Press, New York

Hesse M (2009) Integrated psychological treatment for substance use and co-morbid anxiety or depression vs. treatment for substance use alone. A systematic review of the published literature. BMC Psychiatry 9:6

Horsfall J, Cleary M, Hunt GE, Walter G (2009) Psychosocial treatments for people with co-occurring severe mental illnesses and substance use disorders (dual diagnosis): a review of empirical evidence. Harv Rev Psychiatry 17(1):24–34. doi:10.1080/10673220902724599

Hunt GE, Siegfried N, Morley K, Sitharthan T, Cleary M (2013) Psychosocial interventions for people with both severe mental illness and substance misuse (Review). The Cochrane Library (10)

Jeffrey DP, Ley A, McLaren S, Siegfried N (2007) Psychosocial treatment programmes for people with both severe mental illness and substance misuse (Review). The Cochrane Library 4:1–35
Kelly TM, Daley DC, Douaihy AB (2012) Treatment of substance abusing patients with comorbid psychiatric disorders. Addict Behav 37(1):11–24. doi:10.1016/j.addbeh.2011.09.010
Lubman DI, King JA, Castle DJ (2010) Treating comorbid substance use disorders in schizophrenia. Int Rev Psychiatry 22(2):191–201. doi:10.3109/09540261003689958
Miller WR, Rollnick S (2002) Motivational interviewing: preparing people for change, 2nd edn. Guilford, New York
Mills KL, Teesson M, Back SE, Brady KT, Baker AL, Hopwood S, Sannibale C, Barrett EL, Merz S, Rosenfeld J, Ewer PL (2012) Integrated exposure-based therapy for co-occurring posttraumatic stress disorder and substance dependence: a randomized controlled trial. JAMA 308(7):690–699. doi:10.1001/jama.2012.9071
Moggi F, Brodbeck J, Költzsch K, Bachmann KM (2002) One-year follow-up of dual diagnosis patients attending a 4-months integrative inpatient treatment. Eur Addict Res 8:30–37
Moggi F, Donati R (2004) Psychische Störungen und Sucht: Doppeldiagnosen. Fortschritte der Psychotherapie. Hogrefe, Göttingen
Moggi F, Hirsbrunner HP, Brodbeck J, Bachmann KM (1999) One-year outcome of an integrative inpatient treatment for dual diagnosis patients. Addict Behav 24:589–592
Morrens M, Dewilde B, Sabbe B, Dom G, De Cuyper R, Moggi F (2011) Treatment outcomes of an integrated residential programme for patients with schizophrenia and substance use disorder. Eur Addict Res 17(3):154–163. doi:10.1159/000324480
Mueser KT, Glynn SM, Cather C, Xie H, Zarate R, Smith LF, Clark RE, Gottlieb JD, Wolfe R, Feldman J (2013) A randomized controlled trail of family intervention for co-occurring substance use and severe psychiatric disorders. Schizophr Bull 39:658–672
Murthy P, Chand P (2012) Treatment of dual diagnosis disorders. Curr Opin Psychiatry 25(3):194–200. doi:10.1097/YCO.0b013e328351a3e0
Najavits LM (2002) Seeking safety: a treatment manual for PTSD and substance abuse. Guilford, New York
Najavits LM, Schäfer I, Stubenvoll M, Dilling A (2008) Posttraumatische Belastungsstörung und Substanzmissbrauch: Das Therapieprogramm «Sicherheit finden». Hogrefe, Göttingen
Öjehagen A (2006) Services to persons with concomitant substance use disorders and other psychiatric disorders—the Swedish system. In: Baldacchio A, Corkery J (eds) European Collaborating Centres in Addiction Studies (ECCAS), vol 17, International Centre for Drug Policy, St George's. University of London, London, pp 245–246
Öjehagen A, Schaar I (2003) Mentally ill substance abusers in Sweden. A 5-year follow-up of a multisite study of co-operation between psychiatric services and social authorities. In: Carra G, Clerici M (eds) Dual diagnosis: filling the gap. John Libbey Euorotext, Paris
Osher FC, Kofoed LL (1989) Treatment of patients with psychiatric and psychoactive substance use disorders. Hosp Community Psychiatry 40:1025–1035
Pennay A, Cameron J, Reichert T, Strickland H, Lee NK, Hall K, Lubman DI (2011) A systematic review of interventions for co-occurring substance use disorder and borderline personality disorder. J Subst Abuse Treat 41(4):363–373
Pfammatter M, Junghan UM, Brenner HD (2006) Efficacy of psychological therapy in schizophrenia: conclusions from meta-analyses. Schizophr Bull 32(Suppl 1):S64–S80. doi:10.1093/schbul/sbl030
Prochaska JO, DiClemente CC, Norcross JC (1992) In search how people change. Applications to addictive behaviors. Am Psychologist 47:1102–1114
Riper H, Andersson G, Hunter SB, de Wit J, Berking M, Cuijpers P (2013) Treatment of comorbid alcohol use disorders and depression with cognitive-behavioural therapy and motivational interviewing: a meta-analysis. Addiction. doi:10.1111/add.12441
Roberts LJ, Shaner A, Eckman TA, Tucker DE, Vaccaro JV (1992) Effectively treatment of stimulant-abusing schizophrenics: Mission impossible? New Dir Ment Health Serv 53:55–65

Rosenthal RN, Westreich L (1999) Treatment of persons with dual diagnoses of substance use disorder and other psychological problems. In: McCrady BS, Epstein EE (eds) Addictions. A comprehensive guidebook. Oxford University Press, New York, pp 439–476

Sannibale C, Teesson M, Creamer M, Sitharthan T, Bryant RA, Sutherland K, Taylor K, Bostock-Matusko D, Visser A, Peek-O'Leary M (2013) Randomized controlled trial of cognitive behaviour therapy for comorbid post-traumatic stress disorder and alcohol use disorders. Addiction 108(8):1397–1410

Schaar I, Öjehagen A (2001) Severely mentally ill substance abusers: an 18-month follow-up study. Soc Psychiatry Psychiatr Epidemiol 36(2):70–78

Schaar I, Öjehagen A (2003) Predictors of improvement in quality of life of severely mentally ill substance abusers during 18 months of co-operation between psychiatric and social services. Soc Psychiatry Psychiatr Epidemiol 38(2):83–87. doi:10.1007/s00127-003-0604-9

Schäfer I, Najavits LM (2007) Clinical challenges in the treatment of patients with posttraumatic stress disorder and substance abuse. Curr Opin Psychiatry 20(6):614–618. doi:10.1097/YCO.0b013e3282f0ffd9

Schäfer I, Schulze C, Stubenvoll M (2011) Psychotherapie bei Abhängigkeitserkrankungen und Posttraumatischer Belastungsstörung. Sucht 57(5):353–361

Schneider B (2009) Substance use disorders and risk for completed suicide. Arch Suicide Res 13 (4):303–316. doi:10.1080/13811110903263191

Sher L (2006) Alcoholism and suicidal behavior: a clinical overview. Acta Psychiatr Scand 113 (1):13–22. doi:10.1111/j.1600-0447.2005.00643.x

Tiet QQ, Mausbach B (2007) Treatments for patients with dual diagnosis: a review. Alcohol Clin Exp Res 31(4):513–536. doi:10.1111/j.1530-0277.2007.00336.x

Torchalla I, Nosen L, Rostam H, Allen P (2012) Integrated treatment programs for individuals with concurrent substance use disorders and trauma experiences: a systematic review and meta-analysis. J Subst Abuse Treat 42(1):65–77. doi:10.1016/j.jsat.2011.09.001

van Dam D, Ehring T, Vedel E, Emmelkamp PM (2013) Trauma-focused treatment for posttraumatic stress disorder combined with CBT for severe substance use disorder: a randomized controlled trial. BMC Psychiatry 13:172. doi:10.1186/1471-244X-13-172

van den Bosch LM, Koeter MW, Stijnen T, Verheul R, van den Brink W (2005) Sustained efficacy of dialectical behaviour therapy for borderline personality disorder. Behav Res Ther 43 (9):1231–1241. doi:10.1016/j.brat.2004.09.008

van den Bosch LMC, Verheul R (2007) Patients with addiction and personality disorder: treatment outcomes and clinical implications. Curr Opin Psychiatry 20:67–71

Weiss RD, Griffin ML, Greenfield SF, Najavits LM, Wyner D, Soto JA, Hennen JA (2000) Group therapy for patients with bipolar disorder and substance dependence: results of a pilot study. J Clin Psychiatry 61(5):361–367

Pharmacotherapy of Dual Disorders

19

Michael Soyka and Heinz Grunze

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Abstract

This chapter gives a short overview on the comorbidity and clinical correlates of substance use in affective and anxiety disorders, as well as in schizophrenia. The emphasis is on pharmacotherapies available for the treatment of comorbid disorders. While no specific drugs have been developed for comorbid substance use disorders, psychotropic drugs such as antidepressants or antipsychotics have been tested in dual disorder patients, as well as anticraving compounds. Most studies have included few patients. Very few randomized controlled trials are available in the dual disorder research field. Thus, the empirical basis for evidence-based recommendations is rather limited. The possible benefits of available medications so far are discussed.

List of Abbreviations

BD	Bipolar disorder
BZD	Benzodiazepines
CBT	Cognitive-behavioral therapy
CRF	Corticotrophin-releasing factor
EPMS	Extrapyramidal symptoms
FES	First-episode schizophrenia
FGA	First-generation antipsychotics
GAD	Generalized anxiety disorder
HPA	Hypothalamic–pituitary–adrenocortical
IPT	Interpersonal Group Psychotherapy
LAI	Long-acting injectable
MAOIs	Irreversible monoamine oxidase inhibitors
mPFC	Medial prefrontal cortex
NICE	National Institute of Health and Clinical Excellence
PANSS	Positive and Negative Syndrome Scale
PD	Panic disorder
PET	Positron emission tomography
RCT	Randomized, controlled trial
RIMA	Reversible inhibitor of monoamine oxidase A
SAD	Social anxiety disorder
SFBN	Stanley Foundation Bipolar Network
SGA	Second-generation antipsychotics
SSRIs	Selective serotonin reuptake inhibitors
SNRIs	Selective serotonin noradrenaline reuptake inhibitors
SUD	Substance use disorders
TCAs	Tricyclic antidepressants

19.1 Introduction

Comorbidity of substance use and that of psychiatric disorders are of relevance for diagnosis, prognosis, and treatment of substance use disorders (SUD). A high comorbidity of substance use with affective disorder (Merikangas et al. 1998, 2003; Kessler et al. 2005; Pirkola et al. 2005; Marmorstein et al. 2010), especially bipolar disorder, and schizophrenia as well as anxiety disorders (Kessler et al. 1997, 2005; Grant et al. 2005) has repeatedly been shown. Pharmacotherapy of comorbid substance use and psychiatric disorders is a difficult issue, starting with problems in diagnosis and assessment ("true" comorbid or substance-induced psychiatric disorders), physical condition in substance users (e.g., hepatic or renal impairment, cardiac dysfunction), possible pharmacological interactions between psychotropic drugs and drugs of abuse, side effects, and abuse potential of some psychotropic agents. Substance-induced psychiatric disorders such as depression or anxiety disorders are rather poorly defined in ICD-10 and hence there is little research on this issue. So-called dual disorder patients are excluded in almost all psychopharmacological trials. In addition, there are numerous interactions between pharmacologic drugs and drugs of abuse, and compliance of "dual disorder" patients is mostly poor.

19.2 Anxiety Disorders

19.2.1 Background

Anxiety disorders have different clinical features and are subtyped as generalized anxiety disorder (GAD), panic disorder with and without agoraphobia, social anxiety disorder (SAD), and specific phobias. Obsessive–compulsive disorders, although grouped among anxiety disorders, are not part of this review. Anxiety disorders are very frequent in the general population. In the US National Comorbidity Survey, the lifetime prevalence for any anxiety disorder was 28.8 %, and the 12-month prevalence 18.1 %. There is broad evidence for a significant comorbidity of anxiety and substance use disorders (Conway et al. 2006; Compton et al. 2007).

For comorbid anxiety with substance use disorders, self-medication for tension reduction has been discussed as a possible explanation for use (Chutuape and de Wit 1995; Thomas et al. 2003; Robinson et al. 2011). The relaxing, tension- and stress-reducing, sedating effects of alcohol in particular are well established. Short-term consumption of alcohol or benzodiazepines diminishes anxiety in patients with panic disorder (Kushner et al. 1996; Krystal et al. 2006). Although the chronological relationship between onset of anxiety symptoms and substance use varies considerably, many studies indicate that the onset of anxiety precedes substance use in many cases (Merikangas et al. 1998; Falk et al. 2008). This has been explained by means of cognitive processes and the expectancy of the drug's effect. In contrast, long-term use of alcohol and possibly other drugs may induce anxiety disorders. Substance use often worsens psychiatric symptoms and outcome (Burns et al. 2005; Agosti and Levin 2006). In addition, anxiety is a frequent symptom in alcohol and drug withdrawal. In SAD, clinical findings on the

interrelationship with alcohol use are inconsistent. Anxiety symptoms may be part of a protracted withdrawal syndrome, a still rather ill-defined syndrome (De Soto et al. 1985; Kushner et al. 2000).

There is some empirical and epidemiological evidence for the self-medication theory (Robinson et al. 2011), for a review see (Soyka 2013b).

19.2.2 Neurobiology

The pathophysiology of GAD and other anxiety disorders is not clearly elaborated. There is evidence for a modest hereditary influence. In brief, impaired serotonergic and GABAergic neurotransmission have been discussed as neurobiological basis in GAD, as well as a dysfunction of various other neurotransmitter systems such as adrenaline/noradrenaline and GABA (Bandelow et al. 2008; Trincavelli et al. 2012). In addition, the role of stress and neuropeptides in anxiety (and depression) has been pointed out (Kormos and Gaszner 2013). GABA, dopamine, and serotonin also mediate psychotropic effects of drugs of abuse. For example, alcohol (and benzodiazepines) enhances the GABAergic neurotransmission and chronic alcohol intake is also associated with a serotonergic deficit. Other relevant neurotransmitters possibly involved in the pathophysiology of anxiety disorders are noradrenaline, cholecystokinin, and corticotrophin-releasing factors. For GAD, structural and functional neuroimaging studies have revealed abnormalities in the amygdala, the dorsomedial cortex, and other brain regions (Monk et al. 2008; Nitschke et al. 2009). Of note, overactivation of the central amygdala and impairment of medial prefrontal cortex (mPFC) cognitive function are also key factors that lead to excessive drinking and compulsive seeking and taking of alcohol and cocaine (Lesscher and Vanderschuren 2012; George et al. 2012).

19.2.3 Pharmacotherapy of Comorbid Anxiety Disorders and SUD

Numerous pharmacologic agents are used for the treatment of anxiety disorders without comorbid substance use disorders. Available drugs include selective serotonin inhibitors (SSRIs), selective serotonin noradrenaline reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), the calcium channel modulator pregabalin, the reversible inhibitor of monoamine oxidase A (RIMA) moclobemide, irreversible monoamine oxidase inhibitors (MAOIs), benzodiazepine (BZD), the 5-HT_{1A}-agonist buspirone, antihistamines, atypical antipsychotics, anticonvulsants, beta-adrenergic blockers, and other homeopathic and herbal preparations (National Institute for Health and Clinical Excellence (NICE) 2007; Bandelow et al. 2008).

For the treatment of comorbid patients, pharmacokinetic and pharmacodynamic interactions with alcohol or other drugs of abuse must be taken into account. With the exception of benzodiazepines and probably pregabalin the named drugs have no significant abuse potential.

In panic disorder and agoraphobia without comorbidities, the clearest evidence is available for various SSRIs, the SNRI venlafaxine, the TCAs clomipramine and imipramine, and some BZD. For GAD, there is evidence again for SSRIs, for the SNRIs venlafaxine and duloxetine, the TCA imipramine, pregabalin, the atypical antipsychotic quetiapine, and BZD. For SAD, several SSRIs are recommended, as well as venlafaxine and the MAOI phenelzine.

The risk of interactions of TCAs with alcohol is significant (e.g., blackouts or cardiac dysfunction); therefore these drugs are not first choice, at least in non-abstinent patients.

For short-term use, treatment with benzodiazepines has been established as being effective, although these substances hold the risk for abuse and dependence, especially in patients with substance use disorders. Since long-term treatment of up to 12 months is generally recommended, the risks for BZD use are apparent. The TCA imipramine, buspirone, SSRIs, and SNRIs are established medications for longer use. More recently pregabalin has also been studied, with promising results.

The database for comorbid patients with alcohol dependence and anxiety disorder is limited. One study found that paroxetine reduces anxiety symptoms in patients with comorbidity, and another found that it reduces social anxiety in patients with alcohol use disorders (Randall et al. 2001; Book et al. 2008). A meta-analysis of 5 published studies showed a positive effect of buspirone on treatment retention and anxiety, but the effect on alcohol consumption was less clear (Malec et al. 1996). Buspirone is no longer available in many countries.

Recently, a study on 81 patients with comorbid anxiety disorder and alcohol use disorders treated either with CBT, venlafaxine (225 mg) alone, or in combination has been published (Ciraulo et al. 2013). Only in the latter group heavy drinking significantly decreased after 11 weeks.

Some anticraving drugs are available for alcohol treatment, including the putative glutamatergic drug acamprosate and the opioid antagonists naltrexone and, more recently, nalmefene (Roesner et al. 2010; Soyka 2013a). They have hardly been studied in dual disorder patients. Acamprosate is an anticraving drug with proven efficacy in reducing relapse rates in alcohol-dependent patients (Roesner et al. 2010). Some open-label studies suggest that the drug is effective as an augmentation for anxiety disorders (Hertzman et al. 2009; Schwartz et al. 2010), but no studies are available in comorbid patients.

Taking the important role of hypothalamic–pituitary stress axis for both anxiety and alcohol use disorders into account (Koob 2008), the use of corticotrophin-releasing factor 1 (CRF_1) receptor antagonists have repeatedly been recommended. There are ongoing trials with various CRF antagonists but no clinical data available yet (Zorrilla et al. 2013).

Baillie and colleagues (Baillie et al. 2010) reviewed six randomized controlled trials of treatment for comorbid anxiety and substance use disorder and concluded that for patients with more than moderate substance dependence there is clear and consistent evidence that standard treatment for substance use disorders leads to the best outcomes.

For comorbid PTSD and alcoholism, a recent study showed a good effect of naltrexone on alcohol outcomes (Foa et al. 2013). Concomitant prolonged exposure therapy was not associated with exacerbation of alcohol use.

Usually, both pharmacological and psychotherapeutic approaches are combined for the treatment of anxiety disorders. A number of psychological interventions have been studied and shown efficacy in anxiety disorders. The first step is usually some form of psychoeducation and information about the diagnosis, etiology, and treatment options.

19.3 Affective Disorder

19.3.1 Background

There are numerous theories on the neurobiology and pathophysiology of depression. Historically, a monoamine deficiency and the relevance of serotonin and noradrenaline have been stressed (Kern et al. 2012). The existing antidepressants are mainly targeting these neurotransmitters and their receptors (Willner et al. 2013). Other neurotransmitters of relevance are GABA and dopamine. More recently, other transmitters such as the neuropeptides oxytocin and vasopressin were found to be important for emotional behaviors and anxiety and depression (Neumann and Landgraf 2012). Among the many other factors discussed in the development of depression are changes in neuronal and glial function and structure (Kern et al. 2012) and a stress-related dysfunction of the hypothalamic–pituitary–adrenocortical (HPA) axis mediating vulnerability to depression.

There is robust evidence for a significant comorbidity of depressive disorders and substance use, especially alcoholism. Epidemiological studies indicate an about twofold increased risk for substance use in patients with depression and dysthymia. Even more striking are figures reported for comorbid substance use and bipolar disorder (BD). In fact, BD has the highest lifetime prevalence of comorbid SUD of all major psychiatric disorders (Regier et al. 1990). Similar to anxiety disorders, a self-medication theory may, in part, explain these high rates as affective disorders are regularly accompanied by anxiety, often to a degree that merits a separate comorbid diagnosis of anxiety disorder.

Alcohol is the substance with the highest abuse and dependency potential in patients with BD, followed by cannabis (Merikangas et al. 2007). Odds ratios (OR) reported by a large US epidemiological catchment area study (Regier et al. 1990) for substance abuse in the presence versus absence of mood disorder are 7.9 for Bipolar I and 4.7 for Bipolar II patients. Especially in women with bipolar disorder the risk of alcohol abuse or dependence exceeds by far the risk of the general population (Frye et al. 2003), and makes them also more vulnerable to additional comorbidities, namely anxiety (Levander et al. 2007). The prognosis of BD with comorbid SUD is poor (Frye and Salloum 2006). Evidence is emerging that bipolar patients who also abuse drugs or alcohol have an earlier onset and worse course of illness compared with those who do not. They are more likely to

experience irritable and dysphoric mood states, increased treatment resistance, and a greater need for hospitalization (Brady and Sonne 1995). Of note, this poorer long-term prognosis persists even in patients who have stopped their substance abuse (Gaudiano et al. 2008). Mood-destabilizing effects of substance use in bipolar patients have been repeatedly described, e.g., increased vulnerability to mood switches (Ostacher et al. 2010) and a higher frequency of mania in patients with SUD and a rapid cycling course (Kemp et al. 2009). SUD might impact on treatment-emergent mood switching via direct or indirect effects. The direct action would be by negatively affecting neurons and neuronal circuits. The indirect way is through non-adherence to pharmacological treatments leading to a reduction in efficacy of pharmacological treatments (Manwani et al. 2007).

Most patients with mood and anxiety disorders and substance use have independent mood and anxiety psychiatric disorder while substance-induced depression is rare (Torrens et al. 2011; Magidson et al. 2013).

19.3.2 Neurobiology

Similar to anxiety disorders, an underlying central serotonergic deficit might be a common link between depression and substance use disorders. For bipolar disorder, dysfunction of the dopaminergic and noradrenergic system has been considered as potential underlying common pathophysiology. This is based both on the clinical observation of impulsivity, strong novelty and reward seeking behaviors in mania as well as preliminary genetic findings, such as a Val158Met polymorphism in the catechol-O-methyltransferase gene (COMT) affecting patients with bipolar disorder and substance abuse (but also schizophrenia and ADHD) (Zumarraga et al. 2010; Schellekens et al. 2012). Recent research also suggests a role of glutamatergic, namely NMDA receptor-coupled signal transmission, of intracellular guanine nucleotide-binding protein (G protein)-coupled signaling pathways, and of related calcium-dependent processes in the etiology of bipolar disorder (Mathew et al. 2008), all of which also appear to be involved in alcohol dependence. Thus, it is more than likely that not just one genetic overlap exists between bipolar disorder and substance use, but a pattern of different gene loci with individual contribution to a clinical phenotype. A hereditary connection between bipolar disorder and/or substance use is also supported by a large bipolar cohort study. The investigators of the Stanley Foundation Bipolar Network (SFBN) found that parental alcoholism is significantly correlated with the severity of bipolar disorder in offsprings (Nolen et al. 2004) although factors other than genetic, e.g., adverse environment, may also play a role.

In addition, the endogenous opioid system might be involved not only in SUD, but also in BD through mediation, modulation, and regulation of stress responses. Blockade of kappa opiate receptors results in antidepressant-like properties in animals, and a nonselective kappa agonist (pentazocine) showed anti-manic effect in humans (Zarate and Manji 2008). In line with this, naltrexone has been reported to produce manic-like symptoms in a patient with BD (Losekam et al. 2013).

There is also a linkage between the endogenous cannabinoid system and BD. Carriers of the cannabinoid 1 receptor gene (CNR1) variants may be more susceptible to BD (Monteleone et al. 2010). A growing body of evidence supports that the endocannabinoid system could become a future therapeutic target in BD (Micale et al. 2013).

19.3.3 Pharmacotherapy of Comorbid Unipolar Depression and SUD

Few studies only have addressed the issue of pharmacological treatment in comorbid patients.

In unipolar depression, a small randomized controlled trial (RCT) with fluoxetine showed efficacy in both improving depression and lowering alcohol consumption (Cornelius et al. 1997). Other SSRIs such as sertraline (Kranzler et al. 2006) were not found to be effective in this population, while Moak and colleagues (Moak et al. 2003) reported a modest benefit. Farren and colleagues (Farren et al. 2009) also reported that sertraline plus naltrexone was not more effective than naltrexone alone in alcohol-dependent patients ($N = 113$). More recently, a double-blind, placebo-controlled trial by Pettinati and colleagues (Pettinati et al. 2010) found sertraline plus naltrexone to be effective in dual disorder patients. Thus, the evidence is inconsistent so far.

The meta-analysis conducted by Nunes and Levin (2004) states that tricyclics rather than SSRIs are effective in patients with alcoholism and depression. Modest effects on SUD-related outcomes were only seen in patients who also showed greater effect sizes on depression ratings (depression effect sizes greater than 0.5), demonstrating that substance use effect sizes and depression effect sizes are not independent from each other. Torrens and colleagues (2005) performed another systematic review and meta-analysis on this issue and found that in alcohol dependence without comorbid depression, the use of any antidepressant is not justified which seems to be general consensus in the literature. The authors further stated that in cocaine dependence this still has to be clarified (see below) but that SSRIs do not seem to offer significant advantages compared with tricyclics in substance use disorders.

A meta-analysis by Hobbs and colleagues (2011) on psychiatric treatment (medication plus psychotherapy, CBT) in alcoholic patients with depression and anxiety found that both psychiatric and alcohol-related outcomes were improved by combining approaches effective for substance use and the mental disorder.

Recently, George and colleagues (2011) demonstrated fluoxetine in conjunction with alcohol treatment and CBT to reduce alcohol-induced anger and physical aggression in alcoholic perpetrators.

Muhonen and colleagues (2008b) performed a double-blind, randomized comparison of memantine and escitalopram (20 mg each) for the treatment of major depressive disorder comorbid with alcohol dependence and found that both treatments significantly reduced baseline levels of depression and anxiety. Effects

on alcohol consumption were also evident (Muhonen et al. 2008a). Secondary analyses showed that age at onset of first depressive episode was predictive for response for escitalopram (Muhonen et al. 2009), as was serotonin transporter genotype (Muhonen et al. 2011).

All in all, antidepressants were not found to be effective to improve drinking outcomes at least in nondepressed alcoholics. A combined substance use and psychiatric (including medication) treatment is recommended for dual disorder patients. Since substance-induced depression is rather rare, treatment can be recommended sometime after possible withdrawal symptoms—which may include anxiety and mood disorders—have vanished. No particular antidepressant can be recommended on the limited basis of studies available so far. Clinical and pharmacological interactions with drugs of abuse must be taken into account.

The anticraving drug acamprosate was found to have "antidepressant" effects in mice (Palucha-Poniewiera and Pilc 2012), but probably not in humans (Witte et al. 2012). An individual patient data meta-analysis of RCTs with acamprosate suggests the drug to be equally effective in depressed and nondepressed patients (Lejoyeux and Lehert 2011). A recent randomized, placebo-controlled study of acamprosate added to escitalopram in patients with alcohol use disorder and major depression showed a significant reduction in alcoholic drinks per week and a nonsignificant improvement in depression symptoms.

In opioid dependence, depressive symptoms are frequent with some 40 % of patients affected (lifetime prevalence 44–54 %), representing a risk factor for morbidity and mortality (Rounsaville et al. 1982; Brooner et al. 1997; Darke and Ross 1997; Strain 2002; Ross et al. 2005; Schäfer et al. 2011; Wittchen et al. 2011; Savant et al. 2013). There are few studies on efficacy of antidepressant treatment in heroin users. Stein and colleagues (2004) performed a randomized controlled trial exploring the effects of combined pharmacotherapy (citalopram) plus psychotherapy (CBT) for treatment of depression in active injection drug users ($N = 109$) and found the combined treatment to be superior to a control condition (assessment only) for proportion of patients in remission, but not for improvement of depression as measured by the Hamilton depression scale. Follow-up data of this sample indicate that these differences may not persist (Stein et al. 2005).

A fairly recent Cochrane analysis on pharmacological treatment in opioid dependence included seven studies with 482 participants. Pani and colleagues (Pani et al. 2010) concluded that there is little evidence supporting the clinical use of antidepressants for the treatment of depressed opioid addicts under treatment with opioid agonists. Clinically, taking the high risk for relapse and suicides into account, antidepressant treatment should be favored at least in those individuals with significant depressive symptoms.

Full μ-opioid agonists such as methadone are widely used for the treatment of opioid dependence (Soyka et al. 2011). A first-line alternative is buprenorphine which is a partial agonist and an antagonist at the kappa-opioid receptor. Since kappa-antagonists may have antidepressant effects (Wee and Koob 2010) buprenorphine may be favored in depressed opioid-dependent patients. There are some small reports on antidepressant effects of buprenorphine (Emrich et al. 1982;

Bodkin et al. 1995). In a randomized double-blind study in 164 opioid- and cocaine-dependent patients treated with either methadone or buprenorphine plus desipramine, depressive symptoms at baseline but not during treatment were more frequent in the buprenorphine group. Desipramine was not superior to placebo (Dean et al. 2004).

In a retrospective study Gerra and colleagues (2006) studied the effects of buprenorphine in dual disorder patients ($N = 206$) with major depression (29.6 %), GAD (11.2 %), personality disorders (22 %), schizophrenia (6 %), and others. Depressive heroin-dependent patients had a better retention rate and less opioid-positive urine testings compared to other dual disorder patients or opioid dependents without psychiatric comorbidity. These findings were in line with previous reports by Gerra and colleagues (2004).

The same group also conducted a Cochrane analysis on antidepressant use for cocaine dependents and cocaine use. Mood disorders are typical for cocaine withdrawal. The database was much larger—37 studies with 3,531 participants (Pani et al. 2011). Again, the authors concluded that evidence data do not support the efficacy of antidepressants in the treatment of cocaine disorders. Desipramine has especially been studied for the treatment of cocaine dependence, with some positive studies included in the meta-analysis.

19.3.4 Pharmacotherapy of Comorbid Bipolar Disorder and SUD

Even less is known about the optimal treatment of concomitant substance use and bipolar disorder. Almost all the randomized controlled studies in bipolar disorder excluded patients with current SUD. To date, only four placebo-controlled RCTs have been conducted in BD with comorbid alcohol use disorder (Geller et al. 1998; Brady et al. 2002; Salloum et al. 2005; Kemp et al. 2009) with one of them (Brady et al. 2002) having a mixed study population of unipolar and bipolar affective disorder, and one including also unipolar patients at high risk of bipolarity (Geller et al. 1998).

Historical data from several, noncontrolled studies indicate that the presence of a substance use disorder may be a predictor of poor response to lithium (Brady and Sonne 1995). Open data do not support efficacy of lithium in cocaine users with bipolar spectrum disorder (Nunes et al. 1990). However, in a small but placebo-controlled RCT conducted in adolescents with an established bipolar diagnosis or being at risk of BD, Lithium was significantly better than placebo for both psychopathology measures and weekly random urine drug assays (Geller et al. 1998). Addiction to both alcohol and marijuana was the most frequent category of SUD in these bipolar adolescents. Interestingly, open studies have also demonstrated reduced numbers of drinking days in non-bipolar alcoholics taking lithium after detoxification (Frye and Salloum 2006). However, this did not hold true in two large, placebo-controlled studies in detoxified alcoholics (Dorus et al. 1989; Fawcett et al. 2000).

19.3.4.1 Anticonvulsants

The evidence for mood-stabilizing anticonvulsants is slightly better, although not satisfactory. In an open-label 12-week safety study, nine bipolar I patients with substance dependence (five alcohol dependent) received a mean daily dose of 1583 mg valproate. Significant decreases in symptoms of mania and depression and a decrease in the number of days of substance use were reported. However, a nonsignificant hepatocellular enzyme elevation (i.e., no more than 2× normal) developed in four of the nine patients (Brady et al. 1995).

A 24-week, double-blind, placebo-controlled, randomized parallel-group trial evaluated the efficacy of valproate in decreasing alcohol use and stabilizing mood symptoms in 59 acutely ill patients with bipolar disorder and alcoholism. All study participants received treatment as usual, including lithium and psychosocial interventions, and were randomized to receive valproate or placebo. The valproate group had a significantly lower proportion of heavy drinking days ($P = 0.02$) and a trend toward fewer drinks per heavy drinking day ($P = 0.055$) than the placebo group. Importantly, higher valproate serum concentration significantly correlated with improved alcohol use outcomes. As far as mood symptoms were concerned, patients on valproate had no additional benefits compared to placebo (Salloum et al. 2005).

The same group also conducted a small open-label study of valproate in bipolar I disorder and comorbid cocaine dependence with active cocaine use. Significant improvement on % of cocaine abstinent days, dollars spent on cocaine, ASI's drug use severity index, % of alcohol abstinent days, drinks per drinking day, marijuana use, and cigarette smoking were observed as well as significant improvement on manic, depressive, and sleep symptoms and on functioning. However, limitations of this study are the small number (only seven subjects fulfilling inclusion criteria), the open design, and the uncontrolled effects of concomitant counseling. Thus, double-blind, placebo-controlled studies to fully evaluate the efficacy of valproate in this population are warranted (Salloum et al. 2007).

Addition of valproate to lithium in rapid cycling patients with comorbid SUD did not prolong time to relapse nor relapse rate over 6 months in a randomized controlled study (Kemp et al. 2009). In line with this, SUD predicted nonresponse in an RCT comparing valproate and lithium in rapid cycling patients, independent from treatment arm (Gao et al. 2010).

Although frequently used in the past in both SUD and bipolar disorder, there is a lack of evidence for carbamazepine in dual disorder patients. A small placebo-controlled RCT looked into a mixed population with either unipolar depression or BD and comorbid cocaine use. Carbamazepine had some benefits in patients with affective disorders, reducing depressive symptoms and the number of positive urine screens for cocaine, and prolonging time to first cocaine use. These effects were not observed in cocaine users without comorbid affective disorder (Brady et al. 2002).

Two open-label studies investigated the use of lamotrigine in cocaine users with BD (Brown et al. 2003a, 2006). Both studies report significant improvements in manic and depressive psychopathology as well as in cocaine craving and money spent on cocaine. However, when studying the most severely ill bipolar patients

with SUD, lamotrigine was not successful. An underpowered RCT of adding lamotrigine in nonresponders to dual treatment with valproate and lithium and comorbid recent SUD and rapid cycling bipolar disorder was inconclusive (Wang et al. 2010).

Of the other anticonvulsants, topiramate has some evidence for reducing alcohol consumption and craving (Johnson et al. 2003). However, its efficacy in bipolar disorder remains unproven; if at all, it might be considered as add-on treatment to effective mood stabilizers in bipolar patients with SUD. No studies in this group have been conducted so far with topiramate.

19.3.4.2 Antipsychotics

Despite their widespread use, little research has been done on the effectiveness of antipsychotics in BD with SUD. In all large, randomized studies of atypical antipsychotics (second-generation antipsychotics, SGA)) SUD was an exclusion criterion. However, the use of SGA in this patient group might be appealing. The D_2 antagonist tiapride is actually licensed for the treatment of alcohol dependence. Most SGA act on both the dopaminergic and serotonergic systems. Both dopaminergic and serotonergic deficiencies have also been implied in craving, and thus SGA might exert anticraving effects. However, proof of this hypothesis failed as shown by a meta-analysis of the use of antipsychotics in primary alcohol dependence (Kishi et al. 2013).

The evidence base for SGA in BD with SUD is rather poor. One randomized but open-label study has been conducted with quetiapine in patients with cocaine and amphetamine use. Of the 29 patients included, only 13 had a diagnosis of BD; the rest were suffering from depression, schizophrenia, or schizoaffective disorder. Decreased craving and improved psychiatric symptoms were observed in the group as whole, but a separate subanalysis of the patients with BD has not been conducted (Brown et al. 2003b).

Twelve-week add-on therapy with quetiapine was also tested in an open-label, non-randomized study in 17 bipolar patients. The investigators reported significant improvements for both manic and depressive symptoms, as well as a reduced craving, but no change in urine drug screens (Brown et al. 2002).

The same group also tested aripiprazole in bipolar patients with SUD (alcohol, cocaine, opioids, cannabis) in an open-label design. After 12 weeks, a symptomatic improvement of mood and some reduction in alcohol and cocaine use were observed.

Given the reasonable evidence for clozapine in schizophrenic patients with SUD, and the widespread use of olanzapine, it is quite surprising that these two SGA have not been investigated so far in BD with comorbid SUD—or results have not been published.

19.3.4.3 Other Psychotropics and Anticraving Drugs

The use of antidepressants in BD remains a matter of controversy due to a relative lack of efficacy and a potential risk of inducing a switch to mania (Grunze et al. 2010). SUD has been identified as another potential risk factor for manic

switches (Ostacher et al. 2010). In the absence of data, it can be assumed that antidepressant use and SUD might have additive effects on destabilizing bipolar patients and thus antidepressants should be used with even greater caution in bipolar patients with comorbid SUD.

Addition of stimulants in otherwise treatment refractory bipolar depression is a recommended option in BD without SUD. However, several studies in children and adolescents with BD and ADHD have shown that co-administration of a stimulant to a mood stabilizer caused reversible adverse mood or behavioral changes including mania, hypomania, and suicidality in up to 10 % of patients (Goldsmith et al. 2011). Whereas addictive amphetamine derivatives such as methylphenidate are clearly no treatment option in BD with SUD, the efficacy of medication such as modafinil or armodafinil remains unclear in these patients (as well as their addiction potential).

So far, systematic investigations of anticraving drugs in comorbid bipolar and alcohol use patients are almost absent. A small study of acamprosate in bipolar patients with alcohol dependence reported no worsening of depressive or manic symptoms (Tolliver et al. 2012). A pilot study of the SFBN in bipolar patients without alcohol abuse even suggests mild anti-manic effects of acamprosate, probably due to its calcium antagonistic properties (Dittmann et al. 2009).

In summary, there is a sharp contrast between the frequency and consequences of SUD in BD on the one hand, and the amount of treatment research conducted on the other hand. Currently, and until better evidence is available, the best way forward might be to treat SUD and BD independently and tailored to the individual needs rather than trying to find a "one fits all" medication.

19.4 Schizophrenia

19.4.1 Background

The literature suggests that nearly 50 % of patients with schizophrenia have a co-occurring substance use disorder (Dixon 1999), but prevalence rates for alcohol and illicit drug use in first-episode schizophrenia (FES) patients are already high (Barnett et al. 2007). Dual and polysubstance abuse is frequent (Soyka et al. 1993), and there is a clear demand for specialized dual disorder services with an integrated treatment program (Ziedonis et al. 2005).

Cannabis is the most frequently abused illicit substance among schizophrenic patients (Bersani et al. 2002). Regarding first-episode psychosis, rates of cannabis misuse range between 15 and 65 %, whereas rates of alcohol misuse range between 27 and 43 % in first-episode samples (Compton et al. 2009). Schizophrenic patients are almost five times more likely to smoke than the general population (Hartz et al. 2014), which potentially interferes with the metabolism of antipsychotic medication (Andrade 2012). Several studies in FES demonstrate that substance use initiation typically precedes psychosis onset, often by several years. This is true of cannabis use in particular. It is less clear how often substance abuse precedes

onset of the prodrome; however, two studies found that substance abuse occurs pre-prodromally in 28–34 % of cases (Hambrecht and Haefner 1996; Veen et al. 2004). It has been hypothesized that SUD may be an inappropriate attempt to counteract early symptoms of psychosis, especially negative symptoms and anhedonia (Degenhardt et al. 2003). Another approach is adopted by the "cumulative risk factor hypothesis" according to which schizophrenia patients are at a higher risk for substance abuse because of their poor cognitive abilities, low social, educational, and vocational functioning, and disadvantageous life circumstances (Mueser et al. 1998).

SUD leads to an earlier onset of psychosis with a poorer prognosis (Wobrock and Soyka 2008; Kerfoot et al. 2011). Besides mental health issues, SUD in schizophrenic patients is also associated with significant physical health issues (Beary et al. 2012). Earlier studies demonstrated that illicit drug abuse in schizophrenia is associated with a higher mortality (Allgulander 1989). However, this might not be true for every cause of death and to the same degree for all substances of abuse. A large prospective study found that illicit drug use was associated with a doubling of the risk for suicide but alcohol usage was not (Limosin et al. 2007), and neither hazardous drinking nor illicit drug use were associated with increased cardiac mortality in chronic schizophrenia (Kilbourne et al. 2009).

19.4.2 Neurobiology

Similar to affective and anxiety disorders, research on the neurobiology of schizophrenia has focussed for a long time on a disbalance of neurotransmitter systems. The three neurotransmitter systems most frequently implicated in schizophrenia are dopamine, GABA, and glutamate. Presumed hyperactivity of the mesolimbic dopamine system has been linked to the positive symptoms, and hypoactivity of the mesocortical dopamine system to the negative symptoms of schizophrenia (van Os and Kapur 2009). On the other hand, reduced activity in glutamatergic and GABAergic systems has also been discussed as a relevant process given their importance for inhibitory cortical feedback circuits (McCarley et al. 1999). Of interest, the endogenous opioid system, especially the dynorphin/κ-opioid receptor system, has also been implicated in schizophrenia; however, its role appears rather unspecific. Impairment of the system might result in deficits in learning and memory, emotional control, and response to stress. Thus, besides schizophrenia, dynorphins/κ-opioid receptors are thought to play a role also in the pathophysiology of epilepsy, depression, and certainly addiction (Schwarzer 2009).

The neurobiology underlying the striking epidemiological figures of comorbid schizophrenia and SUD, however, appears manifold and is not satisfactorily researched. The most prominent hypothesis is that schizophrenia patients tend to use drugs to counteract dysfunction of the dopaminergic brain reward circuitry. Altered reward processing has been extensively demonstrated in schizophrenia, and it has been suggested that schizophrenia patients tend to overvalue the positive consequences of drug use and devalue its negative consequences (Thoma and Daum

2013). However, all other neurotransmitter systems which have been implicated in schizophrenia have also a proposed role in SUD and vice versa. The catechol-o-methyl transferase (COMT) is the key enzyme for the degradation of catecholamine neurotransmitters (dopamine, adrenaline, and noradrenaline). Specifically for cannabis, adolescent cannabis use is associated with the development of psychosis in those who have a "high output" variant of the gene for catechol-o-methyl transferase (COMT), suggesting an important gene–environment interaction in this risk group (Caspi et al. 2005).

Finally, preexisting brain abnormalities might predispose some individuals toward developing both psychosis and addiction (Chambers et al. 2010). In turn, alcohol and cannabis abuse have been associated with more frontal lobe and thalamus abnormalities and increased risk for developing psychosis in individuals with high familial risk for developing schizophrenia (Welch et al. 2011a, b).

19.4.3 Pharmacotherapy of Comorbid Schizophrenia and SUD

Pharmacotherapy of schizophrenia with comorbid SUD needs special consideration not only of efficacy, but also of the safety profile. For example, memory problems in schizophrenia may preclude prescribing disulfiram as well as its potential to induce psychosis, and the seizure risk, sedation, and liver disease caused by substance addiction may influence choice of antipsychotic medications. There is some consensus that the first-generation (conventional) antipsychotics (FGA) are not particularly helpful in the treatment of patients with schizophrenia and SUD (Ziedonis et al. 2005). Small improvement in psychotic symptoms and substance use has been observed with fluphenazine and flupentixol decanoate, but the effect size is marginal (Soyka et al. 2003; Wobrock and Soyka 2008). Several investigators have suggested that conventional antipsychotics may actually precipitate or worsen the abuse of substances in patients with schizophrenia. A PET study demonstrated that higher dopamine D(2) receptor occupancy and binding potentials in the striatal (dorsal and ventral), temporal, and insular regions were associated with the subjective experience of dysphoria (Mizrahi et al. 2007). Also injectable FGA seem to be less preferable than a depot atypical antipsychotic (risperidone long-acting injectable (LAI)) as an open study suggests. Long-acting risperidone patients had fewer positive urine tests for drugs of abuse, showed improved scores on the Positive and Negative Syndrome Scale (PANSS), and showed better compliance with the Substance Abuse Management program applied in this study (Rubio et al. 2006).

However, not all studies are in support of a superiority of SGA compared to FGA, at least for substance abuse-related outcomes (Scheller-Gilkey et al. 2003). A large retrospective chart review of Department of Veterans Affairs patients found that after confounding factors were controlled for, there were no differences in improvement on Addiction Severity Index scores between patients treated with atypical antipsychotics (mostly risperidone and olanzapine) and those treated with conventional antipsychotics (Petrakis et al. 2006).

In contrast to concerns that FGA may worsen SUD, preliminary studies suggest that some of the SGA may be helpful for dual disorder patients (Green et al. 2008). For example, there have been reports that for patients treated with clozapine and olanzapine, overall outcomes during treatment are as good among those who have a co-occurring SUD as those who do not. Especially clozapine has also shown encouraging results in avoiding substance abuse relapses (Brunette et al. 2006) and in reducing alcohol. At the end of the study by Drake and colleagues (Drake et al. 2000) after 3 years, 79.0 % of the patients on clozapine were in remission from alcohol use disorder for 6 months or longer, while only 33.7 % of those not taking clozapine were remitted. In a retrospective analysis, treatment with clozapine prevented psychotic relapse to the same degree in patients with treatment-resistant schizophrenia and concomitant drug abuse as in the group without substance use (Kelly et al. 2003).

More, although low grade, evidence for clozapine originates from case studies and small open case series (Wobrock and Soyka 2008). The beneficial effect of clozapine on SUD might be related to clozapine's unique pharmacologic effects (i.e., its weak antagonism at the dopamine D2 receptor and its potent blockade of the noradrenergic α2 receptor, coupled with its ability to release noradrenaline in the brain), which result in an amelioration of the proposed brain reward circuit deficiency in these patients. However, none of these studies were prospective RCTs, and thus the evidence about clozapine's value for these patients remains to some degree speculative.

Other SGA have also been assessed in schizophrenic patients with SUD, but there is even less information about them than about clozapine. The evidence for risperidone is inconclusive. Whereas risperidone appears to be superior to haloperidol in reducing craving and substance abuse relapse in patients with schizophrenia and co-occurring cocaine dependence (Smelson et al. 2004), it seems to be clearly less effective than clozapine for cannabis and alcohol abuse abstinence rates (Green et al. 2003).

The few available results of RCTs with olanzapine in dual disorder patients are mixed.

Switching to olanzapine from FGA seems to have similar advantages in patients with schizophrenia and comorbid SUD than in those without SUD (Wobrock and Soyka 2008). Contradictory results have been reported for olanzapine compared to haloperidol in cocaine users. When comparing olanzapine and risperidone in FES with SUD, they had a similar initial efficacy on psychotic symptoms and substance use (Sevy et al. 2011). Also inconclusive, either due to very small numbers or contradicting results, is the evidence for quetiapine and aripiprazole (Green et al. 2007). An open study reported significant improvement of the psychopathology, less cocaine use than before, and less craving for cocaine and alcohol in aripiprazole-treated dual disorder patients (Beresford et al. 2005). For quetiapine, a prospective randomized switch study from FGA reported a decrease in craving, but no additional significant effects on psychopathology (Brown et al. 2003b).

Comparing different SGA (and FGA) in a retrospective study patients taking risperidone or ziprasidone stayed longer in an inpatient dual disorder treatment

program and were more likely to complete it successfully than patients with olanzapine or fluphenazine and haloperidol decanoate (Stuyt et al. 2006).

Postpsychotic depression is frequent in schizophrenia, and SUD may additionally contribute to low mood and apathy. Older antidepressants, namely the TCAs desipramine and imipramine, have been tried in dual disorder patients. In summary, less craving and use of cocaine, but not cannabis, and no marked improvement in mood were observed (Wobrock and Soyka 2008). The mood-stabilizing antiepileptic drug lamotrigine has also been tried in treatment-resistant schizophrenic patients with comorbid alcohol use disorder, and found to reduce craving and alcohol consumption (Kalyoncu et al. 2005).

Based on the hypothesis that the endogenous opioid system is involved in the pathophysiology of schizophrenia (Gold et al. 1977) some anticraving substances such as naloxone, naltrexone, and nalmefene (e.g., Rapaport et al. 1993) have been tried in schizophrenic patients without SUD. Initial positive results, however, could not be confirmed in subsequent studies, which were rather indicative for a worsening of schizophrenic symptoms (Sernyak et al. 1998). Thus, a potential use of anticraving substances targets SUD only, with the caveat that psychosis may exacerbate.

As expected, anticraving substances (naltrexone) and disulfiram have a positive influence on alcohol use in schizophrenic patients, similar to that in addicted patients without schizophrenia (Batki et al. 2007). However, it is important to remember that disulfiram itself can induce psychoses, probably due to its blockade of dopamine-beta hydroxylase (Major et al. 1979) and can accelerate the metabolism of antipsychotics. For these reasons, the use of disulfiram in patients with schizophrenia and comorbid alcohol dependence remains a matter of controversy. Unfortunately, no controlled data are available for the use of acamprosate as anticraving substance in this patient group. A case report appears promising (Tek et al. 2008), and acamprosate seems to be safe to use in this group without negatively impacting on cognition (Ralevski et al. 2011).

In summary, the evidence for the pharmacological treatment of schizophrenia with comorbid SUD is scarce, the only exception possibly being clozapine. However, clozapine will remain reserved for schizophrenic patients with a most severe course of illness refractory to other medication, whereas the problematic SUD is more widespread and especially prominent in FES. Thus, similar to BD, individual treatment with the most promising medication for the psychosis and the best choice for the SUD might still be the best way forward.

19.5 Summary

To sum up, the pharmacotherapy of dual disorders is a challenging but widely neglected issue. There are no “one fits all” medications, and both conditions may need to be treated separately. Safety issues and pharmacological interactions have always to be taken into account. Selected interactions between substances of abuse and medication for comorbid mental illness are depicted in Table 19.1. This table is

Table 19.1 Selected interactions between substances of abuse and medication for comorbid mental illness

Medication			
Substance of abuse	Antidepressants	Antipsychotics	Benzodiazepines
Alcohol	Sedation ↑, Seizure threshold ↓	Sedation ↑, Seizure threshold ↓,	Sedation ↑ and motor performance ↓ with some BZD
Opioids	All toxic opioid effects ↑ through CYP450 inhibition: Methadone, Codeine and buprenorphine serum levels ↑ through 3A4 and 2D6 inhibition by Fluvoxamine, Fluoxetine; Methadone and codeine ↑ through 2D6 inhibition by paroxetine, sertraline, citalopram, escitalopram, bupropion, doxepin	Methadone and codeine ↑ through 2D6 inhibition by perphenazine, chlorpromazine, haloperidol	BZD are metabolized mainly by CYP450 3A4, 3A5, 2C19 and thus can interact with opioid metabolism. Sedation ↑ (up to apnea). There is an extensive record of deaths related to parallel consumption of opioids and BZD
Amphetamines, Cocaine	↑ Risk of serotonin syndrome with SSRI, SNRI, and MAO-I. Cocaine inhibits venlafaxine and trimipramine metabolism via CYP 2D6	Amphetamines and cocaine may antagonize the antipsychotic effects. Cocaine increases serum concentration of zuclopenthixol and iloperidone via CYP 2D6 inhibition	No relevant interaction reported
Cannabis	Severe tachycardia with TCA due to combined anticholinergic action	Risk of tachycardia with neuroleptics with high anticholinergic potency (e.g., clozapine, chlorpromazine). Cannabis may antagonize antipsychotic effects (but may also improve extrapyramidal motor symptoms)	Potential of synergistic action on sedation and respiratory depression

not a complete overview, but it lists most frequently used medications and interactions. For a complete reference, please refer to comprehensive handbooks (e.g., McCance-Katz 2012; Mozayani and Raymon 2012).

Table 19.2 Summary of the evidence from RCTs for pharmacological treatments to reduce SUD (alcohol intake-related outcome measures) in patients with comorbid mental disorders

	Comorbid mental disorder			
	Any anxiety disorder	Unipolar depression	Bipolar disorder	Schizophrenia
Positive evidence from RCTs	*Naltrexone (in PTSD)*	Fluoxetine, *Acamprosate*	Valproate	*Naltrexone*
Inconsistent evidence from RCTs	Buspirone, Paroxetine	Sertraline	–	–
Negative evidence from RCTS	Venlafaxine	Desipramine, Nefazodone, Imipramine	Lithium	–

RCTs Randomized controlled trials, *SUD* Substance use disorder, *PTSD* Posttraumatic stress disorder. *Evidence for anticraving medication in Italics*

In general, the use of anticraving drugs can also be recommended in dual disorders, based on a small empirical basis. Table 19.2 summarizes the available evidence to reduce alcohol consumption for different medication used in SUD with selected comorbid conditions.

Antidepressants should be used in unipolar affective disorders, with no particular drug to be favored. In anxiety disorders, serotonergic drugs including venlafaxine may be the primary drugs of choice. Novel drugs such as CRF1 antagonists are currently studied in anxious alcoholics. Recommendations for schizophrenia and bipolar disorders are more difficult. Compliance is a critical issue in both. Novel antipsychotics with a lower risk of EPMS may be favored to enhance compliance. Dual disorder patients may have an increased risk for EPMS. For schizophrenia the evidence is relatively best for clozapine. Injectable antipsychotics are an alternative strategy to enhance compliance. And finally: if possible, drugs with an abuse potential should be avoided, if possible, or its use strictly limited.

References

Agosti V, Levin FR (2006) The effects of alcohol and drug dependence on the course of depression. Am J Addict 15:71–75

Allgulander C (1989) Psychoactive drug use in a general population sample, Sweden: correlates with perceived health, psychiatric diagnoses, and mortality in an automated record-linkage study. Am J Public Health 79:1006–1010

Andrade C (2012) Schizophrenia and smoking. J Clin Psychiatry 73:e725–e727

Baillie AJ, Stapinski L, Crome E, Morley K, Sannibale C, Haber P, Teesson M (2010) Some new directions for research on psychological interventions for comorbid anxiety and substance use disorders. Drug Alcohol Rev 29:518–524

Bandelow B, Zohar J, Hollander E, Kasper S, Moller HJ, Zohar J, Hollander E, Kasper S, Moller HJ, Bandelow B, Allgulander C, Yuso-Gutierrez J, Baldwin DS, Buenvicius R, Cassano G, Fineberg N, Gabriels L, Hindmarch I, Kaiya H, Klein DF, Lader M, Lecrubier Y, Lepine JP, Liebowitz MR, Lopez-Ibor JJ, Marazziti D, Miguel EC, Oh KS, Preter M, Rupprecht R,

Sato M, Starcevic V, Stein DJ, Van AM, Vega J (2008) World Federation of Societies of Biological Psychiatry (WFSBP) guidelines for the pharmacological treatment of anxiety, obsessive-compulsive and post-traumatic stress disorders—first revision. World J Biol Psychiatry 9:248–312

Barnett JH, Werners U, Secher SM, Hill KE, Brazil R, Masson K, Pernet DE, Kirkbride JB, Murray GK, Bullmore ET, Jones PB (2007) Substance use in a population-based clinic sample of people with first-episode psychosis. Br J Psychiatry 190:515–520

Batki SL, Dimmock JA, Wade M, Gately PW, Cornell M, Maisto SA, Carey KB, Ploutz-Snyder R (2007) Monitored naltrexone without counseling for alcohol abuse/dependence in schizophrenia-spectrum disorders. Am J Addict 16:253–259

Beary M, Hodgson R, Wildgust HJ (2012) A critical review of major mortality risk factors for all-cause mortality in first-episode schizophrenia: clinical and research implications. J Psychopharmacol 26:52–61

Beresford TP, Clapp L, Martin B, Wiberg JL, Alfers J, Beresford HF (2005) Aripiprazole in schizophrenia with cocaine dependence: a pilot study. J Clin Psychopharmacol 25:363–366

Bersani G, Orlandi V, Kotzalidis GD, Pancheri P (2002) Cannabis and schizophrenia: impact on onset, course, psychopathology and outcomes. Eur Arch Psychiatry Clin Neurosci 252:86–92

Bodkin JA, Zornberg GL, Lukas SE, Cole JO (1995) Buprenorphine treatment of refractory depression. J Clin Psychopharmacol 15:49–57

Book SW, Thomas SE, Randall PK, Randall CL (2008) Paroxetine reduces social anxiety in individuals with a co-occurring alcohol use disorder. J Anxiety Disord 22:310–318

Brady KT, Sonne SC (1995) The relationship between substance abuse and bipolar disorder. J Clin Psychiatry 56(Suppl 3):19–24

Brady KT, Sonne SC, Anton R, Ballenger JC (1995) Valproate in the treatment of acute bipolar affective episodes complicated by substance abuse: a pilot study. J Clin Psychiatry 56:118–121

Brady KT, Sonne SC, Malcolm RJ, Randall CL, Dansky BS, Simpson K, Roberts JS, Brondino M (2002) Carbamazepine in the treatment of cocaine dependence: subtyping by affective disorder. Exp Clin Psychopharmacol 10:276–285

Brooner RK, King VL, Kidorf M, Schmidt CW Jr, Bigelow GE (1997) Psychiatric and substance use comorbidity among treatment-seeking opioid abusers. Arch Gen Psychiatry 54:71–80

Brown ES, Nejtek VA, Perantie DC, Bobadilla L (2002) Quetiapine in bipolar disorder and cocaine dependence. Bipolar Disord 4:406–411

Brown ES, Nejtek VA, Perantie DC, Orsulak PJ, Bobadilla L (2003a) Lamotrigine in patients with bipolar disorder and cocaine dependence. J Clin Psychiatry 64:197–201

Brown ES, Nejtek VA, Perantie DC, Rajan TN, Rush AJ (2003b) Cocaine and amphetamine use in patients with psychiatric illness: a randomized trial of typical antipsychotic continuation or discontinuation. J Clin Psychopharmacol 23:384–388

Brown ES, Perantie DC, Dhanani N, Beard L, Orsulak P, Rush AJ (2006) Lamotrigine for bipolar disorder and comorbid cocaine dependence: a replication and extension study. J Affect Disord 93:219–222

Brunette MF, Drake RE, Xie H, McHugo GJ, Green AI (2006) Clozapine use and relapses of substance use disorder among patients with co-occurring schizophrenia and substance use disorders. Schizophr Bull 32:637–643

Burns L, Teesson M, O'Neill K (2005) The impact of comorbid anxiety and depression on alcohol treatment outcomes. Addiction 100:787–796

Caspi A, Moffitt TE, Cannon M, McClay J, Murray R, Harrington H, Taylor A, Arseneault L, Williams B, Braithwaite A, Poulton R, Craig IW (2005) Moderation of the effect of adolescent-onset cannabis use on adult psychosis by a functional polymorphism in the catechol-O-methyltransferase gene: longitudinal evidence of a gene X environment interaction. Biol Psychiatry 57:1117–1127

Chambers RA, Sentir AM, Conroy SK, Truitt WA, Shekhar A (2010) Cortical-striatal integration of cocaine history and prefrontal dysfunction in animal modeling of dual diagnosis. Biol Psychiatry 67:788–792

Chutuape MA, de Wit HJ (1995) Preferences for ethanol and diazepam in anxious individuals: an evaluation of the self-medication hypothesis. Psychopharmacology (Berl) 121:91–103

Ciraulo DA, Barlow DH, Gulliver SB, Farchione T, Morissette SB, Kamholz BW, Eisenmenger K, Brown B, Devine E, Brown TA, Knapp CM (2013) The effects of venlafaxine and cognitive behavioral therapy alone and combined in the treatment of co-morbid alcohol use-anxiety disorders. Behav Res Ther 51:729–735

Compton WM, Thomas YF, Stinson FS, Grant BF (2007) Prevalence, correlates, disability, and comorbidity of DSM-IV drug abuse and dependence in the United States: results from the national epidemiologic survey on alcohol and related conditions. Arch Gen Psychiatry 64:566–576

Compton MT, Kelley ME, Ramsay CE, Pringle M, Goulding SM, Esterberg ML, Stewart T, Walker EF (2009) Association of pre-onset cannabis, alcohol, and tobacco use with age at onset of prodrome and age at onset of psychosis in first-episode patients. Am J Psychiatry 166:1251–1257

Conway KP, Compton W, Stinson FS, Grant BF (2006) Lifetime comorbidity of DSM-IV mood and anxiety disorders and specific drug use disorders: results from the National Epidemiologic Survey on Alcohol and Related Conditions. J Clin Psychiatry 67:247–257

Cornelius JR, Salloum IM, Ehler JG, Jarrett PJ, Cornelius MD, Perel JM, Thase ME, Black A (1997) Fluoxetine in depressed alcoholics. A double-blind, placebo-controlled trial. Arch Gen Psychiatry 54:700–705

Darke S, Ross J (1997) Polydrug dependence and psychiatric comorbidity among heroin injectors. Drug Alcohol Depend 48:135–141

De Soto CB, O'Donnell WE, Allred LJ, Lopes CE (1985) Symptomatology in alcoholics at various stages of abstinence. Alcohol Clin Exp Res 9:505–512

Dean AJ, Bell J, Christie MJ, Mattick RP (2004) Depressive symptoms during buprenorphine vs. methadone maintenance: findings from a randomised, controlled trial in opioid dependence. Eur Psychiatry 19:510–513

Degenhardt L, Hall W, Lynskey M (2003) Testing hypotheses about the relationship between cannabis use and psychosis. Drug Alcohol Depend 71:37–48

Dittmann S, Grunze H, Kupka RW, Nolen WA, Bauer M, Schaerer LO, Walden J, Post RM, Frye MA (2009) Acamprosate in bipolar disorder: an open-label pilot study. Bipolar Disord 11 (Suppl 1):35

Dixon L (1999) Dual diagnosis of substance abuse in schizophrenia: prevalence and impact on outcomes. Schizophr Res 35(Suppl):S93–S100

Dorus W, Ostrow DG, Anton R, Cushman P, Collins JF, Schaefer M, Charles HL, Desai P, Hayashida M, Malkerneker U (1989) Lithium treatment of depressed and nondepressed alcoholics. JAMA 262:1646–1652

Drake RE, Xie H, McHugo GJ, Green AI (2000) The effects of clozapine on alcohol and drug use disorders among patients with schizophrenia. Schizophr Bull 26:441–449

Emrich HM, Vogt P, Herz A, Kissling W (1982) Antidepressant effects of buprenorphine. Lancet 2:709

Falk DE, Yi HY, Hilton ME (2008) Age of onset and temporal sequencing of lifetime DSM-IV alcohol use disorders relative to comorbid mood and anxiety disorders. Drug Alcohol Depend 94:234–245

Farren CK, Scimeca M, Wu R, Malley SO (2009) A double-blind, placebo-controlled study of sertraline with naltrexone for alcohol dependence. Drug Alcohol Depend 99:317–321

Fawcett J, Kravitz HM, McGuire M, Easton M, Ross J, Pisani V, Fogg LF, Clark D, Whitney M, Kravitz G, Javaid J, Teas G (2000) Pharmacological treatments for alcoholism: revisiting lithium and considering buspirone. Alcohol Clin Exp Res 24:666–674

Foa EB, Yusko DA, McLean CP, Suvak MK, Bux DA Jr, Oslin D, O'Brien CP, Imms P, Riggs DS, Volpicelli J (2013) Concurrent naltrexone and prolonged exposure therapy for patients with comorbid alcohol dependence and PTSD: a randomized clinical trial. JAMA 310:488–495

Frye MA, Salloum IM (2006) Bipolar disorder and comorbid alcoholism: prevalence rate and treatment considerations. Bipolar Disord 8:677–685

Frye MA, Altshuler LL, McElroy SL, Suppes T, Keck PE, Denicoff K, Nolen WA, Kupka R, Leverich GS, Pollio C, Grunze H, Walden J, Post RM (2003) Gender differences in prevalence, risk, and clinical correlates of alcoholism comorbidity in bipolar disorder. Am J Psychiatry 160:883–889

Gao K, Kemp DE, Wang Z, Ganocy SJ, Conroy C, Serrano MB, Sajatovic M, Findling RL, Calabrese JR (2010) Predictors of non-stabilization during the combination therapy of lithium and divalproex in rapid cycling bipolar disorder: a post-hoc analysis of two studies. Psychopharmacol Bull 43:23–38

Gaudiano BA, Uebelacker LA, Miller IW (2008) Impact of remitted substance use disorders on the future course of bipolar I disorder: findings from a clinical trial. Psychiatry Res 160:63–71

Geller B, Cooper TB, Sun K, Zimerman B, Frazier J, Williams M, Heath J (1998) Double-blind and placebo-controlled study of lithium for adolescent bipolar disorders with secondary substance dependency. J Am Acad Child Adolesc Psychiatry 37:171–178

George DT, Phillips MJ, Lifshitz M, Lionetti TA, Spero DE, Ghassemzedeh N, Doty L, Umhau JC, Rawlings RR (2011) Fluoxetine treatment of alcoholic perpetrators of domestic violence: a 12-week, double-blind, randomized, placebo-controlled intervention study. J Clin Psychiatry 72:60–65

George O, Sanders C, Freiling J, Grigoryan E, Vu S, Allen CD, Crawford E, Mandyam CD, Koob GF (2012) Recruitment of medial prefrontal cortex neurons during alcohol withdrawal predicts cognitive impairment and excessive alcohol drinking. Proc Natl Acad Sci U S A 109:18156–18161

Gerra G, Borella F, Zaimovic A, Moi G, Bussandri M, Bubici C, Bertacca S (2004) Buprenorphine versus methadone for opioid dependence: predictor variables for treatment outcome. Drug Alcohol Depend 75:37–45

Gerra G, Leonardi C, D'Amore A, Strepparola G, Fagetti R, Assi C, Zaimovic A, Lucchini A (2006) Buprenorphine treatment outcome in dually diagnosed heroin dependent patients: A retrospective study. Prog Neuropsychopharmacol Biol Psychiatry 30:265–272

Gold MS, Donabedian RK, Dillard M Jr, Slobetz FW, Riordan CE, Kleber HD (1977) antipsychotic effect of opiate agonists. Lancet 2:398–399

Goldsmith M, Singh M, Chang K (2011) Antidepressants and psychostimulants in pediatric populations: is there an association with mania? Paediatr Drugs 13:225–243

Grant BF, Hasin DS, Stinson FS, Dawson DA, June RW, Goldstein RB, Smith SM, Saha TD, Huang B (2005) Prevalence, correlates, co-morbidity, and comparative disability of DSM-IV generalized anxiety disorder in the USA: results from the National Epidemiologic Survey on Alcohol and Related Conditions. Psychol Med 35:1747–1759

Green AI, Burgess ES, Dawson R, Zimmet SV, Strous RD (2003) Alcohol and cannabis use in schizophrenia: effects of clozapine vs. risperidone. Schizophr Res 60:81–85

Green AI, Drake RE, Brunette MF, Noordsy DL (2007) Schizophrenia and co-occurring substance use disorder. Am J Psychiatry 164:402–408

Green AI, Noordsy DL, Brunette MF, O'Keefe C (2008) Substance abuse and schizophrenia: pharmacotherapeutic intervention. J Subst Abuse Treat 34:61–71

Grunze H, Vieta E, Goodwin GM, Bowden C, Licht RW, Moller HJ, Kasper S (2010) The World Federation of Societies of Biological Psychiatry (WFSBP) guidelines for the biological treatment of bipolar disorders: update 2010 on the treatment of acute bipolar depression. World J Biol Psychiatry 11:81–109

Hambrecht M, Haefner H (1996) Substance abuse and the onset of schizophrenia. Biol Psychiatry 40:1155–1163

Hartz SM, Pato CN, Medeiros H, Cavazos-Rehg P, Sobell JL, Knowles JA, Bierut LJ, Pato MT, Abbott C, Azevedo MH, Belliveau R, Bevilacqua E, Bromet EJ, Buckley PF, Dewan MJ, Escamilla MA, Fanous AH, Fochtmann LJ, Kinkead R, Kotov R, Lehrer DS, Macciardi F, Malaspina D, Marder SR, McCarroll SA, Moran J, Morley CP, Nicolini H, Perkins DO, Potkin

SG, Purcell SM, Rakofsky JJ, Rapaport MH, Scolnick EM, Sklar B, Sklar P, Smoller JW, Sullivan PF, Vivar A (2014) Comorbidity of severe psychotic disorders with measures of substance use. JAMA Psychiatry 10

Hertzman M, Patt IS, Spielman LA (2009) Open-label trial of acamprosate as a treatment for anxiety. Prim Care Companion J Clin Psychiatry 11:267

Hobbs JD, Kushner MG, Lee SS, Reardon SM, Maurer EW (2011) Meta-analysis of supplemental treatment for depressive and anxiety disorders in patients being treated for alcohol dependence. Am J Addict 20:319–329

Johnson BA, It-Daoud N, Bowden CL, DiClemente CC, Roache JD, Lawson K, Javors MA, Ma JZ (2003) Oral topiramate for treatment of alcohol dependence: a randomised controlled trial. Lancet 361:1677–1685

Kalyoncu A, Mirsal H, Pektas O, Unsalan N, Tan D, Beyazyurek M (2005) Use of lamotrigine to augment clozapine in patients with resistant schizophrenia and comorbid alcohol dependence: a potent anti-craving effect? J Psychopharmacol 19:301–305

Kelly DL, Gale EA, Conley RR (2003) Clozapine treatment in patients with prior substance abuse. Can J Psychiatry 48:111–114

Kemp DE, Gao K, Ganocy SJ, Elhaj O, Bilali SR, Conroy C, Findling RL, Calabrese JR (2009) A 6-month, double-blind, maintenance trial of lithium monotherapy versus the combination of lithium and divalproex for rapid-cycling bipolar disorder and co-occurring substance abuse or dependence. J Clin Psychiatry 70:113–121

Kerfoot KE, Rosenheck RA, Petrakis IL, Swartz MS, Keefe RS, McEvoy JP, Stroup TS (2011) Substance use and schizophrenia: adverse correlates in the CATIE study sample. Schizophr Res 132:177–182

Kern N, Sheldrick AJ, Schmidt FM, Minkwitz J (2012) Neurobiology of depression and novel antidepressant drug targets. Curr Pharm Des 18:5791–5801

Kessler RC, Crum RM, Warner LA, Nelson CB, Schulenberg J, Anthony JC (1997) Lifetime co-occurrence of DSM-III-R alcohol abuse and dependence with other psychiatric disorders in the National Comorbidity Survey. Arch Gen Psychiatry 54:313–321

Kessler RC, Berglund P, Demler O, Jin R, Merikangas KR, Walters EE (2005) Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. Arch Gen Psychiatry 62:593–602

Kilbourne AM, Morden NE, Austin K, Ilgen M, McCarthy JF, Dalack G, Blow FC (2009) Excess heart-disease-related mortality in a national study of patients with mental disorders: identifying modifiable risk factors. Gen Hosp Psychiatry 31:555–563

Kishi T, Sevy S, Chekuri R, Correll CU (2013) Antipsychotics for primary alcohol dependence: a systematic review and meta-analysis of placebo-controlled trials. J Clin Psychiatry 74:e642–e654

Koob GF (2008) A role for brain stress systems in addiction. Neuron 59:11–34

Kormos V, Gaszner B (2013) Role of neuropeptides in anxiety, stress, and depression: from animals to humans. Neuropeptides 47:401–419

Kranzler HR, Mueller T, Cornelius J, Pettinati HM, Moak D, Martin PR, Anthenelli R, Brower KJ, O'Malley S, Mason BJ, Hasin D, Keller M (2006) Sertraline treatment of co-occurring alcohol dependence and major depression. J Clin Psychopharmacol 26:13–20

Krystal JH, Staley J, Mason G, Petrakis IL, Kaufman J, Harris RA, Gelernter J, Lappalainen J (2006) Gamma-aminobutyric acid type A receptors and alcoholism: intoxication, dependence, vulnerability, and treatment. Arch Gen Psychiatry 63:957–968

Kushner MG, Mackenzie TB, Fiszdon J, Valentiner DP, Foa E, Anderson N, Wangensteen D (1996) The effects of alcohol consumption on laboratory-induced panic and state anxiety. Arch Gen Psychiatry 53:264–270

Kushner MG, Abrams K, Thuras P, Thuras P, Hanson KL (2000) Individual differences predictive of drinking to manage anxiety among non-problem drinkers with panic disorder. Alcohol Clin Exp Res 24:448–458

Lejoyeux M, Lehert P (2011) Alcohol-use disorders and depression: results from individual patient data meta-analysis of the acamprosate-controlled studies. Alcohol Alcohol 46:61–67
Lesscher HM, Vanderschuren LJ (2012) Compulsive drug use and its neural substrates. Rev Neurosci 23:731–745
Levander E, Frye MA, McElroy S, Suppes T, Grunze H, Nolen WA, Kupka R, Keck PE Jr, Leverich GS, Altshuler LL, Hwang S, Mintz J, Post RM (2007) Alcoholism and anxiety in bipolar illness: differential lifetime anxiety comorbidity in bipolar I women with and without alcoholism. J Affect Disord 101:211–217
Limosin F, Loze JY, Philippe A, Casadebaig F, Rouillon F (2007) Ten-year prospective follow-up study of the mortality by suicide in schizophrenic patients. Schizophr Res 94:23–28
Losekam S, Kluge I, Nittel KS, Kircher T, Konrad C (2013) Letter to the Editor: shopping frenzy induced by naltrexone–a paradoxical effect in bipolar disorder? Psychol Med 43:895
Magidson JF, Wang S, Lejuez CW, Iza M, Blanco C (2013) Prospective study of substance-induced and independent major depressive disorder among individuals with substance use disorders in a nationally representative sample. Depress Anxiety 30:538–545
Major LF, Lerner P, Ballenger JC, Brown GL, Goodwin FK, Lovenberg W (1979) Dopamine-beta-hydroxylase in the cerebrospinal fluid: relationship to disulfiram-induced psychosis. Biol Psychiatry 14:337–344
Malec TS, Malec EA, Dongier M (1996) Efficacy of buspirone in alcohol dependence: a review. Alcohol Clin Exp Res 20:853–858
Manwani SG, Szilagyi KA, Zablotsky B, Hennen J, Griffin ML, Weiss RD (2007) Adherence to pharmacotherapy in bipolar disorder patients with and without co-occurring substance use disorders. J Clin Psychiatry 68:1172–1176
Marmorstein NR, Iacono WG, Malone SM (2010) Longitudinal associations between depression and substance dependence from adolescence through early adulthood. Drug Alcohol Depend 107:154–160
Mathew SJ, Manji HK, Charney DS (2008) Novel drugs and therapeutic targets for severe mood disorders. Neuropsychopharmacology 33:2080–2092
McCance-Katz E (2012) Drug-drug interactions in opioid therapy—a focus on buprenorphine and methadone. PCM Healthcare, London
McCarley RW, Niznikiewicz MA, Salisbury DF, Nestor PG, O'Donnell BF, Hirayasu Y, Grunze H, Greene RW, Shenton ME (1999) Cognitive dysfunction in schizophrenia: unifying basic research and clinical aspects. Eur Arch Psychiatry Clin Neurosci 249(Suppl 4):69–82
Merikangas KR, Mehta RL, Molnar BE, Walters EE, Swendsen JD, Aguilar-Gaziola S, Bijl R, Borges G, Caraveo-Anduaga JJ, DeWit DJ, Kolody B, Vega WA, Wittchen HU, Kessler RC (1998) Comorbidity of substance use disorders with mood and anxiety disorders: results of the International Consortium in Psychiatric Epidemiology. Addict Behav 23:893–907
Merikangas KR, Zhang H, Avenevoli S, Acharyya S, Neuenschwander M, Angst J (2003) Longitudinal trajectories of depression and anxiety in a prospective community study: the Zurich Cohort Study. Arch Gen Psychiatry 60:993–1000
Merikangas KR, Akiskal HS, Angst J, Greenberg PE, Hirschfeld RM, Petukhova M, Kessler RC (2007) Lifetime and 12-month prevalence of bipolar spectrum disorder in the National Comorbidity Survey replication. Arch Gen Psychiatry 64:543–552
Micale V, Di Marzo V, Sulcova A, Wotjak CT, Drago F (2013) Endocannabinoid system and mood disorders: priming a target for new therapies. Pharmacol Ther 138:18–37
Mizrahi R, Rusjan P, Agid O, Graff A, Mamo DC, Zipursky RB, Kapur S (2007) Adverse subjective experience with antipsychotics and its relationship to striatal and extrastriatal D2 receptors: a PET study in schizophrenia. Am J Psychiatry 164:630–637
Moak DH, Anton RF, Latham PK, Voronin KE, Waid RL, Durazo-Arvizu R (2003) Sertraline and cognitive behavioral therapy for depressed alcoholics: results of a placebo-controlled trial. J Clin Psychopharmacol 23:553–562
Monk CS, Telzer EH, Mogg K, Bradley BP, Mai X, Louro HM, Chen G, Clure-Tone EB, Ernst M, Pine DS (2008) Amygdala and ventrolateral prefrontal cortex activation to masked angry faces

in children and adolescents with generalized anxiety disorder. Arch Gen Psychiatry 65:568–576
Monteleone P, Bifulco M, Maina G, Tortorella A, Gazzerro P, Proto MC, Di FC, Monteleone F, Canestrelli B, Buonerba G, Bogetto F, Maj M (2010) Investigation of CNR1 and FAAH endocannabinoid gene polymorphisms in bipolar disorder and major depression. Pharmacol Res 61:400–404
Mozayani A, Raymon L (2012) Handbook of drug interactions. A clinical and forensic guide. Springer, New York
Mueser KT, Drake RE, Wallach MA (1998) Dual diagnosis: a review of etiological theories. Addict Behav 23:717–734
Muhonen LH, Lahti J, Sinclair D, Lonnqvist J, Alho H (2008a) Treatment of alcohol dependence in patients with co-morbid major depressive disorder–predictors for the outcomes with memantine and escitalopram medication. Subst Abuse Treat Prev Policy 3:20
Muhonen LH, Lonnqvist J, Juva K, Alho H (2008b) Double-blind, randomized comparison of memantine and escitalopram for the treatment of major depressive disorder comorbid with alcohol dependence. J Clin Psychiatry 69:392–399
Muhonen LH, Lonnqvist J, Lahti J, Alho H (2009) Age at onset of first depressive episode as a predictor for escitalopram treatment of major depression comorbid with alcohol dependence. Psychiatry Res 167:115–122
Muhonen LH, Lahti J, Alho H, Lonnqvist J, Haukka J, Saarikoski ST (2011) Serotonin transporter polymorphism as a predictor for escitalopram treatment of major depressive disorder comorbid with alcohol dependence. Psychiatry Res 186:53–57
National Institute for Health and Clinical Excellence (NICE) (2007). Anxiety (amended): management of Anxiety (Panic Disorder, with and without Agoraphobia, and generalized Anxiety Disorder) in Adults in Primary, Secondary and community Care. http://www.nice.org.uk/nicemedia/pdf/cg022niceguidelineamended.pdf. 23-8-2013. Ref Type: Electronic Citation
Neumann ID, Landgraf R (2012) Balance of brain oxytocin and vasopressin: implications for anxiety, depression, and social behaviors. Trends Neurosci 35:649–659
Nitschke JB, Sarinopoulos I, Oathes DJ, Johnstone T, Whalen PJ, Davidson RJ, Kalin NH (2009) Anticipatory activation in the amygdala and anterior cingulate in generalized anxiety disorder and prediction of treatment response. Am J Psychiatry 166:302–310
Nolen WA, Luckenbaugh DA, Altshuler LL, Suppes T, McElroy SL, Frye MA, Kupka RW, Keck PE Jr, Leverich GS, Post RM (2004) Correlates of 1-year prospective outcome in bipolar disorder: results from the Stanley Foundation Bipolar Network. Am J Psychiatry 161:1447–1454
Nunes EV, Levin FR (2004) Treatment of depression in patients with alcohol or other drug dependence: a meta-analysis. JAMA 291:1887–1896
Nunes EV, McGrath PJ, Wager S, Quitkin FM (1990) Lithium treatment for cocaine abusers with bipolar spectrum disorders. Am J Psychiatry 147:655–657
Ostacher MJ, Perlis RH, Nierenberg AA, Calabrese J, Stange JP, Salloum I, Weiss RD, Sachs GS (2010) Impact of substance use disorders on recovery from episodes of depression in bipolar disorder patients: prospective data from the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD). Am J Psychiatry 167:289–297
Palucha-Poniewiera A, Pilc A (2012) Involvement of mGlu5 and NMDA receptors in the antidepressant-like effect of acamprosate in the tail suspension test. Prog Neuropsychopharmacol Biol Psychiatry 39:102–106
Pani PP, Vacca R, Trogu E, Amato L, Davoli M (2010) Pharmacological treatment for depression during opioid agonist treatment for opioid dependence. Cochrane Database Syst Rev CD008373
Pani PP, Trogu E, Vecchi S, Amato L (2011) Antidepressants for cocaine dependence and problematic cocaine use. Cochrane Database Syst Rev CD002950
Petrakis IL, Leslie D, Finney JW, Rosenheck R (2006) Atypical antipsychotic medication and substance use-related outcomes in the treatment of schizophrenia. Am J Addict 15:44–49

Pettinati HM, Oslin DW, Kampman KM, Dundon WD, Xie H, Gallis TL, Dackis CA, O'Brien CP (2010) A double-blind, placebo-controlled trial combining sertraline and naltrexone for treating co-occurring depression and alcohol dependence. Am J Psychiatry 167:668–675

Pirkola SP, Isometsa E, Suvisaari J, Aro H, Joukamaa M, Poikolainen K, Koskinen S, Aromaa A, Lonnqvist JK (2005) DSM-IV mood-, anxiety- and alcohol use disorders and their comorbidity in the Finnish general population–results from the Health 2000 Study. Soc Psychiatry Psychiatr Epidemiol 40:1–10

Ralevski E, O'Brien E, Jane JS, Dean E, Dwan R, Petrakis I (2011) Effects of acamprosate on cognition in a treatment study of patients with schizophrenia spectrum disorders and comorbid alcohol dependence. J Nerv Ment Dis 199:499–505

Randall CL, Johnson MR, Thevos AK, Sonne SC, Thomas SE, Willard SL, Brady KT, Davidson JR (2001) Paroxetine for social anxiety and alcohol use in dual-diagnosed patients. Depress Anxiety 14:255–262

Rapaport MH, Wolkowitz O, Kelsoe JR, Pato C, Konicki PE, Pickar D (1993) Beneficial effects of nalmefene augmentation in neuroleptic-stabilized schizophrenic patients. Neuropsychopharmacology 9:111–115

Regier DA, Farmer ME, Rae DS (1990) Comorbidity of mental disorders with alcohol and other drug abuse: results from the Epidemiologic Catchment Area (ECA) study. JAMA 264:2511–2518

Robinson J, Sareen J, Cox BJ, Bolton JM (2011) Role of self-medication in the development of comorbid anxiety and substance use disorders: a longitudinal investigation. Arch Gen Psychiatry 68:800–807

Roesner S, Hackl-Herrwerth A, Leucht S, Lehert P, Vecchi S, Soyka M (2010) Acamprosate for alcohol dependence. Cochrane Database Syst Rev CD004332

Ross J, Teesson M, Darke S, Lynskey M, Ali R, Ritter A, Cooke R (2005) The characteristics of heroin users entering treatment: findings from the Australian treatment outcome study (ATOS). Drug Alcohol Rev 24:411–418

Rounsaville BJ, Weissman MM, Crits-Christoph K, Wilber C, Kleber H (1982) Diagnosis and symptoms of depression in opiate addicts. Course and relationship to treatment outcome. Arch Gen Psychiatry 39:151–156

Rubio G, Martinez I, Ponce G, Jimenez-Arriero MA, Lopez-Munoz F, Alamo C (2006) Long-acting injectable risperidone compared with zuclopenthixol in the treatment of schizophrenia with substance abuse comorbidity. Can J Psychiatry 51:531–539

Salloum IM, Cornelius JR, Daley DC, Kirisci L, Himmelhoch JM, Thase ME (2005) Efficacy of valproate maintenance in patients with bipolar disorder and alcoholism: a double-blind placebo-controlled study. Arch Gen Psychiatry 62:37–45

Salloum IM, Douaihy A, Cornelius JR, Kirisci L, Kelly TM, Hayes J (2007) Divalproex utility in bipolar disorder with co-occurring cocaine dependence: a pilot study. Addict Behav 32:410–415

Savant JD, Barry DT, Cutter CJ, Joy MT, Dinh A, Schottenfeld RS, Fiellin DA (2013) Prevalence of mood and substance use disorders among patients seeking primary care office-based buprenorphine/naloxone treatment. Drug Alcohol Depend 127:243–247

Schäfer I, Fischer M, Reimer J, Karow A, Haasen C (2011) Significance of psychiatric comorbidity fort he outcome of maintenance treatment—a review of the literature. Ment Health Subst Use 4:62–71

Schellekens AF, Franke B, Ellenbroek B, Cools A, de Jong CA, Buitelaar JK, Verkes RJ (2012) Reduced dopamine receptor sensitivity as an intermediate phenotype in alcohol dependence and the role of the COMT Val158Met and DRD2 Taq1A genotypes. Arch Gen Psychiatry 69:339–348

Scheller-Gilkey G, Woolwine BJ, Cooper I, Gay O, Moynes KA, Miller AH (2003) Relationship of clinical symptoms and substance use in schizophrenia patients on conventional versus atypical antipsychotics. Am J Drug Alcohol Abuse 29:553–566

Schwartz TL, Siddiqui UA, Raza S, Costello A (2010) Acamprosate calcium as augmentation therapy for anxiety disorders. Ann Pharmacother 44:1930–1932

Schwarzer C (2009) 30 years of dynorphins–new insights on their functions in neuropsychiatric diseases. Pharmacol Ther 123:353–370

Sernyak MJ, Glazer WM, Heninger GR, Charney DS, Woods SW, Petrakis IL, Krystal JH, Price LH (1998) Naltrexone augmentation of neuroleptics in schizophrenia. J Clin Psychopharmacol 18:248–251

Sevy S, Robinson DG, Sunday S, Napolitano B, Miller R, McCormack J, Kane J (2011) Olanzapine vs. risperidone in patients with first-episode schizophrenia and a lifetime history of cannabis use disorders: 16-week clinical and substance use outcomes. Psychiatry Res 188:310–314

Smelson DA, Williams J, Ziedonis D, Sussner BD, Losonczy MF, Engelhart C, Kaune M (2004) A double-blind placebo-controlled pilot study of risperidone for decreasing cue-elicited craving in recently withdrawn cocaine dependent patients. J Subst Abuse Treat 27:45–49

Soyka M (2013a) Drug therapy: reviewing the evidence. In: Boyle P, Boffetta P, Lowenfels AB, Burns H, Brawley O, Zatonski W, Rehm J (eds) Alcohol—science, policy and public health. Oxford University Press, Oxford, pp 332–339

Soyka M (2013b) Treatment of anxiety in substance-using patients. In: Miller PM (ed) Intervention for addiction: comprehensive addictive behaviours and disorders. Elsevier Inc Academic Press, San Diego, pp 489–495

Soyka M, Albus M, Kathmann N, Finelli A, Hofstetter S, Holzbach R, Immler B, Sand P (1993) Prevalence of alcohol and drug abuse in schizophrenic inpatients. Eur Arch Psychiatry Clin Neurosci 242:362–372

Soyka M, Aichmuller C, Bardeleben U, Beneke M, Glaser T, Hornung-Knobel S, Wegner U (2003) Flupenthixol in relapse prevention in schizophrenics with comorbid alcoholism: results from an open clinical study. Eur Addict Res 9:65–72

Soyka M, Kranzler HR, van den BW, Krystal J, Moller HJ, Kasper S (2011) The World Federation of Societies of Biological Psychiatry (WFSBP) guidelines for the biological treatment of substance use and related disorders, Part 2: Opioid dependence. World J Biol Psychiatry 12:160–187

Stein MD, Solomon DA, Herman DS, Anthony JL, Ramsey SE, Anderson BJ, Miller IW (2004) Pharmacotherapy plus psychotherapy for treatment of depression in active injection drug users. Arch Gen Psychiatry 61:152–159

Stein MD, Solomon DA, Anderson BJ, Herman DS, Anthony JL, Brown RA, Ramsey SE, Miller IW (2005) Persistence of antidepressant treatment effects in a pharmacotherapy plus psychotherapy trial for active injection drug users. Am J Addict 14:346–357

Strain EC (2002) Assessment and treatment of comorbid psychiatric disorders in opioid-dependent patients. Clin J Pain 18:S14–S27

Stuyt EB, Sajbel TA, Allen MH (2006) Differing effects of antipsychotic medications on substance abuse treatment patients with co-occurring psychotic and substance abuse disorders. Am J Addict 15:166–173

Tek C, Srihari V, Tek E (2008) Successful acamprosate treatment of alcohol dependence in schizophrenia. Schizophr Res 106:373

Thoma P, Daum I (2013) Comorbid substance use disorder in schizophrenia: a selective overview of neurobiological and cognitive underpinnings. Psychiatry Clin Neurosci 67:367–383

Thomas SE, Randall CL, Carrigan MH (2003) Drinking to cope in socially anxious individuals: a controlled study. Alcohol Clin Exp Res 27:1937–1943

Tolliver BK, Desantis SM, Brown DG, Prisciandaro JJ, Brady KT (2012) A randomized, double-blind, placebo-controlled clinical trial of acamprosate in alcohol-dependent individuals with bipolar disorder: a preliminary report. Bipolar Disord 14:54–63

Torrens M, Fonseca F, Mateu G, Farre M (2005) Efficacy of antidepressants in substance use disorders with and without comorbid depression. A systematic review and meta-analysis. Drug Alcohol Depend 78:1–22

Torrens M, Gilchrist G, Domingo-Salvany A (2011) Psychiatric comorbidity in illicit drug users: substance-induced versus independent disorders. Drug Alcohol Depend 113:147–156

Trincavelli ML, Da PE, Daniele S, Martini C (2012) The GABAA-BZR complex as target for the development of anxiolytic drugs. Curr Top Med Chem 12:254–269

van Os J, Kapur S (2009) Schizophrenia. Lancet 374:635–645

Veen ND, Selten JP, van Der Tweel I, Feller WG, Hoek HW, Kahn RS (2004) Cannabis use and age at onset of schizophrenia. Am J Psychiatry 161:501–506

Wang Z, Gao K, Kemp DE, Chan PK, Serrano MB, Conroy C, Fang Y, Ganocy SJ, Findling RL, Calabrese JR (2010) Lamotrigine adjunctive therapy to lithium and divalproex in depressed patients with rapid cycling bipolar disorder and a recent substance use disorder: a 12-week, double-blind, placebo-controlled pilot study. Psychopharmacol Bull 43:5–21

Wee S, Koob GF (2010) The role of the dynorphin-kappa opioid system in the reinforcing effects of drugs of abuse. Psychopharmacology (Berl) 210:121–135

Welch KA, McIntosh AM, Job DE, Whalley HC, Moorhead TW, Hall J, Owens DG, Lawrie SM, Johnstone EC (2011a) The impact of substance use on brain structure in people at high risk of developing schizophrenia. Schizophr Bull 37:1066–1076

Welch KA, Stanfield AC, McIntosh AM, Whalley HC, Job DE, Moorhead TW, Owens DG, Lawrie SM, Johnstone EC (2011b) Impact of cannabis use on thalamic volume in people at familial high risk of schizophrenia. Br J Psychiatry 199:386–390

Willner P, Scheel-Kruger J, Belzung C (2013) The neurobiology of depression and antidepressant action. Neurosci Biobehav Rev 37:2331–2371

Wittchen HU, Boehringer G, Rehm JT, Soyka M, Träder A, Mark K, Trautmann S (2011) Der Verlauf und Ausgang von Substitutionspatienten unter den aktuellen Bedingungen der deutschen Substitutionsversorgen nach 6 Jahren. Suchtmed 13:232–246

Witte J, Bentley K, Evins AE, Clain AJ, Baer L, Pedrelli P, Fava M, Mischoulon D (2012) A randomized, controlled, pilot study of acamprosate added to escitalopram in adults with major depressive disorder and alcohol use disorder. J Clin Psychopharmacol 32:787–796

Wobrock T, Soyka M (2008) Pharmacotherapy of schizophrenia with comorbid substance use disorder–reviewing the evidence and clinical recommendations. Prog Neuropsychopharmacol Biol Psychiatry 32:1375–1385

Zarate CA Jr, Manji HK (2008) Bipolar disorder: candidate drug targets. Mt Sinai J Med 75:226–247

Ziedonis DM, Smelson D, Rosenthal RN, Batki SL, Green AI, Henry RJ, Montoya I, Parks J, Weiss RD (2005) Improving the care of individuals with schizophrenia and substance use disorders: consensus recommendations. J Psychiatr Pract 11:315–339

Zorrilla EP, Heilig M, de Wit H, Shaham Y (2013) Behavioral, biological, and chemical perspectives on targeting CRF(1) receptor antagonists to treat alcoholism. Drug Alcohol Depend 128:175–186

Zumarraga M, Davila R, Basterreche N, Arrue A, Goienetxea B, Zamalloa MI, Erkoreka L, Bustamante S, Inchausti L, Gonzalez-Torres MA, Guimon J (2010) Catechol O-methyltransferase and monoamine oxidase A genotypes, and plasma catecholamine metabolites in bipolar and schizophrenic patients. Neurochem Int 56:774–779

Comorbidity of Smoking with Psychiatric Disorders

20

Anil Batra

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Abstract

Indications for comorbidity of smoking with psychiatric disorders have been derived from numerous epidemiological studies. This suggests either an involvement of smoking in the development of psychiatric diseases or the importance of smoking as a habit and the neurobiological effects of nicotine in the context of coping strategies for the psychiatric disorders. Neurobiological and genetic research focuses on the cerebral transmitter function including the serotonergic, dopaminergic, and noradrenergic system and cholinergic transmission. Moreover, effects of smoking on medication might motivate medicated psychiatric patients to practice smoking as a form of self-medication.

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This chapter will also discuss the need for an intense psychotherapy and when necessary pharmacotherapeutic support in smokers with a psychiatric comorbidity.

20.1 Introduction

The significance of nicotine or tobacco consumption in correlation with mental disorders is obvious but still not completely clarified up to now.

Numerous epidemiological studies confirm consistently increased smoking prevalence rates among patients with mental disorders. This is most outspoken in the context of other substance use disorders, e.g., alcohol or drug dependence, but also in patients suffering from schizophrenia and depressive disorders (overview in Batra 2000; Rüther et al. 2014). Inversely, smokers and especially heavy smokers show increased rates of psychopathological disorders and psychological disturbances (Lasser et al. 2000). Within clinical populations, comorbidity prevalences are even higher than within general population samples. Patients with substance use disorders (SUDs) in a therapeutic setting show up to four times higher rates of tobacco smoking than age-matched controls in the general population (Cole et al. 2012). Overall, this high prevalence of smoking in patients with psychiatric disorders is associated with a substantial increase of risks for morbidity and premature death (Bobes et al. 2010; Colton and Manderscheid 2006).

Presumed causes for this high comorbidity may be found in a common biological disposition by a concordant influence of the endogenous self-rewarding system, increased affective irritation, avolition, or a need for dopaminergic stimulation, which is related to pathological neurobiological patterns in subjects with psychiatric disorders. In this line of thinking, a (common) genetic background might also account for both the psychiatric diseases and the intensive smoking behavior as well (Batra 2005; Bauer et al. 2007). The high comorbidity between smoking behavior and numerous mental disorders can be, at least partly, explained by the quasi-therapeutic chemical function of both nicotine as a single substance and many other chemicals released in the process of tobacco smoking. The discussion on possible positive effects on the mental abnormalities or symptoms (e.g., enhance cognition and mood) via a therapeutic nicotine supply (e.g., via a transdermal application, administration of nicotine gums or nicotine tablets), however, is still not concluded.

Within the general population, due to prevention campaigns and most importantly more severe regulations the prevalence of smoking has decreased substantially. This effect has not been found within individuals suffering from psychiatric disorders. Indeed, tobacco consumption decrease turns out to be significantly lower in patients with mental disorders compared to the general population during the last couple of years. It is assumed (Lê Cook et al. 2014) that the corresponding prevention policy does not reach this target group sufficiently. Smoking initiation

invariably occurs within the period of adolescence. Many youngsters experiment, but many of them stop smoking after a short time. This seems to be much harder for adolescents with mental disorders and/or alcohol and drug dependence, who are especially vulnerable for continued tobacco consumption.

Overall, therapeutic approaches ("smoking cessation therapy") aiming at achieving abstinence or reduction of smoking have shown only very moderate to low effect sizes when treating nicotine-dependent patients. . Importantly, results of smoking cessation programs seem to have even less effect in patients with psychiatric comorbidities. One of the reasons might be that the occurrence of withdrawal symptoms, intensifying many psychiatric symptoms, makes a tobacco detoxification especially difficult among people with mental disabilities or mental disorders (Smith et al. 2014).

Thus, taken together, given the high prevalence, the outspoken negative consequences, and the low effect sizes of the current treatments, it seems reasonable to adapt treatment strategies to special needs of individual mental clinical pictures and the persons involved (Batra et al. 2010; Thornton et al. 2012).

20.2 Nicotine Has Short-Term and Long-Term Influences on Mental States

Nicotine stimulates numerous biological systems in the brain and one of its effects is an increase of the dopamine concentration. Subjectively this is associated with a feeling of well-being or pleasure. Additionally via noradrenaline, smoking stimulates and improves the vigilance, and also reduces the sensation of hunger. The stimulation of acetylcholine receptors by nicotine leads to an enhancement of cognitive functions. The cognitive enhancing effect of smoking is also attributed to nicotine's effect on vasopressin. The direct stimulation of the serotonergic system is correlated with a positive impact on anxiety, depressive effects, or the sensation of hunger. Finally, also the beta-endorphin system is supposed to be responsible for a reduction of anxiety or tension and is stimulated by nicotine. Relaxation, overcoming boredom, and increased activity but also social-communicative effects of collective smoking, the legitimation of a break, die influence of moods, stimulation and cognitive functions can offer certain advantages of nicotine consumption for patients with mental disorders and thus encourage smoking. The reduction of stress feelings influencing these different mental qualities is connected with the subjective mental state.

The withdrawal symptoms of nicotine are often very similar to some distressing symptoms associated with mental disorders. A lack in nicotine leads to dysphoria, anxiety, depressive moods, diminished experiencing of pleasure and delight, irritability, sleeping disorders, changes in drive, or attentional problems (Hughes et al. 2006; Jähne et al. 2012). By confusing nicotine withdrawal symptoms with mental symptoms associated with mental disorders, due to the similarity of these symptoms, people with mental illnesses are reluctant, much more than any other smoker, to reduce unpleasant sensations by nicotine consumption.

Therefore depressive and anxious individuals but also people with emotional instability resulting in a lower frustration tolerance and increased stress intolerance are especially at risk of continuing tobacco use. Also for individuals withdrawing from other substances, the overlapping symptomatology with nicotine withdrawal symptoms also stimulates a continuation or often an intensification of smoking behavior. Following we will give a differentiated explanation for the comorbidity connected with smoking for each clinical picture.

Regardless of the positive effects for many people with mental problems via the intake of nicotine, i.e., smoking, it has to be taken into account that the intensity of smoking as performed by patients with mental disorders is correlated with an enormous health risk. The excess mortality among schizophrenic patients is estimated by nearly 20 years. This is due to the interaction of tobacco and many other concomitants, e.g., inactivity, medications, and many others. Therefore each smoker, with or without other mental illnesses, should be advised to quit tobacco consumption and offered appropriate treatment interventions (Taylor et al. 2014). Indeed, reducing or abstaining from smoking does not have only major health benefits, but can also positively impact psychological functioning. Tobacco detoxification is associated with reduced depressiveness, anxiety, stress, and improved positive moods all associated with improvement of life quality compared to constant smoking. This holds true for persons both with and without mental disorders. The effect sizes are even larger than the traditional pharmaceutical treatment of anxiety disorders or depressive disorders. This important finding has recently been documented by Taylor and colleagues (2014) on the basis of 26 studies assessed within the scope of a meta-analysis.

Following a short overview on the most important findings on relation of smoking with different psychiatric disorders, specifically those highly associated with smoking, will be given.

20.3 Affective Disorders

Depressive disorders of all types and smoking behavior are closely linked together. The increases in these comorbidities' prevalence go both ways. Within samples of smoking individuals, the probability to suffer from depressive disorders is increased about factor 2 compared to the nonsmoking population (Boden et al. 2010, Rüther et al. 2014). Inversely, numerous epidemiological studies document a high prevalence of smokers among depressive patients (Batra 2000). Female adolescents with depressive disorders or anxiety disorders smoke double as much as healthy individuals (Romans et al. 1993). Additionally, daily number of cigarettes is increased specifically during acute depressive disorders (Breslau et al. 1993).

The causal pathways explaining this comorbidity are complex. Some prospective studies on this subject did not lead to any clarification on the causation even though there are some indications that adolescents, who start nicotine consumption before 20 years, will have a higher risk of developing anxiety disorders or depressive disorders later on in life (Ajdacic-Gross et al. 2009). However, this could also

be an effect of a selection of children and adolescents with increased anxiety symptoms, a higher disposition for risky behavior, or other psychological disturbances, which initially in an unspecific way find expression through substance consumption, but which might also have occurred without nicotine consumption.

Despite numerous studies on the comorbidity between affective disorders and addictive smokers the causes could not be definitely clarified. Many hypotheses are suggested. Some authors assume that smoking supports the development of anxiety disorders and depression via intrinsic aversively perceived psychological stimuli. Bonevski and colleagues (2014) also emphasize the correlation between the socio-economic status, depression, and smoking behavior. Finally, in a study on 227 traumatized smokers with posttraumatic stress disorders and addictive disorders, Hruska and colleagues (2014) could show that the patient's expectations concerning smoking effects reflect a modulation of the negative affect. This group of patients displays higher expectations on beneficial effects of smoking, which should be taken into account concerning efforts for smoking cessations.

Additionally it is assumed that the reduced capability of many depressive patients to achieve smoking cessation could be responsible for the increased smoker prevalence. The expectation of reaching abstinence among depressive smokers only amounts to about 50 % than that of psychologically healthy smokers (Stage et al. 1996; Batra et al. 2008). A common genetic basis associated with underlying abnormalities in the serotonergic transmission has also been suggested as a likely hypothesis explaining the smoking–depression association (Brody et al. 2005; Tsuang et al. 2012).

Clinical observations indicate that nicotine has positive effects on the mental state of depressive patients. Some earlier investigations already suggested a lower concentration and activity of the monoamine oxidase in the thrombocytes of smokers, which can lead to a reduced depletion of monoaminergic neurotransmitters and thus to increased availability of the neurotransmitter serotonin. The neurochemical effect of nicotine to modulate the serotonergic system and its associated anti-depressive effects led to the conclusion that smoking could serve as a form of self-medication. This hypothesis is supported by an inhibition of the monoamine oxidase in smokers. The central inhibition of the monoamine oxidase (MAO)-B, around 40 % in smokers compared to nonsmokers or ex-smokers, initially reported by Fowler and colleagues (1996) can, however, not be assumed as a pure nicotine-mediated effect but rather be attributed to other tobacco smoke ingredients. This effect cannot be elicited by one-time smoking, so that it must be assumed that an anti-depressive effect mediated by the inhibition of the monoaminase oxidase only occurs following chronic cigarette consumption (Fowler et al. 1999).

The MAO-B concentration in thrombocytes correlates with thiocyanate, an ingredient of tobacco smoke and cotinine (Berlin et al. 2000). In both cases the intensity of tobacco consumption, i.e., inhalation of the different tobacco ingredients is reproduced. The number of daily consumed cigarettes probably does, however, not correlate with the reduction of the peripheral MAO-B activity, which is probably associated with inter-individually different inhalation habits (Berlin et al. 2000).

Studies on genetics of smokers and depression still are highly interesting, even if clear evidence for an important impact of single genes is lacking (Tsuang et al. 2012). The question if smoking is specifically correlated with a genetic predisposition for mental disorders could not be clearly evidenced up to now. Various publications deal with this subject (Chen et al. 2012) but could not show a clear connection for individual subforms of candidate genes with mental disorders in interaction with tobacco consumption.

The therapeutic approach using antidepressants in smoking cessation did, however, not lead to any significant results. Tricyclic antidepressants (doxepine or nortriptyline), monoamine oxidase inhibitors (moclobemide), serotonin reuptake inhibitors (various SSRIs, e.g., fluoxetine), as well as the atypical anxiolytic buspirone were applied without any success, i.e., without any indications for a significant superiority over to the established compounds in smoking cessation studies (e.g., nicotine patches, varinecline). Only bupropion, a selective low noradrenaline and dopamine reuptake inhibitor, was approved for smoking cessation due to convincing study results (Jorenby et al. 1999). In later studies, however, the superiority of the new substance does not emerge as clearly as suggested earlier. It has to be assumed that the positive effect was probably initially also caused by expectancy effects. Only future studies will be able to show if a smoking cessation treatment with bupropion will really be more successful than a treatment with nortriptyline or other antidepressants and if the therapy will especially be more successful than the administration of nicotine-substitute compounds). A recent Cochrane review favors individualized behavioral support for depressed patients (van der Meer et al. 2013).

20.4 Schizophrenia and Psychotic Disorders

More recent studies confirm the very high prevalence of tobacco consumption in patients with schizophrenic psychoses. In an Australian investigation, Cooper and colleagues (2012) found that 66.6 % of schizophrenic patients were smoking, and 81 % had already smoked in the course of their lives. The probability for tobacco consumption is especially high in cases, where the disorder started early and patients had a low education level. Male patients smoke more frequently than female. Especially with negative symptoms smoking seems to be of major importance. Sankaranarayanan and colleagues (2014) found data on increased smoking and suicidality in patients with a psychotic disorder indicating the relevance of smoking as an important risk factor for suicidal behaviors.

On the other hand schizophrenic patients seem to benefit from nicotine in many ways. Besides the hepatic enzyme induction mediated by different tobacco ingredients followed by an accelerated decrease of different neuroleptics some positive effects can be attributed to nicotine effects (Wing et al 2012).

Of importance, cognitive impairments, resulting from the administration of neuroleptics, could be improved by nicotine (Levin et al. 1996). Furthermore, an increase in energy with a prevailing negative symptomatology is described, which

might be correlated with dopaminergic stimulation mainly in the prefrontal cortex (McEvoy et al. 1995). Another hypothesis suggests a nicotine-mediated inhibition of an affective psychotic over-excitement. Finally the dopaminergic effect of nicotine against the neuroleptics-induced Parkinsonism increases the disposition to uptake high doses of nicotine.

Furthermore, schizophrenic patients show a neuropsychological deficit described as "filter impairment," i.e., a lacking the ability to separate relevant from irrelevant information. Patients with schizophrenic disorders do not habituate to this stimulation after a temporarily repeated presentation of a stimulus. Nicotine has the "therapeutic feature" to intensify the adaptation performance to acoustic stimuli in the animal model and in smoking and nonsmoking individuals (Kumari et al. 1997). This result can be explained by the "latent inhibition": "Latent inhibition defines the physiological blinding out of irrelevant stimuli by a delayed adaptation of the neuronal information-processing system. An impaired "latent inhibition" in the animal model can be regulated by low doses of nicotine (1.5 mg/kg). This result can also be replicated in the human model (Thornton et al. 1996).

Interestingly, schizophrenic patients as well as some of their relatives also show an impairment of a "latent inhibition," which can be regulated temporarily by nicotine intake, e.g., nicotine gums (Stevens et al. 1995). The impairment of a "latent inhibition" correlates with a polymorphism in the gene of the alpha7-acetylcholine receptor protein, so that a connection with the cholinergic receptor system might be possible. Although a correlation with schizophrenia can be observed, this result is rather related to the vulnerability for a psychotic experience than with the intensity of the psychopathology. It can also be found in healthy individuals, showing a predisposition for psychotic reactions. The impairment of a "latent inhibition" is not specific for schizophrenia or psychotic experiences but can also be determined in manic patients and healthy individuals under stress.

To what extent this will have an impact on smokers remains controversial. While Allan and colleagues (1995) found a less distinct "latent inhibition" in smokers than in nonsmokers, other authors could not replicate these findings (Thornton et al. 1996). Despite the fact that our own investigation could confirm that schizophrenic patients experience a regulation of their delayed adaptation performance to irrelevant stimuli after supply of nicotine, differences between strong smokers and nonsmoking control probands could not be demonstrated. In a classically experimental investigation we presented klick noises 30 dB and 50 dB to probands via headphones above the hearing threshold level. Within 50 ms the EEG records a positive wave (p50) above the lead location CZ. After repeated presentation the amplitude of the p50 was reduced in nonsmokers as well as in strong smokers but not in schizophrenic patients. Only after nicotine supply via cigarettes schizophrenic patients showed a significantly improved and regulated habituation performance. These findings might be correlated with some more genetic associations of schizophrenic symptoms and the intensity of smoking (deLeon and Diaz 2012).

Therapeutic interventions should be offered after stabilization of the patient; medical supply, first of all nicotine replacement, is recommended (Tsoi et al. 2013).

20.5 Alcohol or Drug Dependence

Many hypotheses explaining the high coincidence of alcohol, drug, and tobacco consumption exist, e.g., favoring environmental conditions, milieu, or leisure behavior, during which both substances are normally consumed and the associated availability of both substances is supposed to be responsible. Additionally, addictive effects in connection with an increased positive reinforcing process by a simultaneous effect on the dopaminergic system or a general, partly genetically determined vulnerability for risky behavior, which among others is correlated with increased consumption of addictive substances, are assumed to be a possible cause.

Furthermore, it is reported that a coincident consumption of tobacco, nicotine, and alcohol might partly compensate alcohol-related impairments of cognitive performances. Especially alcohol-related impairments of the perception and reaction ability are supposed to decrease by coincident nicotine stimulation (Batra and Buchkremer 2001). Gould and colleagues (2001), for instance, investigated the effect of a combined administration of alcohol and nicotine in the animal model and confirmed a positive effect of nicotine on alcohol-associated disorders of the "latent inhibition" in alcohol-dependent smokers. The concurrent intake of nicotine and alcohol reversed the alcohol-associated suppression of the inhibition. Presumably a stimulation of neuronal nicotinergic acetylcholine receptors with the consecutive activation of further transmitter systems might be crucial.

Nevertheless alcoholic patients are interested in tobacco abstinence as well and are rather successful in smoking cessation (Batra et al. 2011).

20.6 Neurodegenerative and Other Disorders

For the association of nicotine and the Parkinson's disease and a dementia of the Alzheimer's type contradictive results exist. Nonsmokers carry double the risk for both diseases according to former investigations. Therefore it was assumed previously that smoking would have a direct protective effect on the development of the Alzheimer's disease. Although findings in the literature earlier suggested that smokers would be protected against the development of a Parkinson's disease, more recent studies claim that the observed relative risk of about 0.4 could only be explained by the excess mortality of smokers (Morens et al. 1995). Acetylcholine receptors are located on dopaminergic cells in the substantia nigra pars compacta. Since about one-third of all striatal nicotine receptors are connected with dopaminergic structures, a stimulation of the presynaptic nicotinergic acetylcholine receptors on the dopaminergic neurons also leads to increased central dopamine release. Therefore it might be presumed that this connection of nicotinergic acetylcholine receptors and dopaminergic tracts is the basis for mild improvements in the results, experienced by Parkinson's patients after experimental nicotine intake.

It is also discussed that patients with a disposition for a Parkinson's disease are less responsive for reinforcing nicotine effects. This would mean that the

predisposition for developing the Parkinson's disease would have protective effects concerning the development of nicotine dependence. The lower incidence of the Parkinson's disease among smokers could, however, also be explained by an inhibition of the monoamino oxidase B observed in smokers and with an associated increase of dopamine (Berlin et al. 1997). Prasad and colleagues (1994) finally reported on a retardation of the natural age-related reduction of nigrostriatal dopamine-D1 and D2 receptors. Yet it is unclear whether this possible neuroprotective influence of nicotine is correlated with the lower probability for the Parkinson's disease.

The discussion on the possible protective effects of nicotine against the Alzheimer's disease still continues. Twin studies suggested a reduced risk for the development of the Alzheimer's dementia in smokers (Plassman et al. 1995). A possible explanation could be seen in the nicotine-mediated neuroadaptation in terms of an amplification of nicotinergic acetylcholine receptors. An induction of the synthesis of the Nerve Growth Factor (NGF) and the NGF receptors and an increase of the cerebral blood flow, which could be effective neuroprotectively, are also being discussed. Regardless of this hypothesis some indications of a slight improvement of cognitive functions in patients with Alzheimer's disease after intake of nicotine exist.

More recent prospective studies, however, lead to doubts about the statement that smokers dispose of a lesser risk for developing a dementia of the Alzheimer's disease type. Instead more recent publications discuss the exact opposite. Some earlier studies lead to the assumption that smokers provide a higher risk for the development of dementia disease, especially of the Alzheimer's type (Almeida et al. 2000). These new results challenge the existing investigations based on other methodological approaches (retrospective case–control studies or randomized group comparisons). A final conclusion, however, cannot be made, yet the existing approach postulating a protective effect of nicotine intake for the development of neurodegenerative diseases should be relativized carefully.

In cases of the Gilles de la Tourette syndrome nicotine also showed some therapeutic effects. After intake of transdermal nicotine the frequency of motoric and linguistic tics lessened. This effect still continues after discontinuation of the therapeutically administered nicotine or nicotine chewing gum for a certain time.

Concerning ADHD high smoking prevalences are found in both adolescents and adult ADHD populations (Matthies et al. 2013). An association with a dopaminergic neurotransmission and smoking could be shown. In this case, the immediate effect on the dopaminergic disorder could probably be the correlation to intensive tobacco consumption.

20.7 Smoking and Psychopharmacological Medications

Many patients with psychiatric and addictive disorders receive some form of pharmacotherapy during their treatment. Their smoking status can have a significant effect on their medication. Ingredients of tobacco smoke induce metabolism of

many psychopharmaceutical drugs. The turnover of antidepressants (e.g., tricyclic antidepressants like amitriptyline, clomipramine, serotonin reuptake inhibitors (SSRIs) like fluvoxamine or sertraline, and serotonin-norepinephrine reuptake inhibitors (SNRIs) like duloxetine) and antipsychotics (e.g., butyrophenones, phenothiazines, and—most important—clozapine, olanzapine, and quetiapine) is influenced and in most cases enhanced by induced activation of the cytochrome P450 isoforms. As a result, blood levels of these medications are decreased as a consequence of smoking. So, smokers receive higher daily dosages to obtain the same therapeutic effect as nonsmokers get with lower dosing (e.g., more than 50 % higher clozapine doses) (Cormac et al. 2010). However, these higher dosings result in increased rates of many adverse effects (e.g., tardive dyskinesia) including the risk of toxic serum levels after quitting smoking. Therefore, a ttherapeutic drug monitoring and adjustment of psychopharmacological treatment dosages is mandatory as soon as smoking is significantly reduced or terminated (Lowe and Ackman 2010).

20.8 Practical Recommendations for Interventions in Tobacco Dependence in Mentally Ill

It is of utmost importance that every patient with psychiatric disorders, as part of the therapeutic standard workout, should be screened on and offered the possibility of treatment for smoking cessation. Treatment of tobacco dependence in mentally ill smokers should follow the general recommendations as described in the available guidelines for non-mentally ill smokers. These are summarized and modified for treatment of psychiatric patients in the "European Psychiatric Association (EPA)

Table 20.1 EPA guidance on tobacco dependence and strategies for smoking cessation in people with mental illness (Rüther et al. 2014): Main suggestions

1. Smoking status should be evaluated and documented for every psychiatric patient and the degree of dependence should be documented (preferentially with the Fagerstrom Test for Nicotine Dependence, FTND)
2. As soon as the patient with any psychiatric disorder, excepting a substance-related disorder, is in a stable phase, i.e., with no recent or planned changes in medications and no urgent problems, consequences of tobacco dependence are to be explained and the patient should be actively motivated to quit smoking. Substance-dependent inpatients should be motivated as an integral part of their withdrawal treatment
3. A minimum amount of counseling on smoking cessation should be performed
4. Taking into account the possible side effects and contraindications in the therapeutic decision-making, suggestions to use nicotine replacement therapy, varenicline, or bupropion should be part of the interventions offered
5. In order to minimize relapse rates a contact within the first days after a quit day should be offered for motivational support and supervision of medical treatment
6. Follow-up visits should be arranged in order to increase long-term abstinence rates

Besides relapse prevention (follow-up visits, medication, behavioral techniques) the patients should always be motivated for another quit attempt in case of a relapse

recommendations" (Rüther et al. 2014). Main suggestions of this European Guidance paper are summarized in Table 20.1.

20.9 Summary

A variety of psychiatric and neuropsychiatric disorders are associated with an increased smoking prevalence. The interaction between psychiatric disorders and smoking behavior remains complex and largely unknown. However, one of the key factors is the neurochemical properties of nicotine and in second order the many chemicals released during tobacco smoking. In addition to its highly addictive properties, nicotine can have protective effects in cases of neurological or psychiatric clinical pictures (neurodegenerative disorders), a quasi-therapeutic effect (schizophrenia and affective disorders), or a reinforcing function as desired by patients (other substance disorders). The underlying neurochemical bases of the desired and positive effects are the direct cholinergic or secondary dopaminergic, serotonergic, and noradrenergic effects of nicotine intake.

The causal coherences are of great interest for the understanding of the etiopathogenesis of neuropsychiatric clinical pictures. Also regarding possible therapeutic implications for neurodegenerative diseases and the development of new approaches in the treatment of addictions the research in this field is of major importance.

The presumed positive effects of nicotine are however largely overshadowed by the enormous negative impact of smoking (associated with the inhalation of more than 4,000 chemicals) on the health, morbidity, and mortality of patients with psychiatric disorders. These negative effects and the high prevalences of smoking should motivate the implementation of smoking cessation programs in every mental health care facility.

Finally it has to be taken into account that the obvious significance of the factor "smoking" for the mental state and the cognitive performance as well as the effect of medications has been underestimated in the past. Many investigations on psychiatric and neurological clinical pictures neglect the effects of smoking unreasonably and thus do not describe disorder-specific effects of certain psychotropic drugs but rather show pseudo-correlations caused by smoking or nicotine intake!

References

Ajdacic-Gross V, Landolt K, Angst J, Gamma A, Merikangas KR, Gutzwiller F, Rössler W (2009) Adult versus adolescent onset of smoking: how are mood disorders and other risk factors involved? Addiction 104:1411–1419

Allan LM, Williams JH, Wellman NA, Tonin J, Taylor E, Rawlins JNP (1995) Effects of tobacco smoking, schizotypy and number of pre-exposures on latent inhibition in healthy subjects. Pers Individual Dif 19:893–902

Almeida LEF, Pereira EFR, Alkondon M, Fawcett WP, Randall WR, Albuquerque EX (2000) The opioid antagonist naltrexone inhibits activity and alters expression of alpha7 and alpha4-beta2

nicotinic receptors in hippocampal neurons: implications for smoking cessation programs. Neuropharmacology 39:2740–2755
Batra A (2000) Tobacco use and smoking cessation in the psychiatric patient. Fortschr Neurol Psychiatr 68:80–92
Batra A (2005) Genetics of nicotine and tobacco dependency. J Men Health Gender 2(1):100–105
Batra A, Buchkremer G (2001) Beziehungen von Alkoholismus, Drogen- und Tabakkonsum. Dt Ärztebl 98:A2590–2593
Batra A, Collins SE, Torchalla I, Schröter M, Buchkremer G (2008) Multidimensional smoker profiles and their prediction of smoking following a pharmacobehavioral intervention. J Subst Abuse Treat 35:41–52
Batra A, Collins SE, Schröter M, Eck S, Torchalla I, Buchkremer G (2010) A cluster-randomised trial of smoking cessation tailored to multidimensional smoker profiles. JSAT 38:128–140
Batra A, Niethammer S, Mänz C, Peukert P (2011) Tabakentwöhnung bei stationären Patienten mit einer Alkoholabhängigkeit—Motivationsfaktoren und Erfolgs–aussichten. SUCHT 57 (5):337–346
Bauer P, Collins S, Batra A (2007) Genotypes in smokers: correlations with smoking behavior. Biochemica 2007(3):10–12
Berlin I, Spreux-Varoquaux O, Said S, Launay JM (1997) Effects of past history of major depression on smoking characteristics, monoamine oxidase-A and -B activities and withdrawal symptoms in dependent smokers. Drug Alc Depend 45:31–37
Berlin I, Spreux-Varoquaux O, Launay JM (2000) Platelet monoamine oxidase VB activity is inversely associated with plasma cotinine concentration. Nicotine Tob Res 2:243–246
Bobes J, Arango C, Garcia-Garcia M, Rejas J (2010) Healthy lifestyle habits and 10-year cardiovascular risk in schizophrenia spectrum disorders: an analysis of the impact of smoking tobacco in the CLAMORS schizophrenia cohort. Schizophr Res 119:101–109
Boden JM, Fergusson DM, Horwood LJ (2010) Cigarette smoking and depression: tests of causal linkages using a longitudinal birth cohort. Br J Psychiatry 196:440–446
Bonevski B, Regan T, Paul C, Baker AL, Bisquera A (2014) Associations between alcohol, smoking, socioeconomic status and comorbidities: evidence from the 45 and Up Study. Drug Alcohol Rev 33(2):169–76. doi:10.1111/dar.12104
Breslau N, Kilbey MM, Andreski P (1993) Nicotine dependence and major depression. New evidence from a prospective investigation. Arch Gen Psychiatry 50:31–35
Brody CL, Hamer DH, Haaga DA (2005) Depression vulnerability, cigarette smoking, and the serotonin transporter gene. Addict Behav 30:557–566
Chen LS, Xian H, Grucza RA, Saccone NL, Wang JC, Johnson EO, Breslau N, Hatuskami D, Bierut LJ (2012) Nicotine dependence and comorbid psychiatric disorders: examination of specific genetic variants in the CHRNA5-A3-B4 nicotinic receptor genes. Drug Alcohol Depend 123(Suppl 1):S42–51
Cole J, Stevenson E, Walker R, Logan TK (2012) Tobacco use and psychiatric comorbidity among adolescents in substance abuse treatment. J Subst Abuse Treat 43(1):20–9
Colton CW, Manderscheid RW (2006) Congruencies in increased mortality rates, years of potential life lost, and causes of death among public mental health clients in eight states. Prev Chronic Dis 3:A42
Cooper J, Mancuso SG, Borland R, Slade T, Galletly C, Castle D (2012) Tobacco smoking among people living with a psychotic illness: the second Australian Survey of Psychosis. Aust N Z J Psychiatry 46(9):851–63
Cormac I, Brown A, Creasey S, Ferriter M, Huckstep B (2010) A retrospective evaluation of the impact of total smoking cessation on psychiatric inpatients taking clozapine. Acta Psychiatr Scand 121:393–7
deLeon J, Diaz FJ (2012) Genetics of schizophrenia and smoking: an approach to studying their comorbidity based on epidemiological findings. Hum Genet 131(6):877–901

Fowler JS, Volkow ND, Wang GJ, Pappas N, Logan J, MacGregor RR, Alexoff D, Shea C, Wolf AP, Warner D, Zezulkova I, Cilento R (1996) Inhibition of monoamine oxidase in the brains of smokers. Nature 379:733–736

Fowler JS, Wang GJ, Volkow ND, Franceschi D, Logan J, Pappas N, Shea C, MacGregor RR, Garza V (1999) Smoking a single cigarette does not produce a measurable reduction in brain MAO B in non smokers. Nicotine Tob Res 1:325–329

Gould TJ, Collins AC, Wehner JM (2001) Nicotine enhances latent inhibition and ameliorates ethanol-induced deficits in latent inhibition. Nicotine Tob Res 3:17–24

Hruska B, Bernier J, Kenner F, Kenne DR, Boros AP, Richardson CJ, Delahanty DL (2014) Examining the relationships between posttraumatic stress disorder symptoms, positive smoking outcome expectancies, and cigarette smoking in people with substance use disorders: a multiple mediator model. Addict Behav 39(1):273–281

Hughes JR, Helzer JE, Lindberg S (2006) Prevalence of DSM/ICDdefi ned nicotine dependence. Drug Alcohol Depend 85:91–102

Jähne A, Unbehaun T, Feige B, Lutz U, Batra A, Riemann D (2012) How smoking affects sleep—implications for cessation strategies. Sleep Med 13:1286–1292

Jorenby DE, Leischow SJ, Nides MA, Rennard SI, Johnston JA, Hughes AR, Smith SS, Muramoto ML, Daughton DM, Doan K, Fiore MC, Baker TB (1999) A controlled trial of sustained-release bupropion, a nicotine patch, or both for smoking cessation. N Engl J Med 340:685–689

Kumari V, Toone B, Gray JA (1997) Habituation and prepulse inhibition of the acoustic startle reflex: Effects of smoking status and psychosis-proneness. Pers Individual Dif 23:183–191

Lasser K, Boyd JW, Woolhandler S, Himmelstein DU, McCormick D, Bor DH (2000) Smoking and mental illness: a population-based prevalence study. JAMA 284:2606–10

Lê Cook B, Wayne GF, Kafali EN, Liu Z, Shu C, Flores M (2014) Trends in smoking among adults with mental illness and association between mental health treatment and smoking cessation. JAMA 311(2):172–182

Levin ED, Wilson W, Rose J, McEvoy J (1996) Nicotine-haloperidol interactions and cognitive performance in schizophrenics. Neuropsychopharmacology 15:429–436

Lowe EJ, Ackman ML (2010) Impact of tobacco smoking cessation on stable clozapine or olanzapine treatment. Ann Pharmacother 44:727–32

Matthies S, Holzner S, Feige B, Scheel C, Perlov E, Ebert D, Tebartz van Elst L, Philipsen A (2013) ADHD as a serious risk factor for early smoking and nicotine dependence in adulthood. J Atten Disord 17(3):176–86

McEvoy JP, Freudenreich O, Levin ED, Rose JE (1995) Haloperidol increases smoking in patients with schizophrenia. Psychopharmacology 119:124–126

Morens DM, Grandinetti A, Reed D, White LR, Ross GW (1995) Cigarette smoking and protection from Parkinson's disease: false association or etiologic clue? Neurology 45:1041–1051

Plassman BL, Helms MJ, Welsh KA, Saunders AM, Breitner JCS (1995) Smoking, Alzheimer's disease, and confounding with genes. Lancet 345:387

Prasad C, Ikegami H, Shimizu I, Onairi ES (1994) Chronic nicotine intake decelerates aging of nigrostriatal dopaminergic neurons. Life Sci 54:1169–1184

Romans SE, McNoe BM, Herbison GP, Walton VA, Mullen PE (1993) Cigarette smoking and psychiatric morbidity in women. Aust N Z J Psychiatry 27:399–404

Rüther T, Bobes J, De Hert M, Svensson TH, Mann K, Batra A, Gorwood P, Möller HJ (2014) EPA guidance on tobacco dependence and strategies for smoking cessation in people with mental illness. Eur Psychiatry 29(2):65–82

Sankaranarayanan A, Mancuso S, Castle D (2014) Smoking and suicidality in patients with a psychotic disorder. Psychiatry Res 215(3):634–640

Smith PH, Homish GG, Giovino GA, Kozlowski LT (2014) Cigarette smoking and mental illness: a study of nicotine withdrawal. Am J Public Health 104(2):e127–e133

Stage KB, Glassman AH, Covey LS (1996) Depression after smoking cessation: case reports. J Clin Psychiatry 57:467–469

Stevens KE, Meltzer J, Rose GM (1995) Nicotinic cholinergic normalization of amphetamine-induced loss of auditory gating in freely moving rats. Psychopharmacology (Berl) 119:163–170

Taylor G, McNeill A, Girling A, Farley A, Lindson-Hawley N, Aveyard P (2014) Change in mental health after smoking scessation: systematic review and meta-analysis. BMJ 348:g1151

Thornton JC, Dawe S, Lee C, Capstick C, Corr PJ, Cotter P, Frangou S, Gray NS, Russell MAH, Gray JA (1996) Effects of nicotine and amphetamine on latent inhibition in human subjects. Psychopharmacology (Berl) 127:164–173

Thornton LK, Baker AL, Lewin TJ, Kay-Lambkin FJ, Kavanagh D, Richmond R, Kelly B, Johnson MP (2012) Reasons for substance use among people with mental disorders. Addict Behav 37(4):427–34

Tsoi DT, Porwal M, Webster AC (2013) Interventions for smoking cessation and reduction in individuals with schizophrenia. Cochrane Database Syst Rev 2, CD007253

Tsuang MT, Francis T, Minor K, Thomas A, Stone WS (2012) Genetics of smoking and depression. Hum Genet 131(6):905–15

van der Meer RM, Willemsen MC, Smit F, Cuijpers P (2013) Smoking cessation interventions for smokers with current or past depression. Cochrane Database Syst Rev 8, CD006102

Wing VC, Wass CE, Soh DW, George TP (2012) A review of neurobiological vulnerability factors and treatment implications for comorbid tobacco dependence in schizophrenia. Ann N Y Acad Sci 1248:89–106

Violence and Substance Abuse in Psychotic Patients: A Forensic Psychiatric Perspective

21

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Abstract

In this chapter, a forensic psychiatric perspective on violent behaviour and substance abuse in psychotic patients will be described. First of all, the prevalence of substance abuse in schizophrenia and other psychotic disorders will be discussed. Next, some clinically important issues will be highlighted, such as the

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relationship between substance abuse and violence in psychotic disorders, and the impact of the type of substance on violent behaviour. Co-morbidity of substance abuse and a personality disorder in psychotic offenders will be discussed. Psychiatric services tend to separate mental illness and addiction services, despite evidence that more than half of the patients with a psychotic disorder have problems with alcohol and drug use and dependence. That is why substance abusing forensic patients need special attention. This could be achieved by joined-up working together between forensic and addiction services, and by further broadening forensic psychiatry training to include specialism in substance abuse, and vice versa. Finally we will summarize treatment possibilities. In conclusion, substance abuse has an aggravating effect on criminogenic behaviour, depending on the age at first conviction and the diagnosis.

21.1 Introduction

Professionals in mental health care are more and more often being held responsible for the behaviour of the mentally ill patients that they are treating, some of who turn out to be violent (Goethals 2008). The possibility of violent behaviour among psychotic patients is especially a subject of discussion because of its unpredictability and the diverse responsibilities of public mental health care and the police. A large variety of personal, circumstantial, and environmental factors seem to play a role here (Monahan and Steadman 1994). Some of these patients are less violent than the average of the population, while others are significantly more violent. A study by Swartz et al. (1998) showed that the combination of co-morbid substance abuse and poor compliance with medication increased the risk of violent behaviour in psychotic patients. Differences in studies are probably due to intermediary factors that result in a confounding bias in epidemiological studies of violent behaviour in psychotic patients. Munkner et al. (2003) analysed the records of all Danish patients with schizophrenia born after 1 November 1983. A substance abuse-related diagnosis was associated with a younger age at the time of first contact with a psychiatric hospital (but had no effect on the age at the diagnosis of schizophrenia). Lindqvist and Allebeck (1990) found that patients who had been ill for many years, but had never been hospitalized, committed the most offences. These results underline among others the role of substance abuse and social disintegration in the violent behaviour of patients with schizophrenia.

Do psychotic patients more often show violent behaviour in the presence of substance abuse as co-morbidity? In this chapter correlations will be examined between drug use (in DSM-5 mentioned as Substance-related and Addictive Disorders) and other criminogenic factors (Andrews and Bonta 2010) in their relationship with schizophrenia and personality disorders as co-morbid disorders. Having a psychotic or a personality disorder as such is already a risk factor for

criminal conduct (e.g. listed in the HCR-20), but what influence does substance use have on the antisocial behaviour of these patients? In this regard, can anything be said about preventive factors in order to assure more control on their behaviour?

Since 1990, research has revealed considerable variation in the prevalence of substance abuse in schizophrenic patients. The primary risk factors in this connection are male gender and young age. In a sample of schizophrenic patients, Cantor-Graae et al. (2001) found a lifetime prevalence of substance abuse of 48.3 %, mainly alcohol, alone or in combination with other agents. Significant associations were also found between substance abuse and male gender, criminal behaviour, more frequent hospitalization, and a family history of substance abuse.

When looking at assessment and selection for treatment in this dual diagnosis forensic population, we find some issues in the identification of substance use problems, patient's motivation to engage, patient's mental health status, cognitive impairment, polydrug use, timing of assessment, and individual differences. Assessment measurements must be relevant to the dual diagnosis population if used for treatment evaluation (Long and Hollin 2009).

Proposals for treatment programmes in detained patients depend largely on laws and possibilities in different countries, and are frequently elaborated in cooperation with law defenders and justice. Motivation is different from dual diagnosis patients in the community, since external justicial motivation is often the case. It is a real interesting and special field for realizing an effective treatment programme.

21.2 Co-morbidity of Substance Abuse and Violence in Psychotic Disorders

Swanson et al. (1997) found violent behaviour in psychiatric patients to be related to co-morbid substance abuse, the absence of recent contact with psychiatric services, and psychotic symptoms such as a feeling of being threatened and cognitive disorganization. In 96 adult schizophrenic patients from general psychiatry, greater numbers of misdemeanour convictions were linked to more severe drug and alcohol abuse histories and greater levels of disorganized symptoms, whereas a greater number of felony convictions was only associated with more severe drug abuse histories (Fukunaga and Lysaker 2013). Both the severity of severe drug abuse histories and levels of disorganized symptoms contributed to predicting 24 % of the variance in the number of reported lifetime misdemeanour offences. Soyka (2000) emphasized the importance of recurrent intoxication, so that the increased risk of aggression cannot be interpreted simply as the result of poor social integration. In a systematic review and meta-analysis, Fazel et al. (2009) identified 20 individual studies reporting data from 18,423 individuals with schizophrenia and other psychosis. Patients with schizophrenia and other psychosis were associated with violence and violent offending, particularly homicide. Co-morbidity with substance use disorders substantially increased the risk, with increased OR's between 3 and 25. The increased risk of violence in these disorders with co-morbid substance abuse was not different than the risk of violence in

individuals with diagnoses of substance use disorders. A recent systematic review and meta-regression analysis of 110 studies reporting on 45,533 individuals revealed that 18.5 % of whom were violent (Witt et al. 2013). A total of 39,995 (87.8 %) were diagnosed with schizophrenia, 209 (0.4 %) with bipolar disorder, and 5,329 (11.8 %) with other psychoses. Dynamic or modifiable risk factors included recent drug misuse, among others (p values < 0.0001), and higher impulse control scores, recent substance misuse, and recent alcohol misuse (p value < 0.01). In relation to premorbid factors, violence was moderately associated with parental history of alcohol misuse (OR = 1.8). Finally, Tengström et al. (2001) emphasized the importance of substance abuse in early starters (those schizophrenic patients with first conviction before the age of 18), due to both the presence of a diagnosis of substance abuse and the fact that most early starters were intoxicated at the time of the offence. Moreover, early starters differed from late starters in the prevalence of substance abuse by the parents, low grades at school, and a conduct disorder at an early age.

21.3 Intoxication During Offending

Our own study (Goethals et al. 2008) revealed that violent male psychotic offenders with a substance abuse-related disorder were significantly younger at the time of their first conviction, but they had not committed more violent, sexual offences or offences against property and had not spent more months in prison prior to the index offence than psychotic offenders without a co-morbid diagnosis of substance abuse. However, the prior criminal history was no more serious in those that were intoxicated at the time of the index offence than in those that were not intoxicated. We concluded that the role of substance abuse in psychotic offenders was related directly to the psychotic disorder and less to the criminal environment in which these patients find themselves. Recently, Kraanen et al. (2012) compared different types of offenders in forensic outpatient treatment, such as offenders of general violence, intimate partner violence, sex offences, and other offences such as drug trafficking and property crimes, regarding the prevalence of substance abuse disorders at the time of the offence. However, the principal diagnosis in all these offenders remained unclear. More general violence offenders and less sex offenders fulfilled diagnostic criteria for a substance use disorder. About 30 % of the offenders were intoxicated by substances at the moment they committed the offence. More general violence offenders were intoxicated during the offence. Finally, van Panhuis and Dingemans (2000) compared three Dutch cohorts of mainly male psychotic TBS detainees. This comparison also showed that the use of alcohol and drugs could aggravate violent behaviour in patients with psychosis.

21.4 Type of Substance and Violent Behaviour

In Finland, the likelihood of committing a violent offence was 25 times as high in male schizophrenic patients who used alcohol as in mentally health persons, compared to 3.6 times for patients with schizophrenia who did not use alcohol and 7.7 times for patients with other psychosis (Räsänen et al. 1998). In this study, patients with schizophrenia who did not use alcohol did not have relapses, in contrast to those who did use alcohol. In a New Zealand birth cohort, Arsenault et al. (2000) investigated the relation between mental illness and violence. Individuals with alcohol dependence, cannabis dependence, and a schizophrenic disorder had a 1.9, 3.8, and 2.5 times greater chance, respectively, of displaying violent behaviour. The individuals with at least one of these three disorders constituted one-fifth of the study population but were responsible for half of all violent offences. In persons with alcohol dependence, their violent behaviour could best be explained by the use of alcohol prior to the offence. In persons with cannabis dependence there was an association with a conduct disorder in childhood.

The assumption that substance abuse precedes violence in society was investigated by Cuffel et al. (1994). The chance of displaying violent behaviour was especially high in patients with a pattern of multiple drug use, including illegal drugs; Miles et al. (2003) reported that 34 % of their psychotic patients used alcohol, 22 % alcohol and cannabis, 12 % cannabis alone, and 24 % stimulants. A history of violent behaviour was seen significantly more often in the users of stimulants. There were hardly any other differences between the various subgroups of patients with various types of substance abuse. Corbett et al. (1998) found no indication that patients with schizophrenia prefer a particular type of drugs compared to patients with a personality disorder. Drug-abusing male inpatients with a personality disorder were significantly more likely than patients with schizophrenia to have consumed alcohol at the time of the violent offences. Case series of homicide offenders with schizophrenia show high levels of substance abuse co-morbidity (between 40 % and 71 %) according to Putkonen et al. (2004) and Bennett et al. (2011), which increases the odds ratio to 21 (Schanda et al. 2004). A survey based on a 3-year (1996–1999) consecutive sample of people convicted of homicide ($n = 1{,}594$) in England and Wales showed that more than one-third (42 %) occurred in people with a history of alcohol misuse or dependence and 40 % in people with a history of drug misuse of dependence (Shaw et al. 2006). Alcohol or drug misuse played a contributory role in two-fifths of homicides. Forty-two homicides (17 %) were committed by patients with severe mental illness and substance misuse. In the forensic outpatient sample of Kraanen et al. (2012) more general violence offenders and less other offenders were diagnosed with alcohol dependence, and more general violence dependence offenders were diagnosed with cannabis dependence at the time of the offence. Some authors have postulated that increasing substance use (particularly cannabis, cocaine, and amphetamines) was responsible for the increase of homicides committed by offenders with acute psychotic symptoms in England and Wales between 1997 and 2006 (Swinson et al. 2011).

21.5 Substance Abuse as Mediating Factor

What is the effect of substance abuse on the relation between violence and a psychotic disorder? The relationship between substance abuse and violence in psychotic disorders may be mediated by personality features and/or social problems, and is unlikely to be a simple additive effect (Mullen 2006). According to Smith and Hucker (1994), substance abuse was more prevalent among psychiatric patients than previously supposed. Schizophrenic patients, especially, were more susceptible to the negative effects of substance abuse, such as antisocial and violent behaviour. Philips (2000) arrived at a comparable conclusion: the prevalence of violent behaviour was higher in patients with both a psychiatric disorder and comorbid substance abuse than those with a single diagnosis. Such a dual diagnosis was a significant predictor of violent behaviour. Male schizophrenic patients in a large Finnish birth cohort were also found to be at high risk of committing a violent offence (Tiihonen et al. 1997). The prevalence of registered offences was highest among schizophrenic patients with co-morbid alcohol abuse and patients with an alcohol-induced psychosis. Steinert et al. (1996) compared a group of violent male schizophrenic patients with nonviolent schizophrenic patients; substance abuse was seen in 70 % of the aggressive male schizophrenic patients versus 13 % of the patients who had no history of violent behaviour. This is in agreement with the results of a study by Blanchard et al. (2000). According to them, substance abuse was seen in half of the violent schizophrenic patients, especially in young men.

A large retrospective study of hospitalized Swiss patients and a matched control group from the total Swiss population (Modestin and Ammann 1995) revealed that the number of criminal convictions was significantly higher among users of alcohol and drugs, independent of socio-demographic factors. The chance of a criminal record was twice as high among schizophrenic male patients with co-morbid substance abuse as in schizophrenic male patients without substance abuse (Modestin and Würmle 2005). In comparison with the rest of the population, however, the chance of having committed a violent offence was greater in schizophrenic patients without substance abuse.

21.6 Substance Abuse, Personality Disorder, and Psychosis: Double Trouble

First of all, we can consider the impact of substance abuse in patients with a personality disorder. Howard et al. (2013) followed up 53 male offenders after release from a secure hospital unit and after they had returned to society. Patients with antisocial/borderline co-morbidity took significantly less time to re-offend compared to those without this co-morbidity. Both Psychopathy Checklist Revised factor 2, which is strongly associated with affective dysregulation, disinhibition, and inability to plan (Skeem et al. 2011), and the tripartite risk measure (borderline and antisocial personality disorders in the context of drug/alcohol dependence and

severe childhood conduct disorder) significantly predicted time to re-offence. More in particular, Lewis (2011) examined a group of 41 mid-sentence female felons with a diagnosis of antisocial personality disorder to determine associations with substance abuse and dependence. Substance dependence was highly prevalent (i.e. alcohol dependence, 56.1 %; opiate dependence, 48.8 %; cocaine dependence, 61.0 %). In this study, symptom severity (i.e. age of onset, symptom count, co-morbidity) was associated with violent behaviour in women dependent on opiates, alcohol, and cocaine. With regard to co-morbidity, the mean number of psychiatric diagnoses, other than substance dependence, was 2.2 (most commonly a major depressive disorder and a post-traumatic stress disorder).

Next, let us examine the effect of a combination of substance abuse and a personality disorder in psychotic offenders. The prevalence of a co-morbid personality disorder and substance abuse in male psychotic patients convicted for (attempted) murder was investigated by Putkonen et al. (2004). A lifetime prevalence of substance abuse was found in 74 % and especially alcohol abuse in 72 %. Half of the group had a co-morbid personality disorder, including 47 % with an antisocial personality disorder. It is striking that substance abuse was seen in all offenders with a personality disorder. Only 25 % of the patients did not have a co-morbid disorder. Steele et al. (2003) compared schizophrenic patients with and without substance dependence. Those with substance dependence more often had a criminal history and were more often intoxicated prior to hospitalization. Moreover, they more often had an antisocial personality disorder. In a study by Baxter et al. (1999), schizophrenic patients were followed for 10 years after their discharge from a medium-security treatment facility. Prior to treatment, the patients had a history of frequent intramural psychiatric care, violent offences, substance abuse, alcohol abuse to a lesser degree, and a conduct disorder. Compared to patients with only schizophrenia, those with a co-morbid conduct disorder or problematic use of alcohol had twice as high a risk of violent behaviour. The chance of a relapse was increased by young age, multiple drug, use or a conduct disorder. In our own study of TBS detainees (Goethals et al. 2008), early starters were intoxicated more often, started with substance abuse at an earlier age and more often had a diagnosis of substance abuse at the time of the index offence than late starters. Personality disordered offenders were intoxicated more often and more often had a prior diagnosis of substance abuse at the time of the offence than psychotic offenders. To a limited extend, psychotic offenders with a diagnosis of a substance-related disorder or intoxication at the time of the offence had a more extensive criminal history than personality disordered offenders. We conclude that substance abuse has an aggravating effect on all criminogenic behaviour, depending on the age at first conviction and diagnosis.

21.7 Assessment for Treatment and Risk Assessment

In the introduction we already mentioned some issues concerning assessment. There are several instruments for screening/detection of substance abuse, for the pattern of use, severity of dependence, substance misuse-related problems, and functional assessments and analysis (Long and Hollin 2009). Baseline assessment measures for treatment are self-efficacy, motivation for change, biological markers of substance use, craving, coping skills, problem solving, impulsivity, quality of life, and co-occurring psychopathology. Especially in forensics, it is useful to look at social desirability scales. Risk of violence can be evaluated using HCR-20 (Historical Clinical Risk management measure), Clinical Inventory of Dynamic Reoffending Risk Indicators, the Short-Term Assessment of Risk and Treatability (START), or the Alcohol-Related Aggression Questionnaire.

All taken together, there is a paucity of purpose made, clinically useful, and research-based assessment instruments for assessing the effectiveness of treatment interventions for substance use-related problems in detained psychiatric patient groups.

21.8 Recommendations for Treatment in Drug-Abusing Offenders

Different stages of motivation, active treatment, and relapse prevention are not easy to distinguish in detained dual diagnosis patients. In detention, external motivation to involve in treatment is often the first step. In stages of active treatment and relapse prevention, internal motivation becomes gradually more important to move on to active treatment and relapse prevention. Psycho-educational interventions can stress the influence of substance abuse on the life of the client, also their criminal behaviour to feed their addiction. Psychosocial rehabilitation is an indirect approach on substance abuse by developing compensating abilities and activities that reduce the need and desire to use drugs. So in prison, special attention must go to screening of mental health, working on trust and safety, and preparation for peer group treatments in community (Mueser et al. 2011).

We can synthesize the main components of such a prison dual diagnosis treatment programme as follows:

- Strongly structured programme
- Strategies for psycho-education, self-help, behaviour therapy, and relapse prevention
- Phased treatment: assessment and orientation, intensive treatment, and relapse prevention and transfer
- Smaller caseloads than in substance use disorders alone
- Shorter, simpler meetings, regarding psychotic symptoms and cognitive deficits
- Working on “criminal thinking” and values (CBT)
- Education on medication and drugs

- No confronting
- Specialized training in treatment of dual diagnosis for institute caregivers
- Planning of follow-up care

Empathy, unconditional positive valuing, and intensive care are essential for development of motivation, while discipline and structure are necessary for self-control. This can be done in a "shared decision-making" strategy, where client and caregivers are able to make a treatment plan together.

Follow-up treatment in the community lacks the reachability, the time, and the sober condition that are available in prison. Hence it is essential to make a treatment network and focus again on the contemplation stage, with a lot of persuading treatment work. The role of substance use in the criminogenesis must be taken into account, and plans should be made for dealing with risky situations. Peer group treatment programmes (Alcoholics Anonymous, Dual Recovery Anonymous) can already be started in prison and continued afterwards.

One can also focus on the organizational characteristics of programme, to further understand treatment processes and outcomes (Grella et al. 2007). Community-based treatment programmes are more likely to be specialized in substance abuse treatment, more trained staff, and more commitment to and importance of drug abuse treatment. There is also a broader range of wrap-around services, in addition to core components of drug abuse treatment. Assertive community treatment with an integrated dual diagnosis treatment decreased nuisance acts and stabilized convictions in the following 12 months (Staring et al. 2012). On the contrary, correctional programmes have longer planned treatment durations, more types of patient populations, using more written treatment protocols, no dedicated drug abuse treatment, and a smaller proportion of staff with specialized training in this area, and more Therapeutic Community-based treatment.

Typical for offenders with psychiatric co-morbidity is the two-armed approach from medical and justiciary teams, both with other agendas (Marlowe 2003). In this light, elements of successful programmes are treatment in the community, opportunity to avoid a criminal record or incarceration, close supervision, and certain and immediate consequences. Confidentiality guidelines for integrated approaches depend on the laws of the country you work in.

21.9 Discussion

We can conclude that, compared to late starters, early starters more often have a diagnosis of substance abuse, and more often intoxicated at the time of the offence, and more often have parents that abuse alcohol or drugs. The distinction between early and late starters is important because early starters start criminal behaviour younger, in a more severe fashion, and go on for a longer time (Tengström et al. 2001; Moffitt and Caspi 2001; Van Dongen et al. 2012). Schizophrenic patients that abuse alcohol or drugs have a higher number of criminal convictions

and a greater chance of a criminal record. In schizophrenic offenders, the combination of substance abuse and a personality disorder increases the chance of a relapse.

With regard to the differences found between psychotic and personality disordered offenders, we can conclude that substance abuse in personality disordered offenders fits in with their criminal history. In contrast, the role of substance abuse in psychotic offenders is related directly to the psychotic disorder and less to the criminal environment in which these patients find themselves. Reports in the literature have repeatedly demonstrated that substance abuse can be resorted by psychotic patients as a kind of self-medication for the frightening symptoms of the psychotic disorder (Dixon et al. 1991; Noordsy et al. 1991; Addington and Duchak 1997; Baigent et al. 1995).

Psychiatric services tend to separate mental illness and addiction services, despite evidence that more than half of the individuals with schizophrenia have problems with alcohol and drug use and dependence (Pickard and Fazel 2013). As they stated, alcohol and drug abusing forensic patients need special attention. This could be facilitated by joined-up working between existing forensic and addiction services, and by further broadening forensic mental health training to include specialism in substance abuse.

Conclusion and Recommendations

In summary, we can state that substance abuse has an empirically proven aggravating effect on all kinds of criminal behaviour by psychiatric patients, depending on the age at first conviction and the diagnosis. Special attention to substance abuse must be given in vulnerable people, to be recognized by the early symptoms of a psychosis or a personality disorder. One might wonder whether such early starters first have their first conviction before the age of 18, and then start with substance abuse, or whether the chronology is the opposite (first the start of substance abuse and then the first conviction). National factors, like drug laws and the availability of drugs, e.g. between the Unites States and the Netherlands, play also an important role. In any case, substance abuse seems to be also an important offence-maintaining factor in these early starters. Also, we cannot exclude that early substance abuse is one of the factors that contributed to the onset of the psychosis itself. Surely substance abuse has participated in the continuous isolation, confused behaviour, and social malfunctioning of these patients.

For the future, we recommend that a prospective study to be carried out with a population cohort with and without substance abuse, and offending behaviour and onset of psychosis as dependent variables. With regard to the detection of early risk factors then it would be useful to put less highly correlated criminogenic variables in a predictive logistic regression model. A checklist of prodromal symptoms of people with an ultrahigh risk of deterioration from substance abuse, psychosis, and personality disorder is urgently needed to improve primary mental health care and patient empowerment.

As for treatment, the forced condition of detention can be also an opportunity to treat these patients. In-prison dual diagnosis programmes and assertive

community treatment can both be of help when specific needs are addressed. It is a unique cooperation between health care and justiciary workers. The right attention must go to risk factors for relapse, as well as in delict and as in substance abuse. Outcome must be evaluated not only in recidivism, but also in psychiatric symptoms.

References

Addington J, Duchak V (1997) Reasons for substance abuse in schizophrenia. Acta Psychiatr Scand 96:329–333

Andrews DA, Bonta J (2010) The psychology of criminal conduct, 5th edn. LexisNexis, New Providence, NJ

Arsenault L, Moffitt TE, Caspi A, Taylor PJ, Silva PA (2000) Mental disorders and violence in a total birth cohort. Results from the Duned in study. Arch Gen Psychiatry 57:979–986

Baigent M, Home G, Hafner RJ (1995) Self reports of the interaction between substance abuse and schizophrenia. Aust N Z J Psychiatry 29:69–74

Baxter R, Rabe-Hesketh S, Parrott J (1999) Characteristics, needs and reoffending in a group of patients with schizophrenia formerly treated in medium security. J Forensic Psychiatry 10:69–83

Bennett DJ, Ogloff JR, Mullen PE, Thomas SD, Wallace C, Short T (2011) Schizophrenia disorders, substance abuse and prior offending in a sequential series of 435 homicides. Acta Psychiatr Scand 124(3):226–233

Blanchard JJ, Brown SA, Hornan WP, Sherwood AR (2000) Substance use disorders in schizophrenia: review, integration, and a proposed model. Clin Psychol Rev 2:207–234

Cantor-Graae E, Nordström LG, McNeil TF (2001) Substance abuse in schizophrenia: a review of the literature and a study of correlates in Sweden. Schizophr Res 48:69–82

Corbett M, Duggan C, Larkin E (1998) Substance misuse and violence: a comparison of special hospital inpatients diagnosed with either schizophrenia or personality disorder. Crim Behav Ment Health 8:311–321

Cuffel BJ, Shunway M, Chouljian TL, MacDonald T (1994) A longitudinal study of substance use and community violence in schizophrenia. J Nervous Mental Disord 182:704–708

Dixon L, Haas G, Weiden PJ, Sweeney J, Frances AJ (1991) Drug abuse in schizophrenic patients: clinical correlates and reasons for use. Am J Psychiatry 148:224–230

Fazel S, Gulati G, Linsell L, Geddes JR, Grann M (2009) Schizophrenia and violence: systematic review and meta-analysis. PLoS Med 6(8):e1000120. doi:10.1371/journal.pmed.1000210

Fukunaga R, Lysaker PH (2013) Criminal history in schizophrenia: associations with substance use and disorganized symptoms. J Forensic Psychiatry Psychol 24:293–308

Goethals KR (2008) Diagnostic comorbidity and circumstantial risks in psychotic offenders: an exploratory study (dissertation). PrintPartners Ipskamp, Enschede, The Netherlands

Goethals K, Buitelaar J, van Marle H (2008) The role of substance abuse in psychotic versus personality disordered offenders detained under the Dutch Entrustment Act (TBS): an exploratory study. Int J Mental Health Addict 6:389–401

Grella CE, Greenwell L, Prendergast M, Farabee D, Hall E, Cartier J, Burdon W (2007) Organizational characteristics of drug abuse treatment programs for offenders. J Subst Abuse Treat 32 (3):291–300

Howard R, McCarthy L, Huband N, Duggan C (2013) Re-offending in forensic patients released from secure care: The role of antisocial/borderline disorder co-morbidity, substance dependence and severe childhood conduct disorder. Crim Behav Ment Health 23(3):191–202

Kraanen FL, Scholing A, Emmelkamp PMG (2012) Substance use disorders in forensic psychiatry: differences among different types of offenders. Int J Offender Ther Comp Criminol 56 (8):1201–1219

Lewis CF (2011) Substance use and violent behaviour in women with antisocial personality disorder. Behav Sci Law 29:667–676
Lindqvist P, Allebeck P (1990) Schizophrenia and crime. A longitudinal follow-up of 644 schizophrenics in Stockholm. Br J Pyschiatry 157:345–350
Long CG, Hollin CR (2009) Assessing comorbid substance use in detained psychiatric patients: issues and instruments for evaluating treatment outcome. Subst Use Misuse 44:1602–1641
Marlowe DB (2003) Integrating substance abuse treatment and criminal justice supervision. Sci Pract Perspect 2(1):4–14
Mueser KT, Noordsy DL, Drake RE, Fox L (2011) Geintegreerde behandeling van dubbele diagnose. De Tijdstroom, Utrecht. ISBN 9789058981868
Miles H, Johnson S, Amponsah-Afuwape S, Finch E, Leese M, Thornicroft G (2003) Characteristics of subgroups of individuals with psychotic illness and a comorbid substance use disorder. Psychiatr Serv 54:554–561
Modestin J, Ammann R (1995) Mental disorders and criminal behaviour. Br J Psychiatry 166:667–675
Modestin J, Würmle O (2005) Criminality in men with major mental disorder with and without comorbid substance abuse. Psychiatry Clin Neurosci 59:25–29
Moffitt TE, Caspi A (2001) Childhood predictors differentiate life-course persistent and adolescence-limited antisocial pathways among males and females. Dev Psychopathol 13 (2):355–375
Monahan J, Steadman H (1994) Violence and mental disorder. Developments in risk assessment. University of Chicago Press, Chicago
Mullen P (2006) Schizophrenia and violence: from correlations to preventive strategies. Adv Psychiatr Treat 12:239–248
Munkner R, Haastrup S, Jorgensen T, Andreasen AH, Kramp P (2003) Taking cognizance of mental illness in schizophrenics and its association with crime and substance-related diagnoses. Acta Psychiatr Scand 107:111–117
Noordsy DL, Drake RE, Teague GB, Osher F, Hurlbut SC, Beaudett MS et al (1991) Subjective experiences related to alcohol use among schizophrenics. J Nerv Ment Dis 179:410–414
Philips P (2000) Substance misuse, offending and mental illness: a review. J Psychiatr Ment Health Nurs 7:483–489
Pickard H, Fazel S (2013) Substance abuse as a risk factor for violence in mental illness: some implications for forensic psychiatric practice and clinical ethics. Curr Opin Psychiatry 26:349–354
Putkonen A, Kotilainen I, Joyal CC, Tiihonen J (2004) Comorbid personality disorders and substance use disorders of mentally ill homicide offenders: a structured clinical study on dual and triple diagnoses. Schizophr Bull 30(1):59–72
Räsänen P, Tiihonen J, Isohanni M, Rantakallio P, Lehtonen J, Moring J (1998) Schizophrenia, alcohol abuse, and violent behavior: a 26-year followup study of an unselected birth cohort. Schizophr Bull 24(3):437–441
Schanda H, Knecht G, Schreinzer D, Stompe T, Ortwein-Schwodoba G, Waldhoer T (2004) Homicide and major mental disorders: a 25 year study. Acta Psychiatr Scand 110:98–107
Shaw J, Hunt IM, Flynn S, Amos T, Meehan J, Robinson J et al (2006) The role of alcohol and drugs in homicides in England and Wales. Addiction 101:1117–1124
Skeem JL, Polaschek DLL, Patrick CJ, Lilienfeld SO (2011) Psychopathic personality: bridging the gap between scientific evidence and public policy. Pscyhol Sci Public Interest 12:95–162
Staring ABP, Blaauw E, Mulder CL (2012) The effects of assertive community treatment including integrated dual diagnosis treatment on nuisance acts and crimes in dual-diagnosis patients. Community Ment Health J 48:150–152
Steele J, Darjee R, Thomson LDG (2003) Substance dependence and schizophrenia in patients with dangerous, violent and criminal propensities: a comparison of co-morbid and non-co-morbid patients in a high-security setting. J Forensic Psychiatry Psychol 14:569–584

Swartz MS, Swanson JW, Hiday VA, Borum R, Wagner HR, Burns BJ (1998) Violence and severe mental illness: the effect of substance abuse and nonadherence to medication. Am J Psychiatry 155:226–231

Smith J, Hucker S (1994) Schizophrenia and substance abuse. Br J Psychiatry 165:13–21

Soyka M (2000) Substance misuse, psychiatric disorder and violent and disturbed behaviour. Br J Psychiatry 176:345–350

Steinert T, Hermer K, Faust V (1996) Comparison of aggressive and non-aggressive schizophrenic inpatients matched for age and sex. Eur J Psychiatry 10:100–107

Swanson J, Estroff S, Swartz M, Borum R, Lachicotte W, Zimmer C et al (1997) Violence and severe mental disorder in clinical and community populations: the effects of psychotic symptoms, comorbidity, and lack of treatment. Psychiatry 60:1–22

Swinson N, Flynn S, While D, Roscoe A, Kapur N, Appleby L et al (2011) Trends in rates of mental illness in homicide perpetrators. Br J Psychiatry 198:485–489

Tengström A, Hodgins S, Kullgren G (2001) Men with schizophrenia who behave violently: the usefulness of an early versus late starters typology. Schizophr Bull 27:205–218

Tiihonen J, Isohanni M, Räsänen P, Koiranen M, Moring J (1997) Specific major mental disorders and criminality: a 26-year prospective study of the 1966 Northern Finland birth cohort. Am J Psychiatry 154:840–845

van Dongen JD, Buck NML, van Marle HJC (2012) The role of ideational diestress in the relation between persecutory ideations and reactive aggression. Crim Behav Ment Health 22 (5):350–359

van Panhuis PJA, Dingemans PM (2000) Geweld en psychotische ziekte [Violence and psychotic disorder]. Tijdschr Psychiatr 11:793–802

Witt K, van Dorn R, Fazel S (2013) Risk factors for violence in psychosis: systematic review and meta-regression analysis of 110 studies. PLoS ONE 8(2):e55942. doi:10.371/journal.pone.0055942

Dual Disorders in Adolescent Populations 22

Dirk van West and Robert Vermeiren

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Abstract

Psychiatric comorbidity in adolescents who abuse substances is the rule rather than the exception, and common comorbidities include depression, anxiety disorder, bipolar disorder, conduct disorder, and Attention Deficit Hyperactivity Disorder (ADHD).

Among adolescents, the presence of both mental health problems and substance use disorders (SUD) (also called "dual disorders") is related to more severe symptomatology, greater treatment challenges, and poorer outcomes.

Research showing that mental health problems often precede SUD in adolescents indicates that there is a critical period for the prevention of dual disorders. Early identification and intervention for mental health disorders, coupled with substance abuse prevention, is of great importance in avoiding damage to the developing brain.

Treatment requires an integrated, multidisciplinary plan in which the youngster is actively involved. However, treatment of dual disorders in adolescents is still in its infancy and requires much more evidence-based diagnosis and treatment.

The stigma associated with mental health problems and SUD prevents youth from seeking treatment. The difficulty is further exacerbated by the existence of two separate service systems, one for mental health services and another for SUD treatment.

22.1 Introduction

It is well known that the brain of young people is still in development until the age of 25.

The areas which are necessary for self-regulation develop last. The brain of young people is not yet entirely adjusted to functions as regulating emotions and impulses, which makes it very difficult for planning and overseeing the future consequences of their behavior. Adolescence is a critical period for the development of cognitive, social, and affective skills. Experimental behavior belongs to this developmental age and often also involves the use of drugs.

The Diagnostic and Statistical Manual of Mental Disorders (DSM-5, APA 2013) divides substance-related disorders into substance use disorders (SUD) (which encompasses both substance abuse and substance dependence) and substance-induced disorders. Substance abuse is characterized by a maladaptive pattern of use manifested by recurrent and significant adverse consequences related to the repeated use of substances. Substance dependence, often commonly referred to as addiction, is a cluster of cognitive, behavioral, and physiological symptoms indicating that the individual continues use of the substance despite significant substance-related problems. Substance-induced disorders include groups of symptoms of substance intoxication, and substance withdrawal. Dual disorder

commonly refers to a person who meets DSM-5 criteria for at least one diagnosable mental health disorder, as well as at least one diagnosable SUD.

The diagnostic criteria for substance abuse and substance dependence in adolescents are less standardized than in adults due to differences in psychological and social development (Kaminer and Winters 2011). For example, young people use less frequent substances, but in larger quantities and the use is more common when they are going out. This pattern of binge drinking and drug use increases the risk for direct adverse effects, but reduces the risk for tolerance or withdrawal symptoms. In addition, adolescents with addiction problems often have not all DSM criteria for substance abuse and substance dependence because these criteria have been developed for adults (Deas 2006).

22.2 Epidemiology

The exact prevalence rate of young people with a dual disorder is difficult and complex to determine. For instance, substance abuse may blend with any number of mental disorders to produce a wide range of symptoms and vulnerability. Another difficulty is gathering valid and reliable information; children and adolescents may not have the words or concepts to express their symptoms and they may have less than reliable insight into their behavior. Despite the methodological difficulties, there seems to be a general agreement that dual disorders among adolescents are the norm rather than the exception (Couwenbergh et al. 2006; Gee et al. 2006; Hawkins 2009; Riggs 2003). In community studies, it is estimated that there is a comorbidity rate of 46–76 % (Armstrong and Costello 2002). In clinical studies, prevalence rates may vary between 43 and 90 % (Chan et al. 2008).

The user pattern of adolescents with a dual disorder is characterized by frequent substance use and a more chronic course (Chan et al. 2008; Grella et al. 2001). The highest comorbidity exists between substance abuse and disruptive behavior disorders (DBD); the comorbidity of substance use and anxiety disorders is the lowest (Kaminer and Bukstein 2008). Young people with an SUD have a five to seven times increased risk of developing a DBD (Oppositional Defiant Disorder (ODD), Conduct Disorder, Attention Deficit Hyperactivity Disorder (ADHD)), a fourfold increased risk of developing depression, and a twofold increased risk of developing an anxiety disorder (Armstrong and Costello 2002). Specific comorbid disorder prevalence rates are shown in Table 22.1.

Boys are more prone to illegal drug use, have more risk of polysubstance abuse or dependence (Johnston et al. 2007), and are more diagnosed with externalizing disorders. Girls are more likely to have comorbid internalizing problems (Latimer et al. 2002); older children were more likely to have dual disorders than younger ones (Turner et al. 2004).

Table 22.1 Prevalence rates of comorbid disorders (Riggs 2003)

Comorbid disorder	Prevalence rate
Conduct disorder (CD)	60–80 %
Attention deficit hyperactivity disorder (ADHD)	30–50 %
Depression	15–25 %
Anxiety disorders	15–25 %
Bipolar disorders	10–15 %

Table 22.2 Theoretical models of dual disorders (Mueser et al. 2003)

Theoretical model	Explanation
Common factor model[a]	Genetic or environment factors predispose both disorders
Secondary SUD model[a]	Mental health problems precede SUD
Secondary mental disorder model	SUD precede mental health problems
Bidirectional model	The two disorders develop independently, but have a significant impact on each other

[a]Modest support for these models

It seems that a conduct disorder problem plays a mediating role with respect to the association between ADHD and substance problems. Young people with comorbid conduct disorder and substance abuse are characterized by frequent polydrug use, delinquent behavior, and a worse (therapeutic) prognosis (Deas 2006). Among Dutch incarcerated boys, Vreugdenhil and colleagues (2003) reported a prevalence rate of SUD of 55 %, of which 90 % had at least one comorbid disorder. Within youngsters with a first psychosis, there is also often a problematic cannabis use (60 %). Cannabis use increases the risk of a psychotic disorder and substance abuse has a negative effect on the course of a psychosis (Milin 2008).

22.3 Etiology

Mueser and colleagues (2003) examined four theoretical models: common factor models, secondary SUD models, secondary psychiatric disorder models (self-medication), and bidirectional models (Table 22.2).

They found modest support for the common factor model and the secondary SUD model. In the common factor model, high rates of comorbidity are the result of shared risk factors, including family history, individual personality variables, environmental factors, and traumatic events. In the secondary SUD model, mental disorders preceded SUD in over 80–90 % of dual disorder cases, particularly in those that developed during adolescence. The mental disorder usually occurred first

Table 22.3 Risk factors for SUD in young people (Kaminer and Winters 2011)

• Children of addictive parents or families where addiction occurs
• Children of parents with mild intellectual disability
• Young people with mental health problems (regulation of emotions and behavior)
• Particularly those with ADHD and a behavior disorder, depression, or anxiety
• Traumatized children/young people (maltreatment or abuse)
• Children who are exposed to high stress
• Children from multi-problem families
• Young people with a low socioeconomic status, living in poverty or marginalized
• Young people who deal with delinquent or deviant peers
• School dropouts, truants
• Young people who have already begun to substance use in early childhood

in early adolescence (median age 11), followed by the SUD 5–10 years later (median age 21). Specific risk factors for substance abuse in young people are shown in Table 22.3.

22.4 Course

Substance use has a negative impact on the functioning of the brain as long as the youngster is under influence, but also afterwards. Substance use leads to an imbalance of neurotransmitters and the reward system is affected. Since the brain is still in development, substance use can stagnate this development causing permanent brain damage. In case of damage, the impact is more serious as the youngster starts at an early age. The development of experimental use of cannabis to cannabis addiction lasts among young people 6 up to 18 months, and in adults 2 up to 7 years. It would be most desirable if a youngster would not use alcohol, nicotine, or other drugs till full maturation of the brain.

Compared to youngsters with only one psychiatric problem, youngsters with dual disorders are more severely impaired, have a higher risk for medical problems, trauma, and sexual and physical abuse, have higher rates of hospitalization, incarceration, suicide attempts, and academic difficulties (Lewinsohn et al. 1996), have an earlier onset of substance use, use substances more frequently and over a longer period, and have poorer drug treatment outcomes (Grella et al. 2001). Clinical interview and presentation of youngsters with SUD is respectively shown in Tables 22.4 and 22.5.

Table 22.4 Clinical interview and evaluation of SUD (Riggs and Davies 2002)

• Onset of substance use
• Progression, patterns, and frequency of use
• Use in combination with other substances
• Presence of tolerance of withdrawal symptoms
• Response to any previous treatment
• Triggers for craving and use • Context of use
• Perceived motivation for using
• Positive and negative consequences of use
• Current motivation and goals for treatment

Table 22.5 Clinical presentation of SUD in young people (Kaminer and Winters 2011)

• Many young people come from complicated family situations with disturbed relationships. There is a higher prevalence of psychiatric disorders in the family
• Many young people have a developmental disorder (ADHD, autism spectrum disorder)
• There are often traumatic experiences and there are regular symptoms of a PTSD
• Many youth are worrying and have mood swings, symptoms of depression, lack of future perspective, and suicidality
• Social anxiety symptoms occur regularly
• Many young people have trouble sleeping and their day-and-night rhythm is often disturbed
• Several young people had psychotic experiences, whether or not under the influence of drugs
• The socio-emotional development has stagnated. Many young people have an identity problem
• Many young people suffer from behavioral problems

22.5 Treatment

22.5.1 In General

There is evidence that co-occurring mental health problems are moderators that affect adolescent treatment participation and outcomes. Adolescents with these problems are considered more difficult to engage and retain in treatment.

Ongoing and active support from system members is essential for the treatment of youngsters with a dual disorder. The system members are primarily the parents or caregivers and other family members and friends, but also professionals. *Motivating* the youngster and his system, and building a *working relationship*, requires a lot of attention. At the start of the process, there is often no intrinsic motivation to go to another counselor or therapist. Moreover, the various system members are in different motivational stages. Therefore, there is a big need of building a working relationship with each of the family members and come to a jointly supported treatment program. Much more than in adults, the youngster is very sensitive if someone really listens to him.

In the early stages, it is essential to build good contact and to prevent people from dropping out, while simultaneously realistic therapeutic expectations will be made.

As in the treatment of adults with a dual disorder, the attitude of the care workers is of great importance. Sincere personal interest in young people and their system, real commitment, and respect for the autonomy of the youngster are key components in the therapeutic relation. Moreover, patience and tenacity, humor, honesty, and transparency are essential in the treatment of youngsters with a dual disorder.

The treatment of young people with a dual disorder requires an integrated multimethod treatment program, where both mental health problems and SUD should be considered primary and treated as such (Cleminshaw et al. 2005; Mueser et al. 2003; Riggs and Davies 2002). Currently, youth with dual disorders tend to intermittently drift between primary care, mental health, substance abuse, and criminal justice systems.

Treatment should focus on the psychiatric problems, the problematic substance use, and the related factors. Therefore, treatment aims at stopping substance abuse, maintaining abstinence, and reducing the comorbid psychiatric problems (Kaminer and Bukstein 2008). An integrated treatment should at least consist of a combination of psycho-education, motivational interviewing, cognitive-behavioral therapy and systemic interventions, and psychopharmacotherapy if indicated.

Adolescents must also receive treatment that is appropriate to their developmental stage. They are involved in different environments (e.g., school, family, leisure activities), and these various settings must also be accounted for during treatment. For each disorder, adolescents with a dual disorder may be in a different stage of change or level of engagement. Therefore, engagement strategies should be matched to the youth's specific diagnosis and to the youth's stage of change.

22.5.2 Cognitive-Behavioral and Motivational Enhancement Interventions

Although few studies have examined the effectiveness of Cognitive-Behavioral Therapy (CBT) for the treatment of adolescent dual disorders, it is believed that they would be helpful, especially for youth with comorbid depression and substance abuse (Bender et al. 2006). From a cognitive-behavioral point of view, substance use is a learned behavior that is initiated and maintained by an interplay of cognitive processes, environmental factors, and behavioral reinforcement. Core features of CBT models include motivation-enhancing techniques, performing a functional assessment, and enhancing coping strategies. Studies of adolescents indicate that it is important both to provide individual behavioral therapy and to involve the family in treatment.

Motivational enhancement interventions are often coupled with CBT and may be helpful in increasing treatment engagement, motivation to change, and goal setting.

Motivational interviewing is a client-directed intervention that emphasizes an empathetic nonjudgmental stance, developing discrepancy, avoiding argumentation, and supporting self-efficacy for change.

Motivational Enhancement Therapy (MET), integrated with CBT, has proved effective in treating adolescents with dual disorders (Monti et al. 2001). MET-CBT techniques are useful in treating adolescents, who tend to be more hesitant about committing to behavior change.

The Center for Substance Abuse Treatment's Cannabis Youth Treatment Project tested the effectiveness of five interventions designed to reduce or eliminate marijuana use and associated problems in adolescents (Dennis et al. 2004). Adolescents were assigned to one of five treatment conditions: (1) MET-CBT for five sessions; (2) MET-CBT for 12 sessions; (3) family support network (including MET-CBT) for 12 sessions; (4) adolescent community reinforcement therapy; and (5) multidimensional family therapy (similar to multisystem therapy). All five treatments were found to be effective for treating adolescents with co-occurring disorders. One specific model of interest is the five-session MET/CBT (MET/CBT5), which consists of two individual MET sessions followed by three sessions of group CBT. The MET component focuses on moving the adolescent through the stages of change and developing motivation to change, whereas the CBT component emphasizes learning and practicing coping skills to handle high-risk substance use situations. MET/CBT5 was found to be one of the most cost-effective interventions studied (Dennis et al. 2004).

Seeking Safety (Najavits 2007) was developed in the 1990s for individuals diagnosed with both a substance use disorder and posttraumatic stress disorder (PTSD). The treatment has five principles: (1) safety as a priority; (2) integrated treatment of both disorders; (3) a focus on ideals to counteract the loss of ideals in both PTSD and substance abuse; (4) four content areas: cognitive, behavioral, interpersonal, and case management; and (5) attention to therapist processes. In comparison to adolescents receiving treatment as usual, those who participated in the Seeking Safety condition had decreases in substance use and associated problems (Najavits et al. 2006).

Finally, although outcomes are preliminary, *Dialectical Behavior Therapy* appears to be a very promising treatment model that merits future consideration for the treatment of adolescent co-occurring disorders.

22.5.3 Family-based Therapies

Family-based therapies are based on family systems theory and share the assumption that dysfunctional family dynamics contribute to adolescent SUD and related mental health problems. Parents are taught behavioral management strategies and are assisted in developing behavior management plans for their children. Three family-based therapy models have shown positive significant outcomes for the integrated treatment of adolescent dual disorders (Bender et al. 2006):

1. Family behavior therapy (FBT) is an intervention that targets adolescent substance use and associated behavioral problems using behavioral techniques (Donohue and Azrin 2001). The intervention targets multiple domains that influence behaviors including the family relationship, cognitions, verbal behaviors, and social interaction.
2. Multidimensional family therapy (MDFT) was developed as a family-based treatment for adolescents with substance use and related emotional and behavioral problems (Rowe 2010). MDFT is an intensive treatment with two to three contacts in one week in varying compositions (youngster with parents, youngster alone, parents alone, with school members or friends). After the initial phase of building relationships (alliances), phases of treatment, consolidation, and closing are following. On average, MDFT takes up to six months. In the European (Belgium, France, Germany, the Netherlands, and Switzerland) INCANT (International Cannabis Need for Treatment) trial, MDFT was used in the outpatient treatment of cannabis use disorder among youth who frequently have co-occurring problems. MDFT reduced youth-reported internalizing and externalizing disorder symptoms and increased family functioning (more cohesion, less conflict) (Schaub et al. 2014).
3. Multisystemic therapy (MST) was developed as a family- and community-based treatment approach for youth with co-occurring substance abuse and antisocial behavior (Henggeler et al. 2003). MST has proved effective for decreasing adolescent substance use and psychiatric symptoms, improving family relations and family functioning, increasing mainstream school attendance, and reducing long-term rates of rearrest and out-of-home placements (Henggeler et al. 2003).

Moreover, in an integrated treatment approach, nonverbal therapies such as music therapy, psychomotor therapy, and art therapy are to our clinical opinion of great value. Furthermore, social skill training, assertiveness training, anger management, and emotion regulation training are mostly indicated supporting individual skill shortages.

22.5.4 Psychopharmacotherapy

Medication is not the first-line treatment approach for adolescents with a dual disorder. Until today, almost no controlled trials have been completed in adolescents with a dual disorder.

22.5.5 Role of Primary Care Providers

Primary care providers need to be aware of effective screening and treatment advances and make appropriate referrals. However, there are several reasons why primary care providers rarely screen for co-occurring disorders (Huang et al. 2006). First, there has been little effort to train primary care providers in the use of mental

health and substance abuse screening instruments. Expanding medical and nursing school curricula and developing mental health and addiction rotations within residency and nursing programs could enhance skills in dual disorder for all primary health care professions. Second, health care providers are likely to be reimbursed for the treatment of either an SUD or a mental health disorder, but not both. Third, among adolescents, there is the additional complicating factor of the parents' right to know about assessment and the legal protection of the adolescent's privacy and confidentiality. Fourth, treatment of co-occurring disorders in primary care calls for a new collaborative approach to care and systems-mindedness.

22.6 Discussion

Almost all data regarding comorbidity, diagnosis, and treatment are derived from North American studies. The few European studies on the treatment of dual disorder in adolescents are congruent with the American studies.

Although there is much more knowledge about the diagnosis and treatment of youngsters with a dual disorder, several barriers still remain in the development and implementation of an integrated treatment program: (a) the lack of scientific research concerning therapy models in adolescents with a dual disorder (these young people were usually excluded from clinical trials), (b) diversity in substance use in combination with the high degree of diversity of comorbid psychiatric disorders, (c) the related problems in mostly all life domains, (d) insufficient consistency in the system of care, (e) the lack of care workers with specific expertise, (f) the lack of well-organized financial support, and (g) the fact that the system of care in most countries has otherwise been organized and financed after the age of 18. Future research will be needed to tackle the abovementioned barriers.

22.7 Conclusion

22.7.1 Summary

Adolescents with a dual disorder put a tremendous social and financial strain on the public health care system as substance use and psychiatric problems interact in a circular manner, thus exacerbating subsequent problems such as family and scholar dysfunction and criminality. Epidemiologic research shows that co-occurring disorders are the norm rather than the exception and are to be expected in every adolescent service setting. Results revealed that 60 % of youths with SUD had a comorbid disorder, and conduct disorder was most commonly associated with SUD. Among adolescents, the presence of co-occurring disorders is related to more severe symptomatology, greater treatment challenges, and poorer outcomes. Early identification and intervention for mental health conditions, coupled with substance abuse prevention, may help prevent or lessen the severity of co-occurring disorders.

Both the research and treatment service communities are converging on a consensus that treatment for adolescents is most effective when multimodal treatment services are provided and integrated. Although certain treatment models have shown positive outcomes, there is a further need to develop effective interventions that treat both mental health and SUD simultaneously and to translate evidence-based treatment models into standard clinical practice.

22.7.2 Recommendation About the Clinical Management

- All youth being evaluated for mental health disorders should be screened for SUD and all youth being evaluated for SUD should be screened for mental health problems using appropriate screening tools. Those who screen positive for these problems should have subsequent assessment using appropriate interview and/or assessment tools.
- Implementation of evidence-based screening and assessment in mental health and SUD treatment agencies should include adequate training, supervision, and follow-up on the administration, scoring, and interpretation of the particular instruments used.
- Screening should occur not only in outpatient clinics, but in all hospital, residential, day treatment, and other settings and should be repeated during transition periods in the youth's life.
- Families and caregivers should be involved in the screening, assessment, and treatment process in all cases.
- Evidence-based or evidence-supported treatments should be the mainstays of treatment for youth with co-occurring disorders.
- Ongoing collaboration with primary care should be broadened.

References

American Psychiatric Association (2013) Diagnostic and statistical manual of mental disorders, 5th edn. American Psychiatric Association, Washington, DC

Armstrong TD, Costello EJ (2002) Community studies on adolescent substance abuse, or dependence and psychiatric comorbidity. J Consult Clin Psychol 70(6):1224–39

Bender K, Springer D, Kim J (2006) Treatment effectiveness with dually diagnosed adolescents: a systemic review. Brief Treat Crisis Interv 6:177–205

Chan YF, Dennis ML, Funk RR (2008) Prevalence and comorbidity of major internalizing and externalizing problems among adolescents and adults presenting to substance abuse treatment. J Subst Abuse Treat 34:14–24

Cleminshaw HK, Shepler R, Newman I (2005) The integrated co-occurring treatment (ICT) model: a promising practice for youth with mental health and substance abuse disorders. J Dual Diagn 1:85–94

Couwenbergh C, van den Brink W, Zwart K, Vreugdenhil C, van Wijngaarden-Cremers P, van der Gaag RJ (2006) Comorbid psychopathology in adolescents and young adults treated for substance use disorders: a review. Eur Child Adolesc Psychiatry 15(6):319–28

Deas D (2006) Adolescent substance abuse and psychiatric comorbidities. J Clin Psychiatry 67:18–23

Dennis ML, Godley SH, Diamond GS, Tims FM, Babor T, Donaldson J, Liddle H, Titus JC, Kaminer Y, Webb C, Hamilton N, Funk R (2004) The Cannabis Youth Treatment (CYT) study: main findings from two randomized trials. J Subst Abuse Treat 27:197–213

Donohue B, Azrin NH (2001) Family behavior therapy. In: Wagner EF, Waldron HB (eds) Innovations in adolescent substance abuse interventions. Pergamon, New York, pp 205–27

Gee RL, Espiritu RC, Huang LN (2006) Adolescents with co-occurring mental health and substance use disorders in primary care. Adolesc Med 17:427–52

Grella CE, Hser Y, Joshi V, Rounds-Bryant J (2001) Drug treatment outcomes for adolescents with comorbid mental and substance use disorders. J Nerv Ment Dis 189:384–92

Hawkins EH (2009) A tale of two systems: co-occurring mental health and substance abuse disorders treatment for adolescents. Annu Rev Psychol 60:197–227

Henggeler SW, Rowland MD, Halliday-Boykins C, Ward DM, Randall J, Pickrel SG, Cunningham PB, Edwards J (2003) One-year follow-up of multisystemic therapy as an alternative to the hospitalization of youths in psychiatric crisis. J Am Acad Child Adolesc Psychiatry 42:543–51

Huang LN, Freed R, Espiritu RC (2006) Co-occurring disorders of adolescents in primary care: closing the gaps. Adolesc Med 17:453–67

Johnston LD, O'Malley PM, Bachman JG, Schulenberg JE (2007) Monitoring the Future National Survey Results on drug use, 1975–2006: Volume I, Secondary School Students 2006. NIH Publ. No. 07–6205. Bethesda, MD: Nat Inst Drug Abuse

Kaminer Y, Bukstein OG (eds) (2008) Adolescent substance abuse. Psychiatric comorbidity and high risk behaviors. Taylor & Francis, New York

Kaminer Y, Winters KC (2011) Clinical manual of adolescent substance abuse. American Psychiatric Publishing, Inc., Washington/london

Latimer WW, Stone AL, Voight A, Winters KC, August GJ (2002) Gender differences in psychiatric comorbidity among adolescents with substance use disorders. Exp Clin Psychopharmacol 10(3):310–5

Lewinsohn PM, Rohde P, Seeley JR (1996) Adolescent psychopathology: III. The clinical consequences of comorbidity. J Am Acad Child Adolesc Psychiatry 34(4):510–9

Milin R (2008) Comorbidity or schizophrenia and substance US disorders in adolescent and young adults. In: Bukstein OG, Kaminer Y (eds) Adolescent substance abuse. Psychiatric comorbidity and high risk behaviors. Taylor and Francis, New York, pp 355–78

Monti PM, Barnett NP, O'Leary TA, Colby SM (2001) Motivational enhancement for alcohol-involved adolescents. In: Monti PM, Colby SM (eds) Adolescents, alcohol, and substance abuse: reaching teens through brief interventions. Guilford, New York, pp 145–82

Mueser K, Torrey W, Lynde D, Singer P, Drake R (2003) Implementing evidence- based practices for people with severe mental illnesses. Behav Modif 27(3):387–411

Najavits LM (2007) Seeking safety: an evidence-based model for substance abuse and trauma/PTSD. In: Witkiewitz KA, Marlatt GA (eds) Therapist's guide to evidence-based relapse prevention: practical resources for the mental health professional. Elsevier, San Diego, CA, pp 141–67

Najavits LM, Gallop RJ, Weiss RD (2006) Seeking Safety therapy for adolescent girls with PTSD and substance use disorder: a randomized controlled trial. J Behav Health Serv Res 33 (4):453–63

Riggs P (2003) Treating adolescents for substance use and comorbid psychiatric disorders. NIDA Sci Pract Perspect 2(1):18–29

Riggs P, Davies R (2002) A clinical approach to integrating treatment for adolescent depression and substance abuse. J Am Acad Child Adolesc Psychiatry 41:1253–5

Rowe CL (2010) Multidimensional family therapy: addressing co-occurring substance abuse and other problems among adolescents with comprehensive family-based treatment. Child Adolesc Psychiatr Clin N Am 19(3):563–76

Schaub MP, Henderson CE, Pelc I, Tossmann P, Phan O, Hendriks V, Rowe C, Rigter H (2014) Multidimensional family therapy decreases the rate of externalising behavioural disorder symptoms in cannabis abusing adolescents: outcomes of the INCANT trial. BMC Psychiatry 14:26

Turner W, Muck R, Muck R, Stephens RL, Sukumar B (2004) Co-occurring disorders in the adolescent mental health and substance abuse treatment systems. J Psychoactive Drugs 36:455–61

Vreugdenhil C, Van Den Brink W, Wouters LF, Doreleijers TA (2003) Substance use, substance use disorders, and comorbidity patterns in a representative sample of incarcerated male Dutch adolescents. J Nerv Ment Dis 91:372–8

Somatic Problems and Dual Disorder Patients

23

Marc De Hert, Davy Vancampfort, and Johan Detraux

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Abstract

Individuals with severe mental illness (SMI) are prone to many different physical health problems. While these diseases are, compared with the general population, more prevalent among people with SMI, their impact on individuals with a dual disorder (=the co-occurrence of SMI with substance use disorder, SUD) seems even to be more significant. Although general research is limited, there is sufficient evidence to conclude that dual disorder patients have a significantly greater medical comorbidity than SMI patients without an SUD. This is confirmed by additional research on major medical diseases in these patients. Studies in SMI patients show a strong relationship between SUDs and human immunodeficiency virus and hepatitis C virus infection. Cigarette

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smoking and drug abuse, which are highly prevalent among SMI people, are implicated in a higher risk for developing respiratory tract diseases, such as chronic pulmonary disease, and cardiovascular diseases. However, although medical health problems are more prevalent in dual disorder patients, a substantial proportion of these patients do not receive any treatment for these somatic problems. Specific patient, provider, and system factors act as barriers to the recognition and the management of physical disease in these highly vulnerable patients.

23.1 Introduction

The life expectancy of people with severe mental illness (SMI), including schizophrenia, bipolar disorder, schizoaffective disorder, and major depressive disorder, is shorter compared to the general population. This excess mortality is mainly due to physical illness. Nutritional and metabolic diseases, cardiovascular diseases, viral diseases, respiratory tract diseases, musculoskeletal diseases, stomatognathic disease, and possibly obesity-related cancers are, compared to the general population, more prevalent among people with SMI. An unhealthy lifestyle as well as treatment-specific factors account for much of the increased risk for most of these physical diseases (De Hert et al. 2011a).

Adults with SMI have high rates of co-occurring substance use disorders (SUDs) (Tandon et al. 2009; Testa et al. 2013). The US Substance Abuse and Mental Health Services Administration (SAMHSA) (2010) reported that 11.4 million adults aged 18 or older (5 %) had an SMI in the past year. About a quarter of these adults (25.2 %) had a co-occurring SUD, compared with 6.1 % of adults who did not have a mental illness. Especially patients with schizophrenia or bipolar disorder have comorbidity of SUDs. For example, compared with the general population, persons with schizophrenia are almost five times more likely to have an SUD (Buckley 2006). Obviously, as has been shown by several non-American studies, dual disorder is a substantial problem around the world, with prevalence rates being lower, similar or even higher than those in the United States (Buckley 2006). Moreover, a primary non-substance-related mental disorder often precedes and is a robust risk factor for the later onset of an SUD (Swendsen et al. 2010).

It is commonly reported that the co-occurrence of an SUD with an SMI is generally more severe, chronic, and less likely to result in positive treatment outcomes than a single disorder (Matusow et al. 2013). Co-occurring substance abuse complicates the disease and is associated with a multitude of adverse outcomes including medication noncompliance and increased relapse and rehospitalization rates (Buckley 2006). Substance abuse in addition to an SMI can also be associated with poorer overall health and physical comorbidities, such as a poorer physical and mental hygiene (often including a sedentary lifestyle, poor eating, and sleeping habits), liver disease, and cardiac and pulmonary diseases. Other related medical problems involve the higher risk for infectious diseases, including human

immunodeficiency virus (HIV), hepatitis C virus (HCV) infection, and tuberculosis (Ziedonis et al. 2005). However, few reports have examined the association of SMI, SUDs, and medical disorders in order to clarify to what extent comorbid SUDs increase the prevalence of certain medical disorders beyond the effect of SMI alone.

23.2 Relationship Between SMI, SUDs, and Medical Disorders

A large-scale cross-sectional study ($N = 26{,}332$ of whom 11,185 have been treated for an SMI), controlling for other medical risk factors, such as poverty, did find that patients with an SMI and an SUD had the highest adjusted odds for five (of eight) investigated medical disorders, compared with SMI patients without an SUD and patients with an SUD but no SMI: heart disease (Odds ratio, OR = 4.24, 95 % CI: 3.19–5.63), asthma (OR = 3.29, 95 % CI: 2.63–4.13), gastrointestinal disorders (OR = 2.82, 95 % CI: 2.28–3.49), skin infections (OR = 1.97, 95 % CI: 1.26–1.77), and acute respiratory disorders (OR = 2.04, 95 % CI: 1.78–2.33). The odds ratios for SMI patients without a comorbid SUD were heart disease (OR = 3.19, 95 % CI: 2.51–4.07), asthma (OR = 1.99, 95 % CI: 1.65–2.39), gastrointestinal disorders (OR = 2.28, 95 % CI: 1.92–2.69), skin infections (OR = 1.49, 95 % CI: 1.26–1.77), and acute respiratory disorders (OR = 1.40, 95 % CI: 1.26–1.54). The reference group for all comparisons consisted of Medicaid beneficiaries without a psychotic disorder or SUD. To identify persons with an SUD, the authors used all ICD (International Classification of Diseases)-9 codes for alcohol and drug use or abuse. SMI was defined as having a diagnosis of schizophrenia, bipolar disorder, or another psychotic disorder (Dickey et al. 2002).

Lin et al. (2011) examined the association between mental illness and chronic physical conditions in older adults (≥65 years) and investigated whether co-occurring SUDs (including alcohol or drug abuse or dependence) are associated with greater risk of chronic physical conditions beyond mental illness alone. The study population ($N = 679{,}182$) was classified into three mutually exclusive mental illness groups: SMI (including schizophrenia, bipolar disorder, and major depression), other mental illness (all other psychiatric diagnoses), and no mental illness. Fifteen chronic physical conditions were selected: hypertension, ischemic heart disease, congestive heart failure, atrial fibrillation, stroke, chronic obstructive pulmonary disease or asthma, diabetes mellitus, chronic kidney disease, osteoporosis, arthritis, hip or pelvic fracture, cancer, dementia (including Alzheimer's disease), Parkinson's disease, and eye disease. They found that community-dwelling older adults with co-occurring SUDs and mental illness had the highest adjusted risk for 11 of the 15 selected chronic physical conditions, compared to those without these disorders ($N = 545{,}450$). Mental illness and SUDs were especially associated with a much greater risk of dementia and hip fractures. The adjusted prevalence ratios for older adults with an SMI and co-occurring SUD (vs. older adults with an SMI but without an SUD) for these chronic physical conditions were 9.9 (95 % CI: 9.5–10.2) vs. 5.9 (95 % CI: 5.8–6.0), and 9.5 (95 % CI: 8.3–10.9) vs. 3.9 (95 % CI: 3.7–4.1), respectively.

Table 23.1 Physical diseases with increased frequency in dual disorder patients, compared to severe mental illness patients without co-occurring substance use disorder

Disease category	Physical diseases with increased frequency
Virus diseases	Human immunodeficiency virus (HIV), hepatitis C virus
Neoplasms	Cancer
Musculoskeletal diseases	Osteoporosis/decreased bone mineral density, hip fractures, arthritis
Stomatognathic diseases	Poor dental status
Gastrointestinal diseases	Gastroesophageal reflux disease
Respiratory tract diseases	Chronic obstructive pulmonary disease (COPD), asthma, tuberculosis, bacterial pneumonia
Skin diseases	Skin infections
Cardiovascular diseases	Stroke, myocardial infarction, hypertension, ischemic heart disease, congestive heart failure, atrial fibrillation
Endocrine system diseases	Diabetes mellitus, hyperlipidemia
Mental disorders	Dementia
Kidney diseases	Chronic kidney disease

Batki et al. (2009) characterized the type and severity of medical comorbidity in patients with schizophrenia and co-occurring alcohol dependence ($n = 80$). The authors examined the influence of demographic factors as well as the severity of psychiatric illness, alcohol use, and non-alcohol substance use on medical illness burden. They found that patients with co-occurring alcohol use disorder (AUD) may have significantly more medical illness burden than patients with schizophrenia or schizoaffective disorder alone. Eighty-three percent of dual disorder patients had at least one chronic medical illness, hypertension being the most common (43 %). The medical illness burden was correlated with alcohol use severity (e.g., gamma-glutamyl-transpeptidase levels), but appeared to be independent of psychiatric severity or other substance use.

Although there are few data on HRQOL (Health-Related Quality of Life) in dual disorder patients, most of the studies show a worse HRQOL in these patients, compared with SMI patients without a comorbid SUD and with patients with an SUD alone (Benaiges et al. 2012).

Thus, although general research is limited, there is sufficient evidence to conclude that dual disorder patients have substantially greater medical comorbidity than SMI patients without an SUD. This is confirmed by additional research on major medical diseases in dual disorder patients (see Sect. 23.3). Interventions to decrease substance use and abuse may therefore be critically in reducing medical morbidity in this patient population (Table 23.1).

23.3 Major Medical Diseases in Dual Disorder Patients

23.3.1 Chronic Viral Infections

Individuals with SMI have been shown to be at significantly increased risk for a variety of chronic viral infections, of which the most serious are the diseases associated with human immunodeficiency virus (HIV) and hepatitis C virus (HCV) infection. This increased risk is largely due to co-occurring use of substances and specifically elevated rates of high-risk drug-related behaviors (Meyer 2003). Studies in SMI patients show a strong relationship between SUDs and HIV and HCV infection.

23.3.1.1 HIV Positivity

The role of substance abuse in HIV infection is well documented. According to a report of the US SAMHSA, drug abuse behavior plays the single largest role in the spread of HIV infection in the United States today. Half of all new HIV infections now occur among injection drug users (Department of Health and Human Services 2008).

Although the prevalence of HIV positivity in people with SMI varies substantially (1.3–23.9 %), it is much higher than the HIV prevalence rate found in the general population (De Hert et al. 2009a, 2011a). Next to injection drug use, substance abuse-associated sexual risk behaviors, as well as a reduced knowledge about HIV-related issues, contribute to these higher HIV prevalence rates (Himelhoch et al. 2007; De Hert et al. 2011a, b). Meade (2006), for example, found that among persons with dual disorders, active substance abusers engaged in the highest rates of sexual activity (56 %), followed by persons with remitted SUD (46 %), and, finally, by those with no lifetime history of SUD (23 %). SMI persons with lifetime SUD were more than 14 times more likely than persons with no SUD to report partner-related risks, including multiple partners, non-monogamous partners, sex with prostitutes or strangers, and sex trade. Individuals with SMI who have a history of childhood abuse may be at particularly high risk for HIV. Childhood abuse, and in particular associated cognitive, emotional, and social impairments, in people with SMI is directly and indirectly related to HIV risk behavior with substance abuse and adult victimization as mediators (Meade et al. 2009).

A longitudinal analysis (Prince et al. 2012), exploring the relationships between diagnosis of SMI and subsequent new diagnoses of HIV among Medicaid beneficiaries in eight US states ($N = 6{,}417{,}676$), underscored the link between substance abuse and the risk of new HIV diagnoses in SMI patients. Among people with major depressive disorder, bipolar disorder, and schizophrenia, those with substance abuse or dependence were, respectively, 3 (adjusted OR = 3.04), 2.5 (adjusted OR = 2.45), and 1.6 (adjusted OR = 1.63) times as likely ($p < 0.001$) as those without substance abuse or dependence to be diagnosed with HIV during the next 3 years. These results therefore suggest once again that assessing and addressing substance abuse, as well as associated high-risk behaviors, are essential

factors to reduce HIV/AIDS risk among persons with SMI. In contrast to what might be expected on the basis of earlier reports of associations between SMI and HIV risk, the authors did not find SMI diagnosis in the absence of substance abuse to be associated with increased risk of HIV/AIDS. People with SMI but without an SUD in 2001 were 23 % less likely (adjusted OR = 0.77, $p < 0.001$) than people without SMI or an SUD to receive a new HIV diagnosis during the next 3 years. Only major depressive disorder seemed to confer such risk (12 % increase, adjusted OR = 1.12, $p < 0.01$). After adjustment for substance abuse or dependence diagnosis and demographic and selecting other characteristics, the presence of bipolar disorder was not associated with higher odds of new HIV/AIDS diagnoses, and the presence of schizophrenia was even associated with lower odds of new HIV/AIDS diagnoses (OR = 0.56, $p < 0.001$). Prince et al. (2012) therefore conclude that it remains unclear whether behavioral factors associated with SMI, other than those captured by a substance abuse or dependence diagnosis, also increase the risk of HIV/AIDS diagnoses.

Nevertheless, because of the high HIV prevalence rates, it is important that dual disorder patients are tested for HIV. However, studies investigating HIV testing rates among individuals with an SMI indicate that fewer than half of these patients (percentages ranging from 17 % to 47 %) have been tested in the past year (De Hert et al. 2011a). Since many patients with SMI are exposed to atypical antipsychotics, which have been associated with metabolic abnormalities, and since patients infected with HIV and on highly active antiretroviral therapy may also develop metabolic abnormalities, this group of patients is at particularly high risk for developing the metabolic syndrome and ultimately cardiovascular diseases (Vergara-Rodriguez et al. 2009).

23.3.1.2 Hepatitis C Virus (HCV) Infection

Across different continents, markedly elevated rates of hepatitis virus infection have been reported in persons with SMI, compared to the general population. Overall, an estimated 20–25 % of persons with SMI are infected with HCV (De Hert et al. 2011a). Several studies have shown that SMI patients with SUDs even have higher rates of HCV infection (Mistler et al. 2006; Huckans et al. 2006; Matthews et al. 2008). Matthews et al. (2008) collected retrospectively data on 325,410 patients from electronic medical records and compared HCV prevalence rates in bipolar disorder patients with and without SUDs ($N = 9{,}750$). Compared with a control group with no history of either bipolar disorder or SUD, patients in the dual disorder group ($N = 4{,}724$) had a 5.46-fold increase in the relative risk of HCV infection, followed by the SUD group without a bipolar disorder ($N = 37{,}970$) (4.86-fold risk increase) and the bipolar disorder group without an SUD ($N = 5{,}026$) (1.31-fold risk increase). Huckans et al. (2006), utilizing a Veterans Healthcare Administration medical record database, found that, of those tested for HCV, 31.1 % (943/3,029) of veterans with comorbid schizophrenia and SUD were confirmed to have HCV, compared with 9.9 % (219/2,207) of veterans with schizophrenia but no documented history of SUD. Respectively, these groups were approximately eight (OR = 8.12, 95 % CI:7.47–8.82, $p < 0.001$) and two

times (OR = 1.98, 95 % CI: 1.71–2.28, $p < 0.001$) as likely as the control group of patients without these diagnoses to have HCV infection. As even patients in the schizophrenia group with no SUD history were twice as likely as those in the control group to have HCV infection, these results equally show that a diagnosis of schizophrenia may be a risk factor independent of SUD.

HCV infection is a major cause of liver disease, including cirrhosis and hepatocellular carcinoma (Loftis et al. 2006). The most common routes of HCV transmission for persons with SMI are drug-use behaviors and sexual behaviors related to drug use (Mistler et al. 2006). For example, increased risk of bipolar disorder patients for both HCV and its related hepatic morbidity may come from some patients' participation in high-risk behaviors like intermittent/episodic drug use or hypersexuality when manic. In addition, AUDs are relatively common in bipolar patients, which may increase the likelihood of high-risk behaviors as well as increase risk of progression of liver disease secondary to alcohol use in those patients with HCV (Matthews et al. 2008). Rosenberg et al. (2001) found, in a large sample ($N = 931$) of patients with an SMI undergoing inpatient or outpatient treatment, that being positive for HCV was associated with several substance using variables, including the presence of an SUD (alcohol, cannabis, and cocaine), a lifetime history of injection drug use, a lifetime history of sniffing or snorting drugs, and a lifetime use of crack. Injection drug use, compared with those without injection drug use, increased the risk of HCV infection to more than 31-fold (OR = 31.25, 95 % CI: 18.47–49.52, $p < 0.001$). A study of Klinkenberg et al. (2003), trying to estimate the prevalence of HCV among homeless persons with dual disorders, found 29.8 % (34/114) were antibody positive for HCV. Substance use variables having a significant bivariate relationship with HCV status were having a history of injection drug use ($p < 0.01$) and needle sharing ($p < 0.01$). SMI persons with a history of injection drug use were about three times more likely (OR = 3.19) to have a reactive test for HCV as SMI persons without a history of injection drug use.

These results underline the centrality of SUD, particularly injection drug abuse, in HCV infection. Therefore, especially patients with dual disorders should have routine screening and treatment for HCV infection to prevent associated morbidity and mortality (De Hert et al. 2011a). Unfortunately, although there is an overwhelming body of evidence that HCV-infected patients with psychiatric and addiction comorbidities can safely and effectively undergo antiviral treatment with similar sustained viral responses, many dual disorder patients are left untreated. If these patients undergo therapy, it is important that such treatment is delivered within the context of a multidisciplinary setting. In particular multidisciplinary approaches that combine HCV treating providers with mental health, addictions, and other support systems can facilitate preparation and successful treatment of these patients (Bonner et al. 2012).

23.3.2 Respiratory Tract Diseases

Up until 50 years ago, respiratory diseases, such as pneumonia and tuberculosis, accounted for the majority of deaths among people with SMI who lived in institutions. Nevertheless, respiratory diseases are still prevalent in people with SMI (De Hert et al. 2011a). Studies consistently show a higher incidence of tuberculosis among patients with schizophrenia compared with the general population (De Hert et al. 2011a). Filik et al. (2006) found that people with SMI have a higher prevalence of angina and respiratory symptoms and impaired lung function when compared with the general population. A nationwide, population-based study found schizophrenia to be associated with a 1.37 times greater risk of acute respiratory failure and a 1.34-fold greater risk of mechanical ventilation, compared to those without schizophrenia. In this study patients with an SUD were excluded from both the schizophrenia and comparison groups (Chen et al. 2011).

Several risk factors are implicated in adverse outcomes for respiratory diseases. In particular cigarette smoking and alcohol abuse, which are more prevalent among SMI people, are important in this regard (Chen et al. 2011). For example, a meta-analysis of worldwide studies demonstrated that, compared with the general population, patients with schizophrenia have a higher prevalence of ever smoking, heavy smoking, and high nicotine dependence, as well as of risk factors that make them more vulnerable to start smoking (De Leon and Diaz 2005). Moreover, up to 85 % of individuals with SMI will die and/or have a reduced quality of life because of a tobacco-related disease (De Hert et al. 2011c). As chronic obstructive pulmonary disease (COPD), i.e., chronic bronchitis and emphysema, is caused primarily by cigarette smoking (Forey et al. 2011), individuals with SMI are likely to be at higher risk for developing this disease (De Hert et al. 2011a). In a sample of 200 SMI patients, overall, the reported prevalence of COPD was 22.6 %. Compared to national comparison subjects who were matched on age, gender, and race, those with SMI were significantly more likely to report a diagnosis of chronic bronchitis (19.5 % versus 6.1 %, OR = 3.75, 95 % CI: 2.53–5.55) as well as emphysema (7.9 % versus 1.5 %, OR = 5.69, 95 % CI: 3.08–10.48). Not surprisingly, smoking was the strongest independent predictor of COPD, with smokers having 8 times higher risk of COPD than the nonsmokers in the same group (adjusted OR = 8.83, 95 % CI: 1.98–39.34, $p = 0.004$) (Himelhoch et al. 2004).

Smoking of illicit drugs has been associated with the transmission of respiratory pathogens including bacterial pneumonia and tuberculosis (Welsh et al. 2012). "Shotgunning" or "doing a shotgun," referring to the practice of one individual forcibly exhaling (blowing) smoke into the mouth (or, rarely, nose) of another, has been associated with potential increased transmission of respiratory pathogens, including tuberculosis. However, a recent study ($n = 236$) demonstrated shotgunning was not associated with tuberculosis, or history of positive purified protein derivative tuberculin skin test in SMI patients with a lifetime substance abuse history and engaged in shotgunning (61 %) (Welsh et al. 2012).

23.3.3 Cardiovascular Diseases

In SMI patients, cardiovascular diseases (CVD) are the commonest cause of death. The prevalence of CVD in people with schizophrenia and bipolar disorder is approximately two- to threefold increased. The risk of coronary heart disease seems to be 2- to 3.6-fold higher in patients with schizophrenia; people with bipolar disorder have a 2.1-fold higher risk. The risk of cerebrovascular accident is 1.5- to 2.9-fold higher in patients with schizophrenia, and 2.1- to 3.3-fold higher in patients with bipolar disorder (De Hert et al. 2011a).

Next to obesity, physical inactivity, hypertension, dyslipidemia, diabetes mellitus, and use of psychotropic medication, smoking undoubtedly is a risk factor for CVD (ischemic heart disease, cerebrovascular disease, atherosclerosis, aneurysm) and associated mortality in SMI patients (Kelly et al. 2011; De Hert et al. 2009b, 2011a, 2012). A US study of patients with mental disorders, including SMI patients, found that smoking (Hazard ratio, HR = 1.32, 95 % CI: 1.26–1.39, $p < 0.001$) was the second most important behavioral cardiovascular mortality risk factor, behind physical inactivity (HR = 1.66, 95 % CI: 1.59–1.74, $p < 0.001$) (Kilbourne et al. 2009). Kelly et al. (2011), examining the effects of cigarette smoking on mortality risk in 1,213 persons with schizophrenia-related psychotic disorders, identified cardiac causes in 43 % of deaths in smokers versus 19 % of deaths in nonsmokers ($p < 0.006$). For those aged 35–54 years, the odds of cardiac-related death was increased by 12-fold in smokers relative to nonsmokers (HR = 12.4, $p = 0.0005$). SUDs, including the use of cocaine or stimulants, also are a risk factor for cardiovascular events (De Hert et al. 2011d; Testa et al. 2013). Cocaine's toxic effects on the cardiovascular system include hypertensive crisis, myocardial infarction, tachyarrhythmia, and sudden death (Devlin and Henry 2008; Testa et al. 2013). Other substances associated with cardiac arrhythmias and sudden death include 3,4-methylenedioxymethamphetamine (MDMA or "ecstasy"), amphetamines, and cannabis (Devlin and Henry 2008). Although excessive alcohol use increases the likelihood of developing a wide range of medical problems, it also harms the cardiovascular system (Batki et al. 2009). Binge drinking is a significant risk factor for stroke, particularly in hypertensive patients (Hillbom et al. 2011).

Despite the increased risk for cardiovascular morbidity and mortality, SMI patients have a limited access to general health care with less opportunity for cardiovascular risk screening and prevention (De Hert et al. 2009b; Testa et al. 2013), as well as a significantly reduced chance of receiving many specialized interventions or circulatory medications (De Hert et al. 2011a).

23.4 Quality of Medical Care in Psychiatric Patients with Dual Disorder

A substantial proportion of adults with comorbid mental health problems and an SUD do not receive any treatment. Therefore, medical problems may go undetected or undiagnosed in these dual disorder patients. Harris and Edlund (2005) examined

the rates of substance abuse treatment and mental health care use among five groups that were formed on the basis of the presence of an SUD (alcohol or any drug), mental health problems, or both in the past year. Although the likelihood of receiving any substance abuse treatment increased with the presence and severity of mental health problems, still 45.9 % of dual disorder patients with an SMI (defined as having at least one 12-month DSM-IV disorder, excluding SUDs, along with functional impairment, $N = 7{,}530$) and 65 % of those with one or more mental health symptoms (representing key constructs from the major disorders, $N = 13{,}759$) received neither mental health nor substance abuse treatment. Only 31.2 % of mental health users with SMI and an SUD ($N = 1{,}872$) received any substance abuse treatment. This low rate of substance abuse treatment among SMI patients who use mental health care raises policy concerns, because mental health treatment alone for co-occurring disorders may be ineffective.

Possible reasons for these low rates of treatment include stigma, denial, financial barriers, inadequate recognition of medical illness and poor access to care, a shortage of trained providers, and the lack of a strong clinical consensus about the best way to treat dual disorder patients (Harris and Edlund 2005; Ziedonis et al. 2005; De Hert et al. 2011c). Under these circumstances, SMI patients may continue to engage in risky behavior. Moreover, it also seems that dual disorder patients underreport their medical problems significantly more than patients with an SUD only. Meszaros et al. (2011) showed that patients with schizophrenia or schizoaffective disorder and co-occurring AUD underreport their medical problems significantly more than patients with AUD only and controls. Accuracy of self-report also was significantly lower in patients with schizophrenia-spectrum disorders and co-occurring alcohol dependence than in patients with AUD only or in controls. The most commonly underreported diagnoses included coronary artery disease, chronic renal failure, seizure disorder, hyperlipidemia, asthma, and hypertension.

To improve the care of dual disorder patients, screening should include testing medical comorbidity, as well as risky behaviors such as intravenous needle use. Furthermore, assessment should include an evaluation of the severity of the SMI and the addiction, the scope of the patient's disabilities, as well as the patient's capacity and resources of support to overcome the dual disorder (Buckley 2006). Although integrated treatment should be the new standard for evidence-based treatment for this population (Ziedonis et al. 2005), there are still barriers to overcome. In our nationwide cross-sectional study ($N = 1{,}420$), evaluating to which extent treatment programs in Belgian psychiatric services were in accordance with an integrated treatment philosophy, we found only 50 % of the clinicians in this study mentioned the use of cross-trained teams in the treatment of dually diagnosed patients (De Hert et al. 2010). Therefore, there is still a high need for cross-trained teams and a high need to develop specific integrated treatment programs that address both disorders. Finally, after an integrated dual disorder treatment plan, aftercare should be provided, as well as other care, to address the social and vocational needs of the patient.

Conclusion

Physical disorders are, compared to the general population and SMI patients without a co-occurring SUD, more prevalent in dual disorder patients. In spite of this, the screening and assessment of physical health aspects in these patients remains poor, even in developed countries. Specific patient (e.g., unawareness of physical problems due to cognitive deficits, difficulties in communicating physical needs), provider (e.g., tendency of psychiatrist to focus on mental rather than physical health, poor communication with patient or primary care health workers), and system (lack of awareness of the physical health and health care access problems for people with SMI, stigma and discrimination, gap between physical and mental health care) factors act as barriers to the recognition and the management of physical diseases in dual disorder patients (De Hert et al. 2011c). This highlights the urgent need to improve the coordination of care across the physical, mental, and addiction health care delivery systems. Although medical staff, guided by negative stereotypes, often tend to treat the physical illnesses of people with SMI less thoroughly and less effective, even simple and very basic monitoring and treatment actions, undertaken by the treating clinician, can already improve the problem of suboptimal medical care in this population. Adhering to monitoring and treatment guidelines will result in a substantial enhancement of physical health outcomes in this vulnerable population (De Hert et al. 2011c).

References

Batki SL, Meszaros ZS, Strutynski K et al (2009) Medical comorbidity in patients with schizophrenia and alcohol dependence. Schizophr Res 107(2–3):139–146

Benaiges I, Prat G, Adan A (2012) Health-related quality of life in patients with dual diagnosis: clinical correlates. Health Qual Life Outcomes 10:106

Bonner JE, Barritt AS 4th, Fried MW et al (2012) Time to rethink antiviral treatment for hepatitis C in patients with coexisting mental health/substance abuse issues. Dig Dis Sci 57(6):1469–1474

Buckley PF (2006) Prevalence and consequences of the dual diagnosis of substance abuse and severe mental illness. J Clin Psychiatry 67(Suppl 7):5–9

Chen YH, Lin HC, Lin HC (2011) Poor clinical outcomes among pneumonia patients with schizophrenia. Schizophr Bull 37(5):1088–1094

De Hert M, Detraux J, Vancampfort D et al (2012) Severe mental illness and diabetes mellitus type 2. Die Psychiatrie 9(3):159–164

De Hert M, Correll CU, Bobes J et al (2011a) Physical illness in patients with severe mental disorders. I. Prevalence, impact of medications and disparities in health care. World Psychiatry 10(1):52–77

De Hert M, Trappeniers L, Wampers M et al (2011b) Knowledge about HIV in people with schizophrenia: a general population comparison. Clin Schizophr Relat Psychoses 5(2):80–86

De Hert M, Cohen D, Bobes J et al (2011c) Physical illness in patients with severe mental disorders. II. Barriers to care, monitoring and treatment guidelines, plus recommendations at the system and individual level. World Psychiatry 10(2):138–151

De Hert M, Detraux J, van Winkel R et al (2011d) Metabolic and cardiovascular adverse effects associated with antipsychotic drugs. Nat Rev Endocrinol 8(2):114–126

De Hert M, Katarina R, Benoit G et al (2010) Dual diagnosis among schizophrenic patients in Belgian psychiatric services: prevalence and available treatment options. Acta Psychiatr Belg 110(2):43–50
De Hert M, Wampers M, Van Eyck D et al (2009a) Prevalence of HIV and hepatitis C infection among patients with schizophrenia. Schizophr Res 108(1–3):307–308
De Hert M, Dekker JM, Wood D et al (2009b) Cardiovascular disease and diabetes in people with severe mental illness position statement from the European Psychiatric Association (EPA), supported by the European Association for the Study of Diabetes (EASD) and the European Society of Cardiology (ESC). Eur Psychiatry 24(6):412–424
De Leon J, Diaz FJ (2005) A meta-analysis of worldwide studies demonstrates an association between schizophrenia and tobacco smoking behaviors. Schizophr Res 76(2–3):135–157
Department Of Health And Human Services, Substance Abuse and Mental Health Services Administration Center for Substance Abuse Treatment (2008). Drugs, alcohol and HIV/AIDS. A consumer Guide. U.S. http://www.samhsa.gov. Accessed 28 June 2013
Devlin RJ, Henry JA (2008) Clinical review: major consequences of illicit drug consumption. Crit Care 12(1):202
Dickey B, Normand SL, Weiss RD et al (2002) Medical morbidity, mental illness, and substance use disorders. Psychiatr Serv 53(7):861–867
Filik R, Sipos A, Kehoe PG et al (2006) The cardiovascular and respiratory health of people with schizophrenia. Acta Psychiatr Scand 113(4):298–305
Forey BA, Thornton AJ, Lee PN (2011) Systematic review with meta-analysis of the epidemiological evidence relating smoking to COPD, chronic bronchitis and emphysema. BMC Pulm Med 14(11):36
Harris KM, Edlund MJ (2005) Use of mental health care and substance abuse treatment among adults with co-occurring disorders. Psychiatr Serv 56(8):954–959
Hillbom M, Saloheimo P, Juvela S (2011) Alcohol consumption, blood pressure, and the risk of stroke. Curr Hypertens Rep 13(3):208–213
Himelhoch S, Lehman A, Kreyenbuhl J et al (2004) Prevalence of chronic obstructive pulmonary disease among those with serious mental illness. Am J Psychiatry 161(12):2317–2319
Himelhoch S, McCarthy JF, Ganoczy D et al (2007) Understanding associations between serious mental illness and HIV among patients in the VA health system. Psychiatr Serv 58:1165–1172
Huckans MS, Blackwell AD, Harms TA et al (2006) Management of hepatitis C disease among VA patients with schizophrenia and substance use disorders. Psychiatr Serv 57(3):403–406
Kelly DL, McMahon RP, Wehring HJ et al (2011) Cigarette smoking and mortality risk in people with schizophrenia. Schizophr Bull 37(4):832–838
Kilbourne AM, Morden NE, Austin K et al (2009) Excess heart-disease-related mortality in a national study of patients with mental disorders: identifying modifiable risk factors. Gen Hosp Psychiatry 31(6):555–563
Klinkenberg WD, Caslyn RJ, Morse GA et al (2003) Prevalence of human immunodeficiency virus, hepatitis B, and hepatitis C among homeless persons with co-occurring severe mental illness and substance use disorders. Compr Psychiatry 44(4):293–302
Lin WC, Zhang J, Leung GY et al (2011) Chronic physical conditions in older adults with mental illness and/or substance use disorders. J Am Geriatr Soc 59(10):1913–1921
Loftis JM, Matthews AM, Hauser P (2006) Psychiatric and substance use disorders in individuals with hepatitis C: epidemiology and management. Drugs 66(2):155–174
Matthews AM, Huckans MS, Blackwell AD et al (2008) Hepatitis C testing and infection rates in bipolar patients with and without comorbid substance use disorders. Bipolar Disord 10(2):266–270
Matusow H, Guarino H, Rosenblum A et al (2013) Consumers' experiences in dual focus mutual aid for co-occurring substance use and mental health disorders. Subst Abuse 7:39–47
Meade CS (2006) Sexual risk behavior among persons dually diagnosed with severe mental illness and substance use disorder. J Subst Abuse Treat 30(2):147–157

Meade CS, Kershaw TS, Hansen NB et al (2009) Long-term correlates of childhood abuse among adults with severe mental illness: adult victimization, substance abuse, and HIV sexual risk behavior. AIDS Behav 13(2):207–216

Meszaros ZS, Dimmock JA, Ploutz-Snyder R et al (2011) Accuracy of self-reported medical problems in patients with alcohol dependence and co-occurring schizophrenia or schizoaffective disorder. Schizophr Res 132(2–3):190–193

Meyer JM (2003) Prevalence of hepatitis A, hepatitis B, and HIV among hepatitis C-seropositive state hospital patients: results from Oregon State Hospital. J Clin Psychiatry 64(5):540–545

Mistler LA, Brunette MF, Marsh BJ et al (2006) Hepatitis C treatment for people with severe mental illness. Psychosomatics 47(2):93–107

Prince JD, Walkup J, Akincigil A et al (2012) Serious mental illness and risk of new HIV/AIDS diagnoses: an analysis of Medicaid beneficiaries in eight states. Psychiatr Serv 63(10):1032–1038

Rosenberg SD, Goodman LA, Osher FC et al (2001) Prevalence of HIV, hepatitis B, and hepatitis C in people with severe mental illness. Am J Public Health 91(1):31–37

Swendsen J, Conway KP, Degenhardt L et al (2010) Mental disorders as risk factors for substance use, abuse and dependence: results from the 10-year follow-up of the National Comorbidity Survey. Addiction 105(6):1117–1128

Tandon R, Nasrallah HA, Keshavan MS (2009) Schizophrenia, "just the facts" 4. Clinical features and conceptualization. Schizophr Res 110(1–3):1–23

Testa A, Giannuzzi R, Sollazzo F et al (2013) Psychiatric emergencies (part II): psychiatric disorders coexisting with organic diseases. Eur Rev Med Pharmacol Sci 17(Suppl 1):65–85

U.S. Department of health and human services. Substance Abuse and Mental Health Services Administration Center for Behavioral Health Statistics and Quality. Results from the 2010 National Survey on Drug Use and Health: Mental Health Findings. http://www.samhsa.gov/data/nsduh/2k10MH_Findings/2k10MHResults.pdf. Accessed 28 June 2013

Vergara-Rodriguez P, Vibhakar S, Watts J (2009) Metabolic syndrome and associated cardiovascular risk factors in the treatment of persons with human immunodeficiency virus and severe mental illness. Pharmacol Ther 124:269–278

Welsh C, Goldberg R, Tapscott S et al (2012) "Shotgunning" in a population of patients with severe mental illness and comorbid substance use disorders. Am J Addict 21(2):120–125

Ziedonis DM, Smelson D, Rosenthal RN et al (2005) Improving the care of individuals with schizophrenia and substance use disorders: consensus recommendations. J Psychiatr Pract 11(5):315–339

Psychiatric Comorbidity in Heroin Maintenance and Methadone Maintenance Treatments

24

Ambros A. Uchtenhagen

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Abstract

Psychiatric disorders occur frequently in individuals with opiate dependence in epidemiology and in clinical studies. A relief from emotional distress is considered to contribute to these elevated rates. Such an effect may contribute to the attractiveness of opioid maintenance treatment for dual diagnosis patients.

Psychiatric disorders risk to be overlooked in addiction treatment resulting in frequent dropouts. In opioid maintenance treatment, including methadone maintenance, lack of mental health care may lead to continued use of street heroin and other non-prescribed substances. Heroin maintenance was designed and tested in the 1990s as a response to such failures.

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In contrast to the traditional practice in the UK of handing out heroin prescriptions to addicts, the new maintenance concept includes a comprehensive assessment and care programme. It is reserved for otherwise treatment-refractory patients. Rates of psychiatric comorbidity are high at entry to heroin maintenance. The potential to provide a safe and efficient answer to such treatment-refractory patients was researched in six countries. The good retention, reductions in illicit drug use and crime, and improvements in somatic and mental health were confirmed repeatedly. New heroin maintenance became part of the routine treatment system in five countries.

In three out of six randomised controlled trials, comparing heroin and methadone maintenance, heroin maintenance resulted in a significantly better outcome for comorbid patients.

In conclusion, maintenance treatment for opiate addicts must be prepared to take care of dual diagnosis patients; for treatment-refractory patients the new heroin maintenance treatment is a valuable rescue option.

24.1 Introduction: The Role of Maintenance Treatment for Opiate Dependence

Opiate maintenance treatment for opiate addicts has a long history (Uchtenhagen 2014), but only since the introduction of methadone maintenance (Dole and Nyswander 1965) the prescribing of opioid agonists—mainly methadone and buprenorphine—for maintenance therapy became the cornerstone of treatment for opioid dependence. Today, methadone and buprenorphine are on the list of essential medicines of World Health Organisation (WHO) (2004a, b). Maintenance on these substances is considered to be the most important approach for heroin dependence (WHO 2009).

24.2 Prevalence of Psychiatric Disorders in Opiate Dependence

Psychiatric comorbidity in opiate-dependent populations has been observed in many clinical and epidemiological studies. A review of 16 studies found prevalence rates of at least one comorbid disorder in almost half of individuals involved. The most frequent comorbid disorders were personality disorders followed by affective and anxiety disorders, while the rates of schizophrenic disorders were low (see Table 24.1).

A very recent study among patients with nonmedical prescription opioid use found rates of psychiatric comorbidity within the ranges of that meta-analysis (27 % affective disorders, 29 % anxiety disorders; Goldner et al. 2013).

How are the differences in comorbidity rates understood? The findings of clinical studies depend much on the sample selection of patients. Settings, reference

Table 24.1 Psychiatric disorders in opiate dependence (meta-analysis of 16 studies; Frei and Rehm 2002)

Diagnosis	Range
At least one comorbid disorder	47–97 %
Personality disorder	26–68 %
Affective disorder	18–54 %
Anxiety disorder	3–49 %
Schizophrenic disorder	0–14 %

period, and differences in diagnostic instruments used for clinical assessment are other factors involved (European Monitoring Center for Drugs and Drug Addiction [EMCDDA] 2013). Psychotic patients are less likely to be accepted in drug treatment services than those with personality, affective, or anxiety disorders. Moreover, diagnostic data from mental health services show substance use disorders in schizophrenic patients at a rate of about one-third (review in National Institute for Health and Clinical Excellence [NICE] 2011), mainly alcohol and cannabis abuse. Cannabis has a potential to provoke psychotic disorders; opiates do not have this effect. A review of European studies found among the most common combinations cannabis use and schizophrenia as well as opioid use and personality or behavioural disorders (EMCDDA 2013).

24.3 From Methadone Maintenance to Heroin Maintenance Treatment

Mental disorders may lead to substance use in an attempt to alleviate unpleasant feelings (Phillips and Johnson 2001). Opiates are known for sedative effects; they may be regarded as instrumental for self-medication in emotional distress occurring with affective and anxiety disorders as well as with negative environmental reactions to personality disorders. Opiate use and opioid agonist treatment may mask psychotic proneness (Maremmani et al. 2003) or even prevent the development of schizophrenic psychosis (Khantzian 1997). A possible consequence could be the preference for opioid substitution treatment. In fact, high rates of psychiatric comorbidity have been documented for methadone maintenance treatment (e.g. two-thirds in the study of Ball and Ross 1991). The Dutch national Reitox (Réseau Européen d'Information sur les Drogues et les Toxicomanies) report 2010 found 84 % psychiatric comorbidity among patients in methadone maintenance treatment (EMCDDA 2011).

Addiction services must be prepared to cope with mental disorders. Looking at retention rates and outcome findings, addiction services seem to achieve this competence over time. Earlier studies found a clear relationship between more severe psychiatric symptomatology and lower retention (McLellan et al. 1993), while no such relationship was found in other studies (Ball and Ross 1991). An improvement of psychiatric care in methadone maintenance treatment followed:

recent studies found higher retention in comorbid patients as compared to non-comorbid ones (Gelbkopf et al. 2006; Maremmani et al. 2008).

In this context, it is of interest to see whether pharmaceutical diamorphine (heroin) is a helpful medication for maintenance treatment and whether methadone patients continue to use street heroin and other non-prescribed substances during treatment. A new concept for supervised injectable heroin maintenance treatment (HMT) was set up and researched in a Swiss national prospective cohort study 1994–1996 (Uchtenhagen et al. 1999; Rehm et al. 2001). It comprised a comprehensive assessment and care programme. Entry was restricted to otherwise treatment-resistant heroin addicts. Patients presented themselves for supervised injections of individual dosages of pharmaceutical diamorphine, clinics were open daily, and no take-out of injectables is permitted. The concept was designed to avoid overdose risk and misuse. Ensuing randomised controlled trials in Switzerland, The Netherlands, Germany, Spain, Canada, and England compared the outcomes of injectable (in one trial inhalable) heroin and of oral methadone as agonist medications for maintenance treatment. An overall summary of findings was recently published in an EMCDDA monograph (Strang et al. 2012). Based on positive outcomes, new heroin maintenance has become part of the regular treatment system in Switzerland, The Netherlands, Germany, Denmark, and England, with a total capacity of ca. 2,900 slots in 55 clinics.

24.4 Heroin Maintenance and Psychiatric Comorbidity

24.4.1 Psychiatric Disorders at Entry to Heroin Maintenance Treatment

As expected, a high rate of psychiatric disorders can be found in patients entering HMT. Data are available from the Swiss, the German and the Dutch studies.

In the Swiss cohort study, patients had at entry a history of any Axis I disorder in 65.9 % lifetime and 38.8 % during the last 4 weeks. The highest frequencies were found for affective disorders (55.3 % and 27.1 %, respectively) and anxiety disorders (25.9 % and 18.5 %, respectively). At least one Axis II, personality disorder, was found in 57.6 % (66.7 for men, 57.2 % for women). Altogether, 86 % of patients entering HMT had an Axis I or Axis II disorder (Frei and Rehm 2001). This is substantially higher than the rates of psychiatric disorders found on average in opiate dependence according to the review mentioned above of Frei and Rehm (2002; see Table 24.1). These rates of psychiatric comorbidity at entry to HMT were more or less stable up to 2011.

The Dutch trials also found a high rate of psychiatric disorders; 30 % had at least one Axis I disorder at entry (Blanken et al. 2005).

In the German trial, 48.9 % of all patients entering had at least one psychiatric disorder during the last 12 months. The rate of comorbidity did not differ significantly between patients randomised to heroin or methadone prescription (Schaefer et al. 2010).

24.4.2 Outcomes in Heroin Maintenance Treatment for Comorbid Patients

In all five countries (Switzerland, The Netherlands, Germany, Spain, and Canada) the same treatment concept for heroin maintenance was used, and the comparison groups were patients on oral methadone. However, diagnostic instruments, measurements of outcome, and periods of follow-up observation were quite diverse.

Retention in heroin maintenance treatment in general was high after 2 years (44 %; Oviedo-Joekes et al. 2010), 2.5 years (50 %; Rehm et al. 2001), 4 years (56 %; Blanken et al. 2010), and 6 years (40 %; Güttinger et al. 2003).

The Swiss national prospective cohort study found a significant improvement of overall mental health during the first 18 months in treatment, according to medical examination. The decrease of severe depressive disorders, of severe anxiety and delusional disorders, and of highly aggressive behaviour was already observed during the first 12 months (Uchtenhagen et al. 1999). The randomised trial in Geneva used SF-36 for assessment and the score as outcome after 9 months. Mental health scores in patients receiving heroin improved significantly (Perneger et al. 1998).

The Dutch trials tested injectable and inhalable heroin against oral methadone, using for assessment the European version of the Addiction Severity Index (EuropASI) and the Symptom Checklist 90-revised (SCL-90-R) in a follow-up of 12 months (Blanken et al. 2005). Outcome was determined by a dichotomous multi-domain outcome index (including validated indicators of physical health, mental status, and social functioning). Treatment response was lower in comorbid patients (43.8 %) as compared to non-comorbid patients (55.5 %) at 12-month follow-up. However, because the significance threshold was a difference of at least 20 %, this result was considered to be not significant (Blanken et al. 2005).

In the German trial, SCL-90-R and DSM IV diagnosis were used for assessment and a composite score for measuring outcome (at least 20 % improvement in the Opiate Treatment Index [OTI] health scale and/or at least 20 % improvement in the Global Severity Index [GSI], without a deterioration of more than 20 % in the other area of health, and reduction in the use of street heroin with at least 3 of 5 negative urines in the month prior to the end of the trial, and no increase in cocaine use). Two years after entry, 75.25 % of patients with at least one psychiatric disorder were retained in the heroin maintenance programme, whereas non-comorbid patients had a retention rate of 80.72 %; the difference was considered to be not significant. Improvements in physical and mental health were found in 80 % of patients receiving heroin (Haasen et al. 2007; Schaefer et al. 2010).

The Spanish patients were assessed by use of the EuropASI, the OTI, and the outcome by a EuropASI composite score. After 9 months, the psychological status score had improved significantly from 0.5 to 0.3 (March et al. 2006).

The Canadian trial used also the EuropASI as assessment instrument and an ASI score on the psychiatric status as determinant for outcome. Twelve months after

entry to treatment, patients receiving heroin showed a reduction in the psychiatric score (Oviedo-Jokes et al. 2008).

24.5 Comparing Outcomes in Methadone Maintenance and Heroin Maintenance Treatments

The Cochrane Collaboration performed a meta-analysis of eight randomised controlled trials comparing heroin and methadone maintenance treatments. It included the early British trial on the traditional heroin-prescribing model and the new randomised trial with injectable heroin, the Randomised Injectable Opiate Treatment Trial (RIOTT) from the UK. Retention in general was found to be significantly superior in heroin maintenance as compared to methadone maintenance. In all six trials featuring supervised heroin prescribing the heroin patients were more likely to meet the criteria for responders, generally reflecting illicit drug use and/or health and crime. Generally the advantages conferred by heroin were statistically significant. The reviewers conclude: "The available evidence suggests an added value of heroin prescribed alongside flexible doses of methadone for long-term, treatment refractory, opioid users, to reach a decrease in the use of illicit substances, involvement in criminal activity and incarceration, a possible reduction in mortality; and an increase in retention in treatment. Due to the higher rate of serious adverse events, heroin prescription should remain a treatment for people who are currently or have in the past failed maintenance treatment, and it should be provided in clinical settings where proper follow-up is ensured" (Ferri et al. 2011).

Data on the comparative analysis on psychiatric comorbidity are available from the Dutch, German, Spanish, and Canadian trials, as well as from the randomised Swiss trial. No data are available from the RIOTT study which excluded patients with psychiatric comorbidity.

In the Dutch trials, patients receiving psychiatric medication (as an indicator for comorbidity) on heroin prescription showed a treatment response rate of 43.8 %, in comparison to 29.6 % of patients on oral methadone only. Again, this was not considered to be significant, because the threshold was set at a difference of at least 20 % (Blanken et al. 2005).

The German trial resulted in different responder rates among completers after 12 months. Among the diagnoses assessed by the Composite International Diagnostic Interview (CIDI) according to the International Classification of Diseases (ICD-10), only neurotic, stress-related, and somatoform disorders (F 40–48) showed a significant difference, whereas differences for schizophrenic disorders (F 20–29), affective disorders (F 30–39), and behavioural syndromes (F 50–59) did not reach statistical significance (Schaefer et al. 2010).

In the Spanish trial, improvements in psychological status did not differ significantly between comorbid patients receiving heroin and those receiving methadone after 9 months in treatment (March et al. 2006).

The Canadian data show a significant difference in mental health status between comorbid patients receiving heroin versus patients receiving methadone, after 12 months in treatment (Table 24.2) (Oviedo-Jokes et al. 2008).

Table 24.2 Results of randomised controlled trials on outcomes of heroin and methadone maintenance treatment for dual disorder patients

Country	Source	Sample size	Follow-up period	Outcome HMT	Outcome MMT	Significance
Switzerland	Perneger et al. (1998)	$n = 51$	6 months	SF-36 score 54.5	SF-36 score 49.3	$p < 0.025$
The Netherlands	Blanken et al. (2005) Blanken et al. (2010)	$n = 430$ $n = 430$	12 months 12 months	43.8 % responders SCL-90 score 38.8	29.6 % responders SCL-90 score 40.3	n.s. n.s.
Germany	Schaefer et al. (2010)	$n = 1{,}015$	12 months	CIDI F 40–48: 26.7 %	CIDI F 40–48: 41.0 %	$p < 0.002$
Spain	March et al. (2006)	$n = 251$	9 months	ASI score reduced $p < 0.009$	ASI score reduced $p < 0.017$	n.s.
Canada	Oviedo-Jokes et al. (2008)	$n = 127$	12 months	ASI score psych 0.16	ASI score psych 0.20	$p < 0.01$

24.6 Implications for Service Provision

24.6.1 Competence for Dual Diagnosis Assessment and Treatment in Agonist Maintenance of Opiate Dependence

The risks of dual diagnosis patients to drop out of treatment and to relapse are elevated. One of the factors is a lack of competence in assessing and treating the condition. Dual disorder patients rarely receive both mental health and substance abuse treatment (Substance Abuse and Mental Health Service Administration [SAMHSA] 2012). Many services providing agonist maintenance treatment do not have staff sufficiently trained in diagnosing and caring for patients with mental health conditions. Maintenance treatment in private practice is frequently provided by family doctors and generalists, without links to psychiatric facilities.

Another problem is a deficit in proper diagnostic assessment. Validated tools for diagnosis are available and should be used (e.g. Mestre-Pintó et al. 2014). A further problem is improving the competence to care for dual disorder patients. Specific treatment approaches have been reviewed (Drake et al. 2006; De Witte et al. 2014).

Given the attractiveness of agonist maintenance treatment for dual disorder patients, the use of such tools and an appropriate link to specialist services could help to improve the care for these patients.

24.6.2 Implementation of Heroin Maintenance

The new heroin maintenance treatment model as described above is a useful instrument for reaching out to and caring effectively for otherwise treatment-resistant opioid addicts. Its implementation therefore makes sense if other therapeutic approaches, including agonist maintenance, are available and accessible in sufficient numbers and adequate quality, and if additional resources for heroin maintenance are in place. If so, the setting up of a pilot clinic in a region with such a target population is advisable, before multiplying facilities at national level. Comprehensive clinics offering other maintenance treatment as well are feasible. Training of staff may include exchange with an existing system practising heroin maintenance. Starting with a research project is an option, but not indispensible as the Danish example demonstrates. A monitoring system recording continuously entries, pathways, and intended outcomes, as well as dosages and unintended side effects, is highly recommended.

Conclusions and Recommendations

High rates of psychiatric comorbidity are documented for opiate dependence. Psychiatric disorders contribute to elevated dropout rates in the treatment of opiate dependence, including methadone maintenance treatment without special mental health care.

Maintenance treatment with injectable pharmaceutical diamorphine (heroin) is designed as a rescue option for opiate addicts for whom other treatments

failed. Retention rates are high as they are for non-comorbid patients. Improvements in mental health status were reported for comorbid patients after 9 and 12 months.

A meta-analysis of randomised controlled trials with heroin versus methadone maintenance found a significantly better overall outcome for heroin prescribing in regard to illicit drug use, health, and crime. In some trials, comorbid patients in heroin maintenance showed more improvements in mental health compared to those in methadone maintenance.

Opioid maintenance treatment in general is an attractive option for the care of patients with psychiatric comorbidity if the services provides the respective diagnostic and therapeutic competence. If such treatment fails, patients with psychiatric comorbidity can still profit from heroin maintenance and should not be excluded.

References

Ball JC, Ross A (1991) The effectiveness of methadone maintenance treatment: patients, programs. Services and outcome. Springer, NY

Blanken P, Hendriks VM, Koeter MWJ, van Ree JM, van den Brink W (2005) Matching of treatment-resistant heroin-dependent patients to medical prescription of heroin or oral methadone treatment: results from two randomized controlled trials. Addiction 100:89–95

Blanken P, van den Brink W, Hendriks VM, Huijsman IA, Klousd MG, Rook EJ, Wakelin JS, Barendrecht C, Beijnend JH, van Ree JM (2010) Heroin-assisted treatment in the Netherlands: history, findings, and international context. Europ Neuropsychopharmacol 20(Suppl 2): 105–158

De Witte NAJ, Crunelle CL, Sabbe B, Moggi F, Dom G (2014) Treatment for outpatients with comorbid schizophrenia and substance use disorders: a review. Eur Addict Res 20:105–114. doi:10.1159/000355267

Dole VP, Nyswander ME (1965) A medical treatment for diacetylmorphine (heroin) addiction. JAMA 193:646–650

Drake RE, Mueser KT, Brunette MF, McHugo GJ (2006) A review of treatments for people with severe mental illnesses and co-occurring substance use disorders. Psychiatr Rehabil J 27: 360–374

EMCDDA (2011) Reitox National reports 2010. European Monitoring Centre for Drugs and Drug Addiction (available at: www.emcdda.europa.eu/publications/national-reports)

EMCDDA (2013) Co-morbid substance use and mental disorders in Europe: a review of the data, EMCDDA Papers, European Monitoring Centre for Drugs and Drug Addiction. Publications Office of the European Union, Luxembourg

Ferri M, Davoli M, Perucci CA (2011) Heroin maintenance for chronic heroin-dependent individuals. Cochrane Database of Systematic Reviews 2011, Issue 12. Art. No.: CD003410. DOI: 10.1002/14651858.CD003410.pub4.

Frei A, Rehm J (2001) Komorbidität: Psychische Störungen bei Opiatabhängigen zu Beginn einer heroingestützten Behandlung. In: Bundesamt für Gesundheit (Ed.) Suchtforschung des BAG 1999–2001 Bd. 3, pp. 92–99

Frei A, Rehm J (2002) Die Prävalenz psychischer Komorbidität unter Opiatabhängigen: eine Metaanalyse bisheriger Studien. Psychiatrische Praxis 29:258–262

Gelbkopf M, Weizman T, Melamed Y, Adelson M, Bleich A (2006) Does psychiatric comorbidity affect drug abuse treatment outcome? A prospective assessment of drug abuse, treatment

tenure and infectious diseases in an Israeli methadone maintenance clinic. Isr J Psychiatry Relat Sci 43:126–136
Goldner EM, Lusted A, Roerecke M, Rehm J, Fischer B (2013) Prevalence of Axis-1 psychiatric (with focus on depression and anxiety) disorder and symptomatology among non-medical prescription opioid users in substance use treatment: systematic review and meta-analyses. Addict Behav. doi:10.1016/j.addbeh.2013.11.022
Güttinger F, Gschwend P, Schulte B, Rehm J, Uchtenhagen A (2003) Evaluating long-term effects of heroin-assisted treatment: the results of a 6-year follow-up. Eur Addict Res 9:73–79
Haasen C, Verthein U, Degkwitz P, Berger J, Krausz M, Naber D (2007) Heroin assisted treatment for opioid dependence: randomised controlled trial. Br J Psychiatry 191:55–62
Khantzian E (1997) The self-medication hypothesis of substance use disorders: a reconsideration and recent applications. Harv Rev Psychiatry 4:231–244
March JC, Oviedo-Joekes E, Perea-Milla E, Carrasco F (2006) Controlled trial of prescribed heroin in the treatment of opioid addiction. J Subst Abuse Treat 31:203–211
Maremmani I, Pacini M, Lovrecic M, Lubrano S, Perugi G (2003) Agonist opioid maintenance. Usefulnes in treatment of comorbid diseases. In: Waal H, Haga E (eds) Maintenance treatment of heroin addiction. Evidence at the crossroads. Cappelen, Oslo, pp 221–233
Maremmani I, Pacini M, Lubrano S, Perugi G, Tagliamonte A, Pani PP, Gerra G, Shinderman M (2008) Long-term outcomes of treatment-resistant heroin addicts with and without DSM-IV Axis 1 psychiatric comorbidity (Dual diagnosis). Eur Addict Res 14:134–142
McLellan AT, Arndt IO, Metzger IS, Woody GE, O'Brien CP (1993) The effects of psychosocial services in substance abuse treatment. JAMA 269:1953–1959
Mestre-Pintó JI, Domingo-Salvany A, Martín-Santos R, Torrens M (2014) Dual diagnosis screening interview to identify psychiatric comorbidity in substance users: development and validation of a brief instrument. Eur Addict Res 20:41–48. doi:10.1159/000351519)
NICE (2011) Psychosis with coexisting substance misuse. The NICE guideline on assessment and management in adults and young people. National clinical guidelines Nr 120. National Collaborating Centre for Mental Health, London
Oviedo-Jokes E et al (2008) The North American Opiate Medication Initiative (NAOMI): profile of participants in North America's first trial of heroin-assisted treatment. J Urban Health 85: 812–825
Oviedo-Joekes E, March JC, Romero M, Perea-Milla E (2010) The Andalusian trial on heroin-assisted treatment: a 2 year follow-up. Drug Alcohol Rev 29:75–80
Perneger TV, Giner F, del Rio M, Mino A (1998) Randomized trial of heroin maintenance programme for addicts who fail in conventional drug abuse treatments. Br Med J 317:13–18
Phillips P, Johnson S (2001) How does drug and alcohol misuse develop among people with psychotic illness? A literature review. Soc Psychiatry Psychiatric Epidemiol 36:269–276
Rehm J, Gschwend P, Steffen T, Gutzwiller F, Dobler-Mikola A, Uchtenhagen A (2001) Feasibility, safety and efficacy of injectable heroin prescription for treatment-refractory heroin addicts: a follow-up study. Lancet 358:1417–1420
SAMHSA (2012) Results from the 2011 National Survey on Drug use and Health: summary of national findings. Substance Abuse and Mental Health Services Administration, Rockville, MD, p 2012
Schaefer I, Eiroa-Orosa FJ, Verthein U, Dilg C, Haasen C, Reimer J (2010) Effects of psychiatric comorbidity on treatment outcome in patients undergoing diamorphine or methadone maintenance treatment. Psychopathology 43:88–95
Strang J, Groshkova T, Metrebian N (2012) New heroin-assisted treatment. Recent evidence and current practices of suppervised injectable heroin treatment in Europe and beyond. EMCDDA Insight nr 11. European Monitoring Centre for Drugs and Drug Addiction, Lisbon
Uchtenhagen A (2014) A short history of opioid maintenance treatment -how a treatment was born and spread around the World. In: Bruinsma G, Weisburd D (eds) Encyclopedia of criminology and criminal justice. Springer, New York

Uchtenhagen A, Dobler-Mikola A, Steffen T, Gutzwiller F, Blättler R, Pfeifer S (1999) Prescription of narcotics for heroin addicts. Main results of the Swiss National Cohort Study. Karger, Basel
WHO (2004a) Proposal for the inclusion of methadone in the WHO model list of essential medicines. World Health Organisation, Geneva
WHO (2004b) Proposal for the inclusion of buprenorphine in the WHO model list of essential medicines. World Health Organisation, Geneva
WHO (2009) Guidelines for the psychosocially assisted pharmacological treatment of opioid dependence. World Health Organisation, Geneva

Toward a New Model of Care: Integrating Mental Health, Substance Use, and Somatic Care

25

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Abstract

Although research and clinical interventions for patients with dual disorders have been described since as early as the 1980s, the day-to-day treatment of these patients remains problematic and challenging in many countries. Throughout this book, many approaches and possible pathways have been outlined. Based upon these experiences, some key points can be extracted in order to guide to future developments. (1) New diagnostic approaches are warranted when dealing with patients who have multiple problems, given the limitations

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of the current categorical systems. (2) Greater emphasis should be placed on secondary prevention and early intervention for children and adolescents at an increased risk of later-life dual disorders. (3) Mental, addiction, and somatic care systems can be integrated, adopting a patient-focused approach to care delivery. (4) Recovery should be taken into consideration when defining treatment intervention and outcome goals. (5) It is important to reduce societal risk factors, such as poverty and early childhood adversity. (6) More resources are needed to provide adequate mental health care in the various countries. The development of European guidance initiatives would provide benefits in many of these areas, making it possible to ensure a more harmonized standard of care for patients with dual disorders.

25.1 Introduction

In spite of a long tradition of developing effective treatment models for patients with severe psychiatric disorders, outcome results remain modest to weak overall. This includes all types of outcome variables covering broad areas, such as psychiatric symptoms, substance use, psychosocial functioning, disability, quality of life, and life expectancy. As to the latter, it is remarkable that even in Europe's most reputed health systems, in the Nordic countries, the life expectancies of patients with complex psychiatric disorders remain substantially shorter than those of the general population (i.e., approximately 15 years shorter for women and 20 years for men) (Nordentoft et al. 2013). This loss of life years illustrates the risks and burden that characterize patients with multiple disorders (comorbidity). Indeed, the excess mortality is because most of these patients suffer from comorbid psychiatric, substance use, and somatic disorders. Early death is due to medical (e.g., cancer, cardiovascular diseases, gastrointestinal problems) and external (e.g., suicide, injuries, accidents, accidental overdoses) causes. Many of these negative consequences are at least partially driven by the effects of excessive substance use. Specifically, alcohol and smoking have a major impact, although many other factors also play an important role (Bobes et al. 2010).

Although various European guidelines have been published in the last couple of years offering guidance in the treatment of comorbidities (e.g., smoking cessation, medical risk management in antipsychotic pharmacotherapy) (Mortimer 2003; Ruther et al. 2014), consistent implementation of these good practices within European countries has been limited. One of the problems is the enormous variety of medical systems and treatment models across the different European countries, making it hard to develop uniform quality indicators and treatment strategies (Gaebel et al. 2012).

Another major pitfall across Europe, and worldwide, is the increasing trend toward specialization and the resulting division of care systems that characterizes modern medicine and health care. Examples of this trend are the division between

mental health versus somatic-medical health on the one hand and mental health versus addiction treatment on the other hand. The increased specialization of care systems according to diagnostic groups has made it possible to develop "specialized excellence," but also has proven to build enormous barriers between these same systems. As a result, patients who have multiple needs (i.e., who require a more holistic approach) are negatively impacted by these barriers. Importantly, this is not exclusively a mental health versus medical care problem. On the contrary, increased specialization is a general trend in medicine, with organ or disease-oriented specializations dividing health care into many subfields. Specialization leads to a fragmentation and discontinuity of care, resulting in an overall loss of efficiency and higher costs. Indeed, any improvements in care and reductions in cost resulting from having more highly trained specialists deliver specific services appear to be offset by the quality-eroding and cost-increasing effects of the communication required between multiple specialties when numerous independent specialists treat the same patient. This coordination problem is particularly relevant for patients with complex comorbidities, who often have several chronic diseases. A specialist is likely to focus on "his" or "her" disease, perhaps overlooking the patient's other important health needs and potentially leading to adverse outcomes (Detsky et al. 2012). The split between mental health and addiction care might be prototypical of the negative consequences of a specialization paradigm.

In conclusion, given that in the "real" clinical world patients increasingly tend to present with comorbidities, the trend toward single-disease specialization might have passed its point of efficiency. Although disorder-specific interventions are efficacious, there is a clear need for a broader treatment spectrum and a more collaborative approach to comorbidity in the health care of the future.

25.2 Dual Disorders: A Categorical Psychiatric Diagnostic Fallacy?

Many critics have accused the categorical diagnostic systems (e.g., Diagnostic and Statistical Manual, DSM) to be at the root of the "comorbidity" hype. Does Europe need to plead guilty? Historically, descriptive psychiatry was initially introduced in Europe two centuries ago in the classifications proposed by Pinel (Paris, France), and later by Kraepelin (Munich, Germany) (Frances 2013). After an initial period of more dimensional diagnostic thinking initiated and supported by the American psychoanalyst movement (DSM I & II), severe critics of the validity and specificity of psychiatric diagnoses in the 1970s (Kendell et al. 1971; Rosenhan 1973) led the American Psychiatric Association (APA) and the National Institute for Mental Health (NIMH) to a drastic reform and a return to a categorical diagnostic system with the publication of the DSM III in 1980 (APA 1980). Since its publication, the number of separate psychiatric diagnosis has substantially increased with each revision and new edition. The great hope that the DSM-5 would mark a return to a more dimensional diagnostic system, closely linked to underlying neurobiological disease markers, has not been fulfilled. The latest version of the DSM has turned out

to be a slightly ameliorated but largely similar and equally categorical version of the previous manual.

Parallel with the increase in "psychiatric diagnoses," epidemiological studies based upon the DSM diagnostic criteria have documented an increasingly high prevalence of comorbidity within both clinical and general population samples. Indeed, it became possible to give several diagnoses at the same time, because diagnoses were no longer theoretically (or sometimes even ideologically) founded, suggesting a certain treatment of the disorder but until now seem to be purely descriptive and based strictly on the type and number of relatively disorder-specific symptoms.

Europe has traditionally been a "cold lover" of the DSM system, and most European countries have adopted the International Classification of Diseases (ICD) developed by the World Health Organization. However, the ICD is also a categorical diagnostic system, carrying the same risk of inflated comorbidity. Both systems create the illusion of separate diseases—the same illusion that stimulates the creation of disease or pathology specialists not only in the mental health field but also in somatic medicine. Indeed, the concept of clear-cut, independent diseases has proven highly attractive for many partners in the broad healthcare industry. Governmental and administrative bodies, healthcare financing organizations, and even patient and family organizations cherish the simplicity of the model. Diagnoses are often used as a way of identifying a problem, but also of providing the rationale that is often mandatory to acquire important benefits (e.g., special accommodations at school, financial reimbursements, etc.). Although it has the advantage of clarity and may have some benefits for those individuals who need a specialized treatment for one specific disorder, the disadvantage of such a system lands largely on the shoulders of those who suffer from multiple, complex, and interacting chronic disorders. These patients are at risk of being underserved by a mental healthcare system that is already struggling with limited financial and human resources.

25.3 Dual Disorders: A Developmental Process?

A growing amount of evidence suggests that psychiatric vulnerabilities early in life underlie an increased risk of loss of control over substance use and/or other addictive behaviors during adolescence or early adulthood (Swendsen et al. 2010). When substance abuse becomes active during adolescence, it negatively influences the course of the initial psychiatric impairment, creating a vicious circle that leads to a full-blown "dual disorder" phenotype in (early) adulthood. The importance of early psychiatric vulnerability is illustrated by the finding that patients with dual disorders whose psychiatric disorders are present prior to the onset of a substance use disorder (SUD) have a worse prognosis than those with an SUD onset that predates a secondary psychiatric disorder. Unfortunately, most patients with dual disorders belong the former "psychiatry first" group (Najt et al. 2011).

Looking at comorbidity from this developmental perspective might offer windows of opportunity. Identifying children or adolescents who are at risk of developing dual disorders in the future may make it possible to provide targeted early prevention and intervention services.

Although the research on risk factors in children and young adolescents is ongoing, a number of factors have been identified that can provide guidance in the development of early interventions. The broader categories of the internalizing and externalizing spectra can be helpful within this context. The early expression of internalizing disorders such as depression or posttraumatic stress disorder (PTSD) during childhood or adolescence (or, more broadly, the sequelae of early childhood adversity, ECA) may open the door to substance abuse (Najt et al. 2011). Crum and colleagues showed that childhood depression is a vulnerability factor for binge drinking and early alcohol dependence among young adolescents (Crum et al. 2008). This is also of great importance given the critical interaction between mood disorders and substance abuse, which serves as a mediating factor in suicidal acts in adolescence. Identifying and treating mood disorders in young people might help to prevent the subsequent development of comorbid addictive behaviors. Even more prevalent are the effects of ECA. Although the prevention of ECA extends far beyond the scope of psychiatry, the early screening and remediation of the negative consequences of ECA should be a high priority in child and adolescent mental health care. Studies increasingly show that ECA with or without PTSD is an important vulnerability factor for a broad range of addictive and other psychiatric disorders (e.g., personality disorders, schizophrenia, mood and anxiety disorders) and their comorbidity. A textbook example is the finding that patients with schizophrenia and substance use disorders report much higher levels of early life stress and PTSD (Scheller-Gilkey et al. 2004).

Within the externalizing spectrum, evidence is accumulating that impairments in self-regulation processes manifested during childhood are associated with an increased risk of developing the adult psychiatric disorders (both internalizing and externalizing) that frequently co-occur with addictive disorders (Tarter et al. 2002, 2003; Reef et al. 2011). For example, children with ADHD run an increased risk of developing substance use disorders in young adulthood, particularly when their ADHD is associated with disruptive behavioral disorders (conduct disorder) (Bihlar Muld et al. 2013; Wilens et al. 2011; Harty et al. 2013). Early treatment with psychostimulant medications seems to reduce the risk of later substance use problems (Purgato and Cortese 2014). Moreover, the early identification and treatment of children with severe behavioral problems has proven to reduce the risk of developing psychiatric disorders and addictions later in life (Furlong et al. 2013).

Finally, within the psychotic spectrum, the relationship between early and continued cannabis use, subthreshold psychotic symptoms, and the risk of developing chronic schizophrenia at a later age has been documented extensively (Kuepper et al. 2011). The early identification and treatment of young people who experience psychotic symptoms as a reaction to cannabis might help reduce the incidence of schizophrenia with comorbid substance abuse (Lower et al. 2014).

Even taken together, these types of early intervention and screening for high-risk individuals are only in their infancy. However, this might be an important direction to take to help young people deal with a world characterized by a high availability of potentially addictive substances (legal and illegal) and behaviors (e.g., internet, gambling, and gaming). For these high-risk young people, selective, personality-targeted prevention programs appear promising and effective (Conrod et al. 2013).

Within the context of early identification and treatment, important ethical questions need to be addressed. The risk of labeling (and stigmatizing) too many children who may have risk factors or subthreshold symptoms, but who will never develop problems in adulthood, remains a real danger. However, the negative effects of early externalizing behavioral problems on later-life trajectories are currently so well documented that the gains of early interventions will probably outweigh the potential negative effects.

25.4 Integration of Treatment Systems and Disorder-specific Interventions

The integration of treatment systems and disorder-specific interventions was proposed many years ago and has been assumed to be effective for patients with dual disorders. According to experts in the treatment of patients with dual disorders, it is more effective to treat two or more disorders using an integrated treatment approach than it is to use parallel treatments (i.e., simultaneous but uncoordinated treatments) or serial treatments (i.e., one treatment at a time) provided by different healthcare providers. Integration addresses two fundamental concerns: (a) improving access to mental health and addiction interventions by offering them at the same time, in the same setting, and by the same health professionals and (b) improving individualization and clinical relevance by combining multiple intervention types (Drake et al. 2008).

25.4.1 Integrating Mental Health and Addiction Care

Although there is a great deal of variability between the different European countries, overall, the division between mental health and addiction care still holds strong. As has become evident throughout this book, the traditional split between the two care systems is doing more harm than good to the management of patients with dual disorders as it builds unnecessary barriers impairing the organization of effective care. Consequently, treatments that focus on a single disorder and deal with only a part of the patient's problems result in poor treatment engagement, high dropout rates, and a ping-pong effect between facilities. The consequences are poor overall treatment outcomes and low treatment satisfaction among patients (Schulte et al. 2011). Overall, the many examples presented throughout the chapters of this book make a strong case for the development of one mental healthcare system that integrates addiction care.

However, the concept of integrated treatment can be divided into two different levels. The first level is often referred to as a coordination strategy for the delivery of treatment to patients with dual disorders, which may sometimes include integration between different healthcare systems (e.g., psychiatric and addiction systems) as is the case in Scandinavian countries. For example, standard or intensive case management could be considered an integrated treatment strategy that brings interventions for substance use disorders together under a single psychiatric team or coordinates various treatments available in psychiatric and addiction systems, sometimes through a case manager. Case management certainly supports multiple interventions, but these interventions are not considered single, dual, or triple disorder-specific treatments.

The second level is the integration of disorder-specific treatment interventions for psychiatric and substance use disorders into a single program. Unfortunately, it is not often clear how to best integrate these disorder-specific interventions. Adding one or more disorder-specific interventions to treatment as usual reflects more of a parallel treatment approach than an integrated treatment program. Having an integrated treatment program also means that healthcare professionals must be provided with training in both mental health and addiction treatments. With dual training, they will have skills to help their patients develop an understanding of how their psychiatric and substance use disorders interact, motivate their patients to make sustained behavioral changes by overcoming ambivalence, set joint treatment goals, and help them take steps to reach their goals while supporting quality of life (Moggi et al. 2002).

In Chap. 18, Moggi and Öjehagen extensively discuss important ingredients of effective integrated psychosocial treatments. First, efficacious treatments for psychiatric disorders also tend to work in patients with dual disorders. Second, efficacious treatments for reducing substance use also decrease substance use in patients with dual disorders. Third, although the efficacy of integrating treatments and treatment systems is still unclear, programs that combine motivational enhancement with the simultaneous administration of disorder-specific cognitive-behavioral interventions for both psychiatric and substance use disorders, along with family interventions when necessary, are more likely to meet the treatment goals of patients with dual disorders. Finally, a reduction and/or stabilization of substance use appear necessary to obtain clinically significant improvements and effectively treat the psychiatric disorder. However, there is one more domain to consider: the integration of somatic care.

25.4.2 Integrating Mental Health and Somatic-Medical Care Systems

Compared with individuals in the general population, patients with severe and complex psychiatric disorders have increasingly high rates of severe somatic problems that are often undertreated. As indicated in the introduction of this chapter, mental and somatic health problems result in a higher burden of medical

Table 25.1 Factors underlying the excess in mortality due to diseases and medical conditions

1. Effects of comorbid substance abuse, specifically alcohol and tobacco smoking
2. Unhealthy lifestyle, related to a lack of health literacy and the failure of health promotion initiatives to target this vulnerable population, among which there may be a reduced ability to understand the need for behavioral changes
3. Underdiagnosis and under-treatment of somatic disorders among people with mental illnesses
4. Iatrogenic morbidity, i.e., obesity, cardiovascular diseases, and diabetes due to the adverse effects of psychotropic medication (Manu et al. 2014)
5. Common genetic risk factors for psychiatric and somatic disorders (Hansen et al. 2011)

diseases and higher mortality rates (Nordentoft et al. 2013). After important external causes, such as suicide, overdoses, and accidents, the surplus of mortality is largely attributed to a broad range of medical disorders (e.g., cardiovascular diseases, diabetes, infectious diseases; see Table 25.1). These and other data point to the real need to screen much more closely for medical disorders in psychiatric patients and to effectively treat the medical disorders that are identified. Specifically, comorbid substance abuse is associated with high disease morbidity. It is important to note that homeless individuals, many of whom suffer from comorbid disorders, are particularly vulnerable to severe medical conditions (Nielsen et al. 2011). These and other examples strongly point to the need to more closely integrate medical and psychiatric care services, especially for patients with complex dual disorders.

25.5 Recovery: Outcomes of Real-life Importance

To date, most studies exploring the effectiveness of treatments for patients with dual disorders have used rather traditional outcome variables, such as abstinence from substance use and a reduced severity of psychiatric symptoms. However, it is increasingly evident that outcome variables need to reflect much more than just psychiatric symptoms, especially with chronic, complex disorders. Indeed, given the chronicity and continuous risk of relapse that these disorders entail, it might be much more valuable for patients to achieve gains in other aspects of their lives, such as obtaining good housing and work situations. Furthermore, users of the mental health system (patients, clients) in many countries have lodged strong objections against the existing mental health system, indicating that their treatment professionals' goals of symptom stabilization do not correspond to their aspirations for recovery (Drake and Latimer 2012). Although very different for each individual, *recovery* typically encompasses opportunities for education, work, independent living, and community participation. Based on this view of recovery, service users argue that they want to play a more meaningful role in decisions regarding their care and in the delivery of services.

Focusing on outcomes relevant from the recovery perspective is a meaningful approach to the treatment of patients with dual disorders. In an interesting 10-year longitudinal follow-up study, Xie and colleagues identified their outcome variables

in collaboration with their patients through a shared decision-making process (Xie et al. 2010). They established six domains of interest to both patients and care providers: (1) control over psychotic symptoms; (2) remission of problematic substance use; (3) independent living; (4) competitive (paid) work; (5) social contact with non-substance users; and, (6) general quality of life. A 3-year integrated outpatient treatment program produced improvements in all domains for a majority of patients. Interestingly, these changes occurred during the active treatment phase and continued to occur during the posttreatment follow-up phase. This suggests that making positive changes in areas that the patients themselves consider important might stimulate further growth and recovery, even after active treatment. Engaging patients and caregivers in a process of shared decision making with respect to treatment goals and service delivery has proven to be effective in both reducing substance use and increasing patient autonomy (Joosten et al. 2009, 2011).

Employment has become a central goal of mental health treatment for patients with serious mental illnesses. Indeed, improved psychiatric and substance use symptom severity, autonomy, and quality of life on the one hand, and highly significant reductions in healthcare service use and related costs on the other hand, are associated with steady employment among patients with dual disorders (Bush et al. 2009; McHugo et al. 2012). Thus, helping patients achieve competitive employment should be a prime goal with integrated treatment delivery. However, it is important to note that some programs need to be tailored to the patient. Recently, in a large European study, Knapp and colleagues showed that an Individual Placement and Support (IPS) program is a promising approach to establishing patients in paid employment (Knapp et al. 2013). In this study, IPS produced better outcomes than alternative (standard) vocational services, at a lower overall cost to the healthcare and social service systems. This pattern also held true for five of the six European sites when each site was analyzed separately, indicating that this approach can be implemented within different treatment systems and cultures. Compared to standard vocational rehabilitation services, IPS is therefore probably a cost-saving, cost-effective way to help patients with severe mental health problems secure and retain competitive employment.

Finally, safe, high quality *housing* is of great importance for patients to sustain positive life changes. However, this is currently one of the most difficult goals to achieve. Given the enormous increase in housing prices in most European countries, housing that is affordable for people who have low socioeconomic profiles, as do the majority of patients severely affected by dual disorders, is extremely limited. This shortage leads to hospitalizations, lengthens hospital stays, and increases the use of homeless facilities. Given the immense pressure in many European countries to drastically reduce in-patient capacity, safe housing is increasingly becoming a major problem. Patients with dual disorders in particular tend to find housing problematic. Indeed, sheltered housing facilities organized within the healthcare system are still largely "full abstinence" oriented, filtering out the most severe—and the most needy—patients.

For a long time, *abstinence* was the one and only goal of addiction treatment. Today, however, decreasing the amount of alcohol consumed in order to reduce high-risk drinking behaviors is an accepted treatment goal for many clinicians and some of the most influential agencies, such as the National Institute on Alcohol Abuse and Alcoholism (NIAAA) in the U.S. and the European Medicine Agency (EMA) (van Amsterdam and van den Brink 2013). The results of a randomized controlled trial have recently been published showing that patients with alcohol dependence can learn to reduce their drinking by taking nalmefene (not currently registered in the USA) and participating in a motivational and adherence-enhancing psychosocial intervention (i.e., the BRENDA model). Interestingly, the placebo control group in the BRENDA trial also demonstrated considerable reductions in the number of heavy drinking days and the total amount of alcohol consumed, suggesting that patients can change their alcohol use without a verum medication if they are motivationally supported (Mann et al. 2013). Harm reduction as a treatment strategy has been accepted for drug dependence for many years. The insistence on abstinence caused more harm than good, because many young drug-dependent patients did not succeed in remaining abstinent, which cost them their jobs, their homes, their health, and eventually their lives. Heroin-assisted treatment trials showed that providing heroin on a regular and externally controlled basis brings addicted patients back into treatment and helps them progress toward a higher quality of life (Fischer et al. 2007). Unfortunately, research on the controlled use of alcohol and/or drugs has not been conducted among patients with dual disorders, because studies on controlled substances usually exclude patients with a psychiatric comorbidity. Many of the studies reported throughout this book have shown that patients can obtain improved psychiatric and social functioning outcomes even if they continue using substances. It seems that improvement is possible, as long as the consumption of substances can be reduced and stabilized using external approaches (e.g., heroin-assisted treatment, methadone treatment) and/or internal behavioral management (e.g., controlled drinking). This is a promising observation that might encourage researchers to develop treatments that are open to a variety of substance use goals.

25.6 It Is All About the Money

In most countries, there is typically a great deal of tension between the need for mental health care and the amount of money that society effectively spends on it. There is also a great deal of variation between countries. The proportion of total health expenditures that is allocated to mental health care range from as low as 3 % in Poland to 13 % in the UK, with a mean of about 5–6 % in Western Europe. In comparison, 5–12 % of health expenditures are devoted to behavioral health in the USA and 7.2 % in Canada (Frank et al. 2009). Financial constraints, partly due to the economic crisis in Europe, have forced most countries to either reduce their mental health expenditures (e.g., the Netherlands) or to increasingly force program

developers to take into account the health economics or cost–benefit aspect of care delivery.

Unfortunately, a sizeable proportion of patients with dual disorders belong to the category of patients with the highest treatment costs. Indeed, they are often among those with multiple, severe psychiatric and somatic illnesses, the greatest amount of disability, and the least family or community support; they also need the highest level of treatment integration, rehabilitation, and support services. Providing comprehensive, fully integrated care to these individuals is expensive. However, studies focusing on health economics increasingly show that this investment not only mitigates personal suffering but may also be no more costly when organized efficiently; in addition—and most importantly—this approach avoids shifting the costs to families, communities, and the criminal justice system (Larimer et al. 2009). Even less intensive interventions, such as contingency management (CM) aiming to reduce substance use in patients with severe psychiatric illnesses, can have substantial cost-reducing effects (e.g., fewer emergency hospitalization days) (Angelo et al. 2013; McDonell et al. 2013). Depending on the individual's symptom severity level and related impairments, creative combinations of different therapeutic approaches are likely needed to meet the specific needs of patients with comorbidities; for example, a severely affected patient with schizophrenia and substance abuse may require motivational interviewing (MI) + CM + CBT + pharmacotherapy, while a less-impaired patient with an anxiety disorder and substance abuse may require fewer interventions (Kelly et al. 2012).

Final Considerations and Conclusions

Where should we be going in Europe? First, a major challenge for many (all) European countries is to provide adequate human resources to deliver essential mental health interventions. There are major differences between European countries in terms of national income, and, closely related to this, the health resources that are available. The proportion of national resources being invested in mental health vary widely between countries, reflecting different political priorities, but also cultural differences in attitudes and even levels of stigma toward individuals with mental health problems. In many countries, patients with dual disorders are particularly affected by stigmatization and a lack of appropriate services. In addition, it has been suggested that the economic crisis, which has most severely affected southern European countries, has had a major, negative impact on both the prevalence and course of severe, complex psychiatric problems (Anakwenze and Zuberi 2013). In particular, when combined with early childhood adversity, poverty is associated with an increased risk of both the onset of substance use and the transition toward substance abuse (Benjet et al. 2013). Political action is needed to stimulate a reappraisal of the way mental health expenditures are allocated in order to alleviate the consequences of the economic burden, at least for the most vulnerable families.

An important factor underlying the lower quality of care for patients with dual disorders is the separation between mental healthcare services, addiction

services, and somatic-medical services. Different organizations, different types of professional caregivers, different educational backgrounds, and differences in funding and insurance regulations reflect this separation. Thus, the most important goal for Europe would be to mandate *equal parity* between mental health care (including substance use disorders) and somatic health care in every country, if possible under European guidance. Indeed, the editors sincerely hope that, throughout the different chapters in this book, it has been obvious to readers that this separation should be considered archaic at the current stage of development of psychiatric care, doing (much) more harm than good. The high prevalence of patients with dual disorders within all care systems, with their multiple needs, underscores the urgent need to achieve a fundamental integration of these different care systems. This will make it possible to improve the quality of care and efficiency of care delivery, ultimately with an overall better cost–benefit ratio (Dewa et al. 2009; Hoch and Dewa 2014).

Collaborative care requires integrating a wide variety of services (e.g., somatic care, housing, work-day activities) and adopting a patient-focused approach that links these services to the specific needs of each patient, whenever and wherever the services are needed; for example, when patients are hospitalized for severe somatic complications, this can be an excellent opportunity to engage them in psychiatric and/or substance use treatment. Care systems need to be reorganized in order to make this collaborative process available. Both the mental health and addiction treatment systems need to increase their capability to handle the multiple needs of patients with dual disorders. To enhance this process, practical European guidance mechanisms need to be developed. In addition, within the training curricula of the different mental health professions, more focus needs to be placed on the management of patients with multiple, complex problems. Indeed, most current training programs and clinical guidelines focus on the management (diagnosis, treatment) of single, specific disorders. This contrasts with the clinical reality and the needs of most patients with dual disorders, as well as with the collaborative care approach.

To conclude, research, training programs, and guideline development efforts have focused on reducing psychiatric symptoms, as defined by the DSM or ICD, as the ultimate outcome goals. There is a clear need for a European consensus that, for patients with complex dual disorders, outcome needs to be more broadly defined; the new target outcomes need to include not only a reduction in psychiatric and addiction symptomatology but also—and most importantly—variables reflecting a reconnection with and reintegration into society (e.g., housing, work-day activities), as well as subjective improvements identified by the individuals themselves (e.g., quality of life, self-esteem, and shared decision making in the treatment processes). Indeed, it is the latter category of targets that empowers patients with dual disorders to achieve sustainable change.

References

Anakwenze U, Zuberi D (2013) Mental health and poverty in the inner city. Health Soc Work 38 (3):147–157

Angelo FN, McDonell MG, Lewin MR, Srebnik D, Lowe J, Roll J, Ries R (2013) Predictors of stimulant abuse treatment outcomes in severely mentally ill outpatients. Drug Alcohol Depend 131(1–2):162–165. doi:10.1016/j.drugalcdep.2012.11.017

Benjet C, Borges G, Medina-Mora ME, Mendez E (2013) Chronic childhood adversity and stages of substance use involvement in adolescents. Drug Alcohol Depend 131(1–2):85–91. doi:10.1016/j.drugalcdep.2012.12.002

Bihlar Muld B, Jokinen J, Bolte S, Hirvikoski T (2013) Attention deficit/hyperactivity disorders with co-existing substance use disorder is characterized by early antisocial behaviour and poor cognitive skills. BMC Psychiatry 13:336. doi:10.1186/1471-244X-13-336

Bobes J, Arango C, Garcia-Garcia M, Rejas J (2010) Healthy lifestyle habits and 10-year cardiovascular risk in schizophrenia spectrum disorders: an analysis of the impact of smoking tobacco in the CLAMORS schizophrenia cohort. Schizophr Res 119(1–3):101–109. doi:10.1016/j.schres.2010.02.1030

Bush PW, Drake RE, Xie H, McHugo GJ, Haslett WR (2009) The long-term impact of employment on mental health service use and costs for persons with severe mental illness. Psychiatr Serv 60(8):1024–1031. doi:10.1176/appi.ps.60.8.1024

Conrod PJ, O'Leary-Barrett M, Newton N, Topper L, Castellanos-Ryan N, Mackie C, Girard A (2013) Effectiveness of a selective, personality-targeted prevention program for adolescent alcohol use and misuse: a cluster randomized controlled trial. JAMA Psychiatry 70(3):334–342. doi:10.1001/jamapsychiatry.2013.651

Crum RM, Green KM, Storr CL, Chan YF, Ialongo N, Stuart EA, Anthony JC (2008) Depressed mood in childhood and subsequent alcohol use through adolescence and young adulthood. Arch Gen Psychiatry 65(6):702–712. doi:10.1001/archpsyc.65.6.702

Detsky AS, Gauthier SR, Fuchs VR (2012) Specialization in medicine: how much is appropriate? JAMA 307(5):463–464. doi:10.1001/jama.2012.44

Dewa CS, Hoch JS, Carmen G, Guscott R, Anderson C (2009) Cost, effectiveness, and cost-effectiveness of a collaborative mental health care program for people receiving short-term disability benefits for psychiatric disorders. Can J Psychiatry 54(6):379–388

Drake RE, Latimer E (2012) Lessons learned in developing community mental health care in North America. World Psychiatry 11(1):47–51

Drake RE, O'Neal EL, Wallach MA (2008) A systematic review of psychosocial research on psychosocial interventions for people with co-occurring severe mental and substance use disorders. J Subst Abuse Treat 34(1):123–138. doi:10.1016/j.jsat.2007.01.011

Fischer B, Oviedo-Joekes E, Blanken P, Haasen C, Rehm J, Schechter MT, Strang J, van den Brink W (2007) Heroin-assisted treatment (HAT) a decade later: a brief update on science and politics. J Urban Health 84(4):552–562. doi:10.1007/s11524-007-9198-y

Frances A (2013) The past, present and future of psychiatric diagnosis. World Psychiatry 12 (2):111–112. doi:10.1002/wps.20027

Frank RG, Goldman HH, McGuire TG (2009) Trends in mental health cost growth: an expanded role for management? Health Aff 28(3):649–659. doi:10.1377/hlthaff.28.3.649

Furlong M, McGilloway S, Bywater T, Hutchings J, Smith SM, Donnelly M (2013) Cochrane review: behavioural and cognitive-behavioural group-based parenting programmes for early-onset conduct problems in children aged 3 to 12 years (Review). Evid Based Child Health 8 (2):318–692. doi:10.1002/ebch.1905

Gaebel W, Becker T, Janssen B, Munk-Jorgensen P, Musalek M, Rossler W, Sommerlad K, Tansella M, Thornicroft G, Zielasek J, European Psychiatric A (2012) EPA guidance on the quality of mental health services. Eur Psychiatry 27(2):87–113. doi:10.1016/j.eurpsy.2011.12.001

Hansen T, Ingason A, Djurovic S, Melle I, Fenger M, Gustafsson O, Jakobsen KD, Rasmussen HB, Tosato S, Rietschel M, Frank J, Owen M, Bonetto C, Suvisaari J, Thygesen JH, Petursson H, Lonnqvist J, Sigurdsson E, Giegling I, Craddock N, O'Donovan MC, Ruggeri M, Cichon S, Ophoff RA, Pietilainen O, Peltonen L, Nothen MM, Rujescu D, St Clair D, Collier DA, Andreassen OA, Werge T (2011) At-risk variant in TCF7L2 for type II diabetes increases risk of schizophrenia. Biol Psychiatry 70(1):59–63. doi:10.1016/j.biopsych.2011.01.031

Harty SC, Galanopoulos S, Newcorn JH, Halperin JM (2013) Delinquency, aggression, and attention-related problem behaviors differentially predict adolescent substance use in individuals diagnosed with ADHD. Am J Addict 22(6):543–550. doi:10.1111/j.1521-0391.2013.12015.x

Hoch JS, Dewa CS (2014) Advantages of the net benefit regression framework for economic evaluations of interventions in the workplace: a case study of the cost-effectiveness of a collaborative mental health care program for people receiving short-term disability benefits for psychiatric disorders. J Occup Environ Med 56(4):441–445. doi:10.1097/JOM.0000000000000130

Joosten EA, de Jong CA, de Weert-van Oene GH, Sensky T, van der Staak CP (2009) Shared decision-making reduces drug use and psychiatric severity in substance-dependent patients. Psychother Psychosom 78(4):245–253. doi:10.1159/000219524

Joosten EA, De Jong CA, de Weert-van Oene GH, Sensky T, van der Staak CP (2011) Shared decision-making: increases autonomy in substance-dependent patients. Subst Use Misuse 46(8):1037–1038. doi:10.3109/10826084.2011.552931

Kelly TM, Daley DC, Douaihy AB (2012) Treatment of substance abusing patients with comorbid psychiatric disorders. Addict Behav 37(1):11–24. doi:10.1016/j.addbeh.2011.09.010

Kendell RE, Cooper JE, Gourlay AJ, Copeland JR, Sharpe L, Gurland BJ (1971) Diagnostic criteria of American and British psychiatrists. Arch Gen Psychiatry 25(2):123–130

Knapp M, Patel A, Curran C, Latimer E, Catty J, Becker T, Drake RE, Fioritti A, Kilian R, Lauber C, Rossler W, Tomov T, van Busschbach J, Comas-Herrera A, White S, Wiersma D, Burns T (2013) Supported employment: cost-effectiveness across six European sites. World Psychiatry 12(1):60–68. doi:10.1002/wps.20017

Kuepper R, van Os J, Lieb R, Wittchen HU, Hofler M, Henquet C (2011) Continued cannabis use and risk of incidence and persistence of psychotic symptoms: 10 year follow-up cohort study. BMJ 342:d738. doi:10.1136/bmj.d738

Larimer ME, Malone DK, Garner MD, Atkins DC, Burlingham B, Lonczak HS, Tanzer K, Ginzler J, Clifasefi SL, Hobson WG, Marlatt GA (2009) Health care and public service use and costs before and after provision of housing for chronically homeless persons with severe alcohol problems. JAMA 301(13):1349–1357. doi:10.1001/jama.2009.414

Lower R, Wilson J, Medin E, Corlett E, Turner R, Wheeler K, Fowler D (2014) Evaluating an early intervention in psychosis service for 'high-risk' adolescents: symptomatic and social recovery outcomes. Early Interv Psychiatry. doi:10.1111/eip.12139

Mann K, Bladstrom A, Torup L, Gual A, van den Brink W (2013) Extending the treatment options in alcohol dependence: a randomized controlled study of as-needed nalmefene. Biol Psychiatry 73(8):706–713. doi:10.1016/j.biopsych.2012.10.020

Manu P, Correll CU, Wampers M, van Winkel R, Yu W, Shiffeldrim D, De Hert M (2014) Dysmetabolic features of the overweight patients receiving antipsychotic drugs: a comparison with normal weight and obese subjects. Eur Psychiatry 29(3):179–182. doi:10.1016/j.eurpsy.2012.12.001

McDonell MG, Srebnik D, Angelo F, McPherson S, Lowe JM, Sugar A, Short RA, Roll JM, Ries RK (2013) Randomized controlled trial of contingency management for stimulant use in community mental health patients with serious mental illness. Am J Psychiatry 170(1):94–101. doi:10.1176/appi.ajp.2012.11121831

McHugo GJ, Drake RE, Xie H, Bond GR (2012) A 10-year study of steady employment and non-vocational outcomes among people with serious mental illness and co-occurring substance use disorders. Schizophr Res 138(2–3):233–239. doi:10.1016/j.schres.2012.04.007

Moggi F, Brodbeck J, Költzsch K, Bachmann KM (2002) One-year follow-up of dual diagnosis patients attending a 4-months integrative inpatient treatment. Eur Addict Res 8:30–37

Mortimer AM (2003) Antipsychotic treatment in schizophrenia: atypical options and NICE guidance. Eur Psychiatry 18(5):209–219

Najt P, Fusar-Poli P, Brambilla P (2011) Co-occurring mental and substance abuse disorders: a review on the potential predictors and clinical outcomes. Psychiatry Res 186(2–3):159–164. doi:10.1016/j.psychres.2010.07.042

Nielsen SF, Hjorthoj CR, Erlangsen A, Nordentoft M (2011) Psychiatric disorders and mortality among people in homeless shelters in Denmark: a nationwide register-based cohort study. Lancet 377(9784):2205–2214. doi:10.1016/S0140-6736(11)60747-2

Nordentoft M, Wahlbeck K, Hallgren J, Westman J, Osby U, Alinaghizadeh H, Gissler M, Laursen TM (2013) Excess mortality, causes of death and life expectancy in 270,770 patients with recent onset of mental disorders in Denmark, Finland and Sweden. PloS one 8(1):e55176. doi:10.1371/journal.pone.0055176

Purgato M, Cortese S (2014) Does psychostimulant treatment in children with ADHD increase later risk of substance use disorder? Epidemiol Psychiatr Sci 23:1–3. doi:10.1017/S2045796014000146

Reef J, Diamantopoulou S, van Meurs I, Verhulst FC, van der Ende J (2011) Developmental trajectories of child to adolescent externalizing behavior and adult DSM-IV disorder: results of a 24-year longitudinal study. Soc Psychiatry Psychiatr Epidemiol 46(12):1233–1241. doi:10.1007/s00127-010-0297-9

Rosenhan DL (1973) On being sane in insane places. Science 179(4070):250–258

Ruther T, Bobes J, De Hert M, Svensson TH, Mann K, Batra A, Gorwood P, Moller HJ (2014) EPA guidance on tobacco dependence and strategies for smoking cessation in people with mental illness. Eur Psychiatry 29(2):65–82. doi:10.1016/j.eurpsy.2013.11.002

Scheller-Gilkey G, Moynes K, Cooper I, Kant C, Miller AH (2004) Early life stress and PTSD symptoms in patients with comorbid schizophrenia and substance abuse. Schizophr Res 69(2–3):167–174

Schulte SJ, Meier PS, Stirling J (2011) Dual diagnosis clients' treatment satisfaction—a systematic review. BMC Psychiatry 11:64. doi:10.1186/1471-244X-11-64

Swendsen J, Conway KP, Degenhardt L, Glantz M, Jin R, Merikangas KR, Sampson N, Kessler RC (2010) Mental disorders as risk factors for substance use, abuse and dependence: results from the 10-year follow-up of the National Comorbidity Survey. Addiction 105(6):1117–1128. doi:10.1111/j.1360-0443.2010.02902.x

Tarter RE, Kirisci L, Vanyukov M, Cornelius J, Pajer K, Shoal GD, Giancola PR (2002) Predicting adolescent violence: impact of family history, substance use, psychiatric history, and social adjustment. Am J Psychiatry 159(9):1541–1547

Tarter RE, Kirisci L, Mezzich A, Cornelius JR, Pajer K, Vanyukov M, Gardner W, Blackson T, Clark D (2003) Neurobehavioral disinhibition in childhood predicts early age at onset of substance use disorder. Am J Psychiatry 160(6):1078–1085

van Amsterdam JV, van den Brink W (2013) Reduced-risk drinking as a viable treatment goal in problematic alcohol use and alcohol dependence. J Psychopharmacol. doi:10.1177/0269881113495320

Wilens TE, Martelon M, Joshi G, Bateman C, Fried R, Petty C, Biederman J (2011) Does ADHD predict substance-use disorders? A 10-year follow-up study of young adults with ADHD. J Am Acad Child Adolesc Psychiatry 50(6):543–553. doi:10.1016/j.jaac.2011.01.021

Xie H, Drake RE, McHugo GJ, Xie L, Mohandas A (2010) The 10-year course of remission, abstinence, and recovery in dual diagnosis. J Subst Abuse Treat 39(2):132–140. doi:10.1016/j.jsat.2010.05.011