

---

# Comorbid Anxiety and Alcohol or Substance Use Disorders: An Overview

# 119

Francesco Bartoli, Daniele Carretta, Massimo Clerici, and Giuseppe Carrà

## Contents

119.1	Introduction .....	1972
119.2	Epidemiological and Clinical Issues .....	1972
119.2.1	Epidemiology .....	1972
119.2.2	Etiological Hypotheses and Temporal Relationships .....	1974
119.2.3	Diagnosis and Classification .....	1976
119.2.4	Clinical Features, Course, and Prognosis .....	1978
119.2.5	Treatment and Management .....	1979
119.3	Conclusion .....	1980
	References .....	1981

---

## Abstract

The comorbidity between anxiety and alcohol or substance use disorders represents a common and serious clinical challenge, characterized by a high worldwide prevalence. The co-occurrence of these disorders complicates treatment, management, and prognosis of both disorders, but it remains often unrecognized and untreated. Mental health professionals should accurately assess and evaluate the comorbidity, although related etiological links and temporal relationships are still unclear and, probably, heterogeneous and multifactorial. Alcohol and substances may be misused by individuals to self-medicate their anxiety, avoidant, and phobic symptoms, but also anxiety disorders may be consequences of alcohol and/or substance misuse. Integrated treatment appears the most promising approach, but there is paucity of evidence on pharmacological and

---

F. Bartoli (✉) • D. Carretta • M. Clerici

Department of Surgery and Translational Medicine, University of Milano-Bicocca, Milano, Italy  
e-mail: [f.bartoli@campus.unimib.it](mailto:f.bartoli@campus.unimib.it); [d.carretta1@campus.unimib.it](mailto:d.carretta1@campus.unimib.it); [massimo.clerici@unimib.it](mailto:massimo.clerici@unimib.it)

G. Carrà

UCL Division of Psychiatry, Faculty of Brain Sciences, University College London, London, UK  
e-mail: [g.carra@ucl.ac.uk](mailto:g.carra@ucl.ac.uk)

non-pharmacological treatments addressed to both anxiety and substance use disorders. This chapter provides a comprehensive overview of main epidemiological and clinical issues, etiological/temporal links hypotheses, and treatment options for the comorbidity between anxiety and addictive behaviors.

---

## 119.1 Introduction

Comorbid anxiety and alcohol or substance use disorders represent a serious clinical challenge, influencing both treatment and prognosis (Smith and Randall 2012). Clinical evidence demonstrates that people with anxiety disorders, such as social phobia, generalized anxiety, panic, agoraphobia without history of panic, and specific phobia disorders, often misuse alcohol and prescription (e.g., benzodiazepines) and/or illicit drugs (e.g., stimulants or cannabinoids), developing substance abuse or dependence. At the same time, individuals primarily treated for an alcohol or drug use disorder are more likely to suffer from a comorbid anxiety disorder, due to the effect of substances in inducing anxiety symptoms (Pasche 2012).

All clinicians and mental health professionals who care for people with anxiety and substance use disorders should have a comprehensive knowledge of main relevant clinical and epidemiological issues such as:

- Prevalence and correlates of substance use disorders among subjects suffering from anxiety disorders
- Etiological hypotheses and temporal relationships underlying this comorbidity
- Methods to assess this comorbidity and to classify comorbid anxiety and alcohol/substance use disorders, taking mainly into account important changes introduced by the recently released fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) (American Psychiatric Association 2013)
- Specific clinical features, course, and prognosis of people suffering from this comorbidity
- Main evidence on preventive and treatment strategies

In this chapter, we aimed to present a comprehensive overview on these issues, highlighting data derived from research which may be useful to the clinical routine.

---

## 119.2 Epidemiological and Clinical Issues

### 119.2.1 Epidemiology

Comorbid anxiety and alcohol or substance use disorders are highly prevalent both in general and clinical populations (Pasche 2012). Data from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) on 43,093 adults shows that the 12-month prevalence of any DSM-IV substance use disorder among respondents with a 12 month DSM-IV independent anxiety disorder is 15.0 % (Grant et al. 2004). As regards specific drug use disorders involved, cannabis use was the most common (15.1 %), followed by cocaine (5.4 %), amphetamine (4.8 %),

hallucinogen (3.7 %), opioid (3.2 %), sedative (2.6 %), tranquilizer (2.5 %), and inhalant/solvent (0.6 %) use disorders (Conway et al. 2006). People suffering from any anxiety disorder had an odds ratio (OR) of 1.9 (1.7–2.1) for any substance use disorder and of 1.7 (1.5–2.0) for any alcohol use disorder. The likelihood to develop a dependence syndrome was high with ORs of 2.8 (2.4–3.2) and 2.6 (2.2–3.0) for substance and alcohol dependence, respectively (Grant et al. 2004). Panic disorder with agoraphobia seems to show the strongest association with a co-occurring substance use disorder.

Other relevant data from North American samples are provided by the Mental Health Supplement to the Ontario Health Survey (Gratzer et al. 2004), a Canadian study on 7,195 individuals aged 15–64 years, and interviewed using the World Mental Health Composite International Diagnostic Interview (CIDI). A lifetime alcohol abuse or dependence by diagnostic subgroup was found in 8.7 % of people with any anxiety disorder (OR vs. healthy controls: 3.4; 95 % CI: 1.6–7.1) and in 18.0 % of people with comorbid anxiety and depressive disorders (OR vs. healthy controls: 7.6; 95 % CI: 3.5–16.7).

Relevant epidemiological data are available also from European populations. Data from the French representative sample of the Mental Health in General Population (MHGP) survey (Leray et al. 2011) on 36,105 adults showed a prevalence for alcohol abuse of 7.1 %, 6.5 %, 4.9 %, and 3.6 % among subjects suffering from agoraphobia, panic disorder, social phobia, generalized anxiety disorder, respectively. The results highlighted an OR of 1.7 (1.4–2.0) for alcohol abuse among people with any anxiety disorder. Similar results were found for drug addiction, with a prevalence of 6.5 %, 4.4 %, 3.7 %, and 2.8 % among individuals suffering from panic disorder, social phobia, agoraphobia, and panic disorder, respectively. Drug addiction was significantly associated with the diagnosis of any anxiety disorder, with an overall OR of 2.1 (1.8–2.5).

Baseline data from the Netherlands Study of Depression and Anxiety (NESDA), including 2,329 subjects with lifetime DSM-IV anxiety (social phobia, generalized anxiety disorder, panic disorder, agoraphobia) or depressive disorders and 652 controls, showed a significant association between alcohol dependence and comorbid anxiety disorder (OR: 2.4; 95 % CI: 1.5–3.8) or for an anxiety disorder associated to a depressive disorder (OR: 4.3; 95 % CI: 3.0–6.2) (Boschloo et al. 2011).

Epidemiological data are available also from the National Survey of Mental Health and Well-Being (NSMH&WB) conducted in Australia. This study, involving more than 10,000 adults, showed that the respondents with an alcohol use disorder (abuse or dependence) were three times more likely to suffer from a 12-month anxiety disorder. On the other hand, people suffering from any anxiety disorder had a prevalence of 16.0 % for any past-year alcohol use disorder (Burns and Teesson 2002).

Finally, some relevant epidemiological information is available also from Latin America. For example, a cross-sectional household survey in a sample of 2,302 Brazilian adults from Bahia, Brazil (Almeida-Filho et al. 2007), highlighted a prevalence of comorbid anxiety disorders and alcoholism of 14.4 %, with an OR of 2.7 (1.7–4.2).

Generally, the comorbidity between anxiety and alcohol or substance use disorders appears a worldwide phenomenon, with similar prevalence rates and high and significant risk of co-occurrence as compared with general population.

### 119.2.2 Etiological Hypotheses and Temporal Relationships

The underlying mechanisms influencing the association between anxiety and alcohol/substance use disorders are unclear because of relevant clinical heterogeneity as different drugs and alcohol may not share identical relationships with different anxiety disorders (Kushner et al. 2000). Three main etiological hypotheses are worth to be mentioned.

First, an anxiety disorder may be a direct predictor of addictive behaviors. This direction of the association is supported by evidence suggesting that some individuals may use alcohol and/or illicit substances to self-medicate their anxiety or depressive symptoms (the “self-medication” hypothesis) (Mueser et al. 1998). For example, alcohol shares many pharmacological effects with sedatives, anxiolytic agents, hypnotics, or anticonvulsants drugs (Lingford-Hughes et al. 2002). Further scientific support for the “self-medication” hypothesis comes from longitudinal studies. Data from the NESARC on 34,653 US adults showed that those who had used alcohol or other drugs for the purpose of reducing their fear, anxiety, or avoidance had a significant risk of incident alcohol or substance dependence, with adjusted ORs of 2.6 (1.0–6.7) and 5.0 (1.7–14.2), respectively (Robinson et al. 2011). However, further findings from NESARC (Martins and Gorelick 2011) did not support the self-medication hypothesis, highlighting that both mood and anxiety disorders may influence the transition from substance use to abuse and/or dependence rather than from abstinence to use. The representative National Comorbidity Survey (NCS) showed that a self-medication intent was present in 21.9 % of individuals with any anxiety disorder, with the highest prevalence (35.6 %) among people with a generalized anxiety disorder (Bolton et al. 2006). More generally, social phobia has been predominantly identified as a primary disorder preceding substance use, though the temporality of other anxiety and substance use disorders is less clear (Pasche 2012).

The second etiological hypothesis posits that alcohol and other substances directly promote the development of anxiety syndromes, in terms of consequences of chronic alcohol/substance use and/or related withdrawal syndromes (Kushner et al. 2000). For example, although alcohol is a fast-acting and effective anxiolytic agent, it can also increase the levels of anxiety, when the consumption is excessive and the subjects develop withdrawal symptoms, which determine a vicious cycle between anxiety and alcohol use (Lingford-Hughes et al. 2002). Another relevant example involves early cannabis exposure that may be related to the subsequent development of an anxiety disorder. A recent study (Degenhardt et al. 2013) on a cohort of 1,756 young Australians recruited in secondary schools showed that the continuity of cannabis use from adolescence to the age of 29 was associated to a risk 3–4 times higher of having a comorbid anxiety disorder. Data from the Netherlands

Mental Health Survey and Incidence Study (NEMESIS), a prospective study on 3,854 adults who had no lifetime anxiety disorders at baseline, highlighted a significant association between baseline cannabis use and 3-year incidence of any anxiety disorder (especially generalized anxiety and panic disorders), after adjusting for age, gender, education, urbanicity, employment, and partner status (van Laar et al. 2007).

Furthermore, the existence of anxiety disorders induced by specific classes of substances, such as alcohol, cannabis, cocaine/other stimulants, opioids, is supported by different neurobiological findings. Recent advances on the complex relationships between stress, anxiety, and alcohol use disorders show that synaptic communication in brain regions regulating stress and anxiety-related behaviors, such as amygdala and bed nucleus of the stria terminalis, is modulated by endogenous factors like dopamine and corticotropin-releasing factor (CRF) as well as by acute and chronic use of alcohol (Silberman et al. 2009). The CRF, a stress-related neuropeptide, has been implicated also in the anxiogenic effects of cocaine withdrawal, as well as in some of long-term effects of cocaine (Erb et al. 2006). Cannabis, mainly through the cannabinoid type 1 (CB1) receptors, can induce biphasic responses on anxiety- and fear-related behaviors. Generally, low doses of cannabis tend to induce anxiolytic-like effects, whereas high doses often cause an increase of anxiety symptoms (Moreira and Wotjak 2010). Finally, as regards heroine, morphine, or other opioids, it should be highlighted that the opioid system seems to play a key role in the neural modulation of anxiety. The activation of opioid system leads to anxiolytic effects both in healthy subjects and in individuals suffering from anxiety disorders since the opioid neurotransmission may serve as an adaptive mechanism addressed to blunt acute negative and distressing affective responses (Colasanti et al. 2011). At the same time, blockade or downregulation of opioid systems and second messengers is associated with the occurrence of severe anxiety, similar to opiate withdrawal (Colasanti et al. 2011).

Finally, there may be an independent mediator explaining the relationship between anxiety and alcohol/substance use disorders rather than a direct causal association. Generally, studies on the common-factor models for anxiety and substance use disorders are limited, and publications directly addressing this topic are sparse (Smith and Randall 2012) and focused on alcohol use disorders. Anxiety and alcohol or substance use disorders may share genetic and environmental factors, such as a disruptive family environment and parental abuse or neglect (Kushner et al. 2000). Especially among women, a childhood traumatic event might be at least partially responsible for the association between these two disorders (Marquenie et al. 2007). Mediators of the relationship between anxiety disorders and addictive behaviors may be also some personality traits characterized by a high level of anxiety sensitivity (Smith and Randall 2012). Individuals with increased levels of sensitivity to anxiety, and who do not have a diagnosable anxiety disorder, may be more likely to develop both anxiety and alcohol or substance use disorders. Furthermore, it has been investigated whether some molecular mechanisms could represent the common factor between anxiety and alcohol/substance use disorders. For example, it has been hypothesized that a decreased function of cAMP response

element-binding protein (CREB) in the central nucleus of the amygdala might regulate both anxiety and alcohol intake via the reduced expression of neuropeptide Y (NPY) and, therefore, might provide a common link between anxiety and alcohol use disorders (Pandey 2003).

### 119.2.3 Diagnosis and Classification

Anxiety disorders among people suffering from substance use disorders, as well as alcohol or drug addictive behaviors among people with an anxiety disorder, remain often unrecognized and, consequently, untreated. Despite scientific background of this comorbidity is mainly based on DSM-IV-TR criteria (American Psychiatric Association 2000), future diagnostic issues should necessarily take into account modifications approved by the recently released DSM-5 (American Psychiatric Association 2013). As regards anxiety disorders, these no longer include neither obsessive-compulsive disorder (now in the “obsessive-compulsive and related disorders” chapter) nor posttraumatic and acute stress disorders (included in the “trauma- and stressor-related disorders” chapter). At the same time, DSM-5 includes several changes in criteria of the new chapter “Substance-Related and Addictive Disorders,” such as the exclusion of the abuse/dependence dichotomy, the introduction of craving as a diagnostic criterion, and the dimensional classification of alcohol and substance use disorders. However, no studies on vulnerable populations, such as those suffering from psychiatric disorders, are still available.

Actually, all subjects suffering from any anxiety disorders should be screened for alcohol or substance use disorders at the initial assessment. Early diagnosis and treatment can improve consistently course, prognosis, and treatment outcomes of both disorders. However, often it is difficult to ascertain the diagnosis and to assess whether anxiety symptoms are alcohol or substance induced or represent signs of an independent anxiety disorder (Smith and Randall 2012). Because of the overlapping of symptoms, a detailed interview is often a step needed to fully differentiate symptoms, which should resolve with abstinence, from anxiety and alcohol/substances use disorders. Therefore, it is important to carefully assess not only symptoms but also distinct diagnoses and clinical syndromes using structured diagnostic interviews, such as SCID (Structured Clinical Interview for DSM Disorders) (First et al. 2002), CIDI (Composite International Diagnostic Interview) (Robins et al. 1988), or MINI (Mini-International Neuropsychiatric Interview) (Sheehan et al. 1998). The Psychiatric Research Interview for Substance and Mental Disorders (PRISM) is a semistructured diagnostic interview, designed to maximize reliability and validity in alcohol, drug, and co-occurring disorders, individuals with a good reliability for many psychiatric diagnoses, including substance use and some anxiety disorders (Hasin et al. 1996).

Observing symptoms over a sustained period of abstinence may represent the best way to differentiate substance-induced from independent anxiety disorders. Anxiety may return to baseline levels after the period of withdrawal, so clinicians

should always reevaluate and reassess clinical features after 2–3 weeks of abstinence (Lingford-Hughes et al. 2002). The minimum duration of abstinence to establish the presence of an independent or substance-induced anxiety disorder is heterogeneous and based on half-life of involved drugs. For example, some benzodiazepines or methadone may require several weeks of abstinence to exclude a secondary anxiety disorder, whereas alcohol or cocaine necessitates shorter periods of abstinence to make valid diagnoses (Back and Brady 2008).

In order to diagnose a primary, and not substance-induced, psychiatric disorder, clinicians should verify whether (a) the onset of symptoms occurred before the substance use disorder, (b) the symptoms persist after a period of abstinence according to the characteristics of withdrawal course of each substance, and (c) symptoms exceed those produced by the specific misused substance. On the other hand, clinicians should suspect a secondary anxiety disorder if (a) the anxiety syndrome develops only during periods of active alcohol or substance misuse, (b) the symptoms are well-matched with specific symptoms of intoxication or withdrawal of the involved substance, and (c) the age at onset is atypical for a primary anxiety disorder.

A significant amount of alcohol and substance use screening tools are available and may be helpful to detect potential disorders. For example, the ASSIST (Alcohol, Smoking and Substance Involvement Screening Test), developed for the World Health Organization (WHO), is used to detect substance use and related problems in primary and general medical care settings (Humeniuk et al. 2008). As regards alcohol use disorders, AUDIT (Alcohol Use Disorders Identification Test) (Saunders et al. 1993) is probably the most widely used screening tool. Relatively recent data from the NESDA (Boschloo et al. 2010), including 1,756 individuals suffering from a past-year depressive and/or anxiety disorder, showed that AUDIT accurately detected alcohol dependence in depressed and/or anxious men and women, as compared to the gold standard of a CIDI-based diagnosis. However, the overall accuracy in detecting alcohol abuse was limited, without appropriate and identifiable cutoff scores for sensitivity and specificity.

The Addiction Severity Index (ASI) is a multidimensional and semistructured interview used to measure substance use severity, health-related outcomes, and social problems in individuals suffering from alcohol and other drug use disorders, both at admission to treatment and at follow-up (McLellan et al. 2006). The ASI can be used appropriately for screening of anxiety disorders, since the clusters of psychological composite scores are significantly related to a current psychiatric diagnosis, especially depressive and anxiety disorders (Dixon et al. 1996). Therefore, this instrument may be useful for both evaluation of the substance use severity and screening of patients who need an additional evaluation or treatment for their comorbid psychiatric disorder.

However, psychometric scales and diagnostic interviews need to be always integrated with all other information sources useful to assess and differentiate primary and secondary anxiety disorders. Laboratory data, age of onset of anxiety and substance disorders, collateral information, and a family history for anxiety and/or substance use disorder should be accurately collected.

### 119.2.4 Clinical Features, Course, and Prognosis

According to a recently published systematic review (Whiteford et al. 2013), anxiety, illicit drug, and alcohol use disorders accounted, respectively, for 14.6 %, 10.9 %, and 9.6 % of overall disability-adjusted life years (DALYs) caused by mental and substance use disorders.

The comorbidity between anxiety and substance use disorders makes difficult treatment and management of both disorders, with mutual negative effects. Individuals with an alcohol use and co-occurring anxiety disorders are significantly more disabled and use health services more than individuals without this comorbidity (Burns and Teesson 2002). Furthermore, subjects with comorbid generalized anxiety and substance use disorders are more likely than those with a generalized anxiety disorder only to have a lifetime history of any psychiatric disorder, pathological gambling, and an antisocial personality disorder (Alegría et al. 2010). A severe current alcohol dependence represents an important risk factor for unfavorable course of depressive and/or anxiety disorders, with persistent and unremitted symptoms (Boschloo et al. 2012a). The relationship is bidirectional, since the severity of depressive/anxiety symptoms is an additional independent predictor of the recurrence of an alcohol dependence (Boschloo et al. 2012b). A recent study (Magidson et al. 2012) compares substance users with and without a comorbid generalized anxiety disorder. The results showed that the co-occurring generalized anxiety disorder had a significant impact for what concerns a worse health-related quality of life, higher rates of treatment seeking, and greater self-reported drug use at follow up, supporting the need to define specific treatment options for this clinical population. Similar results were found from the National Comorbidity Survey (NCS) in a variety of clinical domains, such as rates of health-care utilization, additional psychiatric diagnoses, physical health problems, and interpersonal stress. Among most of comorbid individuals, social anxiety disorder onset predated that of alcohol dependence, with the former increasing the vulnerability for misusing alcohol (Buckner et al. 2008).

Anxiety disorders are well-known conditions associated to suicidal behaviors. Patients with anxiety disorders are 3.0–3.5 times more likely to complete suicide, 2.5–3.0 times to have suicidal ideations, and 2.5 times to attempt suicide (Kanwar et al. 2013). A comorbidity for an alcohol or a substance use disorder may consistently increase this risk. Findings from NESARC study (Nepon et al. 2010) highlighted that individuals with both substance use and any anxiety disorder had an OR of 3.2 (2.4–4.3) for suicide attempts as compared with people without these psychiatric conditions. Furthermore, substance users with co-occurring anxiety disorders showed a significant higher risk ( $OR = 1.6$ ; 95 % CI: 1.3–2.0) of suicide attempts than those without this comorbidity.

All these findings support the need of further research on innovative intervention strategies to optimally treat co-occurring anxiety and substance use disorders and to prevent clinically severe consequences.



### 119.2.5 Treatment and Management

Although several pharmacological and psychological treatments such as cognitive-behavioral therapy have been studied for treatment of anxiety disorders, there is a paucity of evidence on effective treatments for the comorbidity with alcohol or substance use disorders. Furthermore, relevant management is complicated because of different patterns of anxiety and substance use disorders may interact, making difficult to generalize results (Watkins et al. 2005). New research directions for treatment of comorbid anxiety and substance use disorders are actually needed and should be focused on (a) identification of specific comorbid relationships between these disorders and their underlying processes (e.g., anxiety sensitivity), (b) mechanisms that may maintain the comorbidity, and (c) well-conducted evaluations of treatments that target these mechanisms (Baillie et al. 2010).

Treatment of co-occurring anxiety and alcohol or substance use disorders can be oriented either by dealing primarily with one of the two disorders (generally the more compelling in terms of severity) or, alternatively, by addressing these together. Over the past several decades, empirical studies and clinical guideline recommendations have undergone a broad shift in approaching this comorbidity, highlighting the importance to provide simultaneous and integrated treatment for both disorders, regardless of the status of the comorbid condition (Watkins et al. 2005). However, research conducted in this field has yielded inconsistent results, with some studies demonstrating no clear advantage for the simultaneous treatment of anxiety disorders and addictive behaviors (Pasche 2012). For example, a relatively recent meta-analysis (Hobbs et al. 2011) suggests that, due to the potential serious consequences of unsuccessful treatment for alcohol use disorders, an integration with interventions addressing co-occurring anxiety disorders could be important, even if the amount of absolute benefit is moderate or even smaller. Inconclusive results were shown also by a systematic review (Hesse 2009) analyzing integrated psychosocial treatment for substance use and comorbid anxiety or depressive disorders, as, though promising, these did not give any significant additional benefit. Generally, a potentially effective strategy may be the early treatment of the disorder the patient is ready to address, while, simultaneously, a motivational approach may be used to improve readiness to change the comorbid problem (Smith and Book 2008).

At the same time, there is a lack of consistent evidence for effective pharmacological interventions for both anxiety and substance use disorders, whereas only sporadic intervention studies are available from the scientific literature, e.g., for alcohol use disorders. Selective serotonin reuptake inhibitors (SSRIs) seem effective in reducing and preventing anxiety symptoms, but there is a lack of clinical trials assessing their efficacy in comorbid patients. In a small placebo-controlled trial (Randall et al. 2001) on 15 outpatients with an alcohol dependence and social phobia, the paroxetine-treated group showed significantly lower symptoms on Clinical Global Index (CGI) and the Liebowitz Social Anxiety Scale, as compared with the placebo group, but there was a nonsignificant effect on quantity/frequency

measures of drinking. Studies on Buspirone, a partial 5-hydroxytryptamine 1A agonist, have shown mixed results on comorbid generalized anxiety and alcohol use disorders (Back and Brady 2008). Although benzodiazepines are effective in the treatment of anxiety disorders, their use in individuals with current or lifetime alcohol or substance use disorders may be complicated by their potential for abuse and dependence. More generally, although the use of medications for comorbid psychiatric disorder is encouraged, evidence is inconclusive whether there is the need of full detoxification before starting psychopharmacological treatment (Watkins et al. 2005).

Finally, use of agents specifically addressed to substance use disorders in individuals suffering from comorbid anxiety disorders is underexplored (Back and Brady 2008). In one randomized study conducted at three Veterans Administration outpatient clinics on 254 patients with an axis I psychiatric disorder and alcohol dependence, the efficacy of disulfiram and naltrexone, or their combination, was investigated. Subjects treated with an active medication showed more consecutive weeks of abstinence and less symptoms of craving than those treated with placebo, but there were no significant differences in other measures of alcohol consumption. Furthermore, subjects treated with disulfiram experienced significantly fewer obsessive-compulsive and phobic symptoms over time, whereas no clear advantage of combining medications was observed (Petrakis et al. 2005).

A secondary analysis of a study evaluating efficacy of naltrexone 50 mg/day in veterans suffering from alcohol dependence showed that among subjects taking antidepressant medications for mood and anxiety symptoms, those randomized to naltrexone had significantly smaller percent drinking days than those receiving placebo. On the other hand, for patients not on antidepressant medication, the difference between naltrexone and placebo groups was not significant (Krystal et al. 2008).

---

### 119.3 Conclusion

The dual diagnosis between anxiety and co-occurring alcohol or substance use disorders is a common but serious clinical problem. This comorbidity tends to complicate treatment, management, and prognosis of both disorders. Clinicians face a number of heterogeneous combinations of anxiety and substance use disorders. The prevalence of alcohol or substance use disorders among subjects with anxiety disorders is high worldwide. Etiological links and temporal relationships of this comorbidity are still unclear and, probably, multifactorial. Alcohol and substance may be misused by individuals in order to self-medicate their anxiety, avoidant, and phobic symptoms, though this remains often unrecognized and untreated. Clinicians should assess this comorbidity using structured diagnostic interviews and observing symptoms over a sustained period of abstinence to differentiate substance-induced from independent anxiety disorders. A comprehensive diagnostic assessment should include also several alcohol and substance use screening tools, such as ASI, ASSIST, and AUDIT questionnaires. While some pharmacological and psychosocial treatments

have shown effectiveness for separate treatment of anxiety and substance use disorders, there is a lack of evidence on treatments addressed to both disorders as dual diagnosis label means more complex needs rather than two distinct problems (Carrà and Clerici 2006).

---

## References

- Alegría AA, Hasin DS, Nunes EV, Liu SM, Davies C, Grant BF, Blanco C (2010) Comorbidity of generalized anxiety disorder and substance use disorders: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *J Clin Psychiatry* 71:1187–1195
- Almeida-Filho N, Lessa I, Magalhães L, Araújo MJ, Aquino E, de Jesus MJ (2007) Co-occurrence patterns of anxiety, depression and alcohol use disorders. *Eur Arch Psychiatry Clin Neurosci* 257:423–431
- American Psychiatric Association (2000) Diagnostic and statistical manual of mental disorders, 4th edn, text rev. Washington, DC, American Psychiatric Association
- American Psychiatric Association (2013) Diagnostic and statistical manual of mental disorders, 5th edn. Arlington, VA, American Psychiatric Association
- Back SE, Brady KT (2008) Anxiety disorders with comorbid substance use disorders: diagnostic and treatment considerations. *Psychiatr Ann* 38:724–729
- 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
- Bolton J, Cox B, Clara I, Sareen J (2006) Use of alcohol and drugs to self-medicate anxiety disorders in a nationally representative sample. *J Nerv Ment Dis* 194:818–825
- Boschloo L, Vogelzangs N, Smit JH, van den Brink W, Veltman DJ, Beekman AT, Penninx BW (2010) The performance of the Alcohol Use Disorder Identification Test (AUDIT) in detecting alcohol abuse and dependence in a population of depressed or anxious persons. *J Affect Disord* 126:441–446
- 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* 131:233–242
- Boschloo L, Vogelzangs N, van den Brink W, Smit JH, Veltman DJ, Beekman AT, Penninx BW (2012a) Alcohol use disorders and the course of depressive and anxiety disorders. *Br J Psychiatry* 200:476–484
- Boschloo L, Vogelzangs N, van den Brink W, Smit JH, Beekman AT, Penninx BW (2012b) Predictors of the 2-year recurrence and persistence of alcohol dependence. *Addiction* 107:1639–1640
- Buckner JD, Timpano KR, Zvolensky MJ, Sachs-Ericsson N, Schmidt NB (2008) Implications of comorbid alcohol dependence among individuals with social anxiety disorder. *Depress Anxiety* 25:1028–1037
- Burns L, Teesson M (2002) Alcohol use disorders comorbid with anxiety, depression and drug use disorders. Findings from the Australian National Survey of Mental Health and Well Being. *Drug Alcohol Depend* 68:299–307
- Carrà G, Clerici M (2006) Dual diagnosis—policy and practice in Italy. *Am J Addict* 15:125–130
- Colasanti A, Rabiner EA, Lingford-Hughes A, Nutt DJ (2011) Opioids and anxiety. *J Psychopharmacol* 25:1415–1433
- 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

- Degenhardt L, Coffey C, Romaniuk H, Swift W, Carlin JB, Hall WD, Patton GC (2013) The persistence of the association between adolescent cannabis use and common mental disorders into young adulthood. *Addiction* 108:124–133
- Dixon L, Myers P, Johnson J, Corty E (1996) Screening for mental illness with the addiction severity index. *Am J Addict* 5:301–307
- Erb S, Kayyali H, Romero K (2006) A study of the lasting effects of cocaine pre-exposure on anxiety-like behaviors under baseline conditions and in response to central injections of corticotropin-releasing factor. *Pharmacol Biochem Behav* 85:206–213
- First MB, Spitzer RL, Gibbon M, Williams JB (2002) Structured Clinical Interview for DSM-IV-TR Axis I Disorders, research version, Patient edition (SCID-I/P). Biometrics Research, New York State Psychiatric Institute, New York
- Grant BF, Stinson FS, Dawson DA, Chou SP, Dufour MC, Compton W, Pickering RP, Kaplan K (2004) Prevalence and co-occurrence of substance use disorders and independent mood and anxiety disorders: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Arch Gen Psychiatry* 61:807–816
- Gratzer D, Levitan RD, Sheldon T, Toneatto T, Rector NA, Goering P (2004) Lifetime rates of alcoholism in adults with anxiety, depression, or co-morbid depression/anxiety: a community survey of Ontario. *J Affect Disord* 79:209–215
- Hasin DS, Trautman KD, Miele GM, Samet S, Smith M, Endicott J (1996) Psychiatric Research Interview for Substance and Mental Disorders (PRISM): reliability for substance abusers. *Am J Psychiatry* 153:1195–1201
- 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
- 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
- Humeniuk R, Ali R, Babor TF, Farrell M, Formigoni ML, Jittiwutikarn J, de Lacerda RB, Ling W, Marsden J, Monteiro M, Nhwatiwa S, Pal H, Poznyak V, Simon S (2008) Validation of the Alcohol, Smoking and Substance Involvement Screening Test (ASSIST). *Addiction* 103:1039–1047
- Kanwar A, Malik S, Prokop LJ, Sim LA, Feldstein D, Wang Z, Murad MH (2013) The association between anxiety disorders and suicidal behaviors: a systematic review and meta-analysis. *Depress Anxiety* 30(10):917–929
- Krystal JH, Gueorguieva R, Cramer J, Collins J, Rosenheck R, VA CSP No. 425 Study Team (2008) Naltrexone is associated with reduced drinking by alcohol dependent patients receiving antidepressants for mood and anxiety symptoms: results from VA Cooperative Study No. 425, “Naltrexone in the treatment of alcoholism”. *Alcohol Clin Exp Res* 32:85–91
- Kushner MG, Abrams K, Borchardt C (2000) The relationship between anxiety disorders and alcohol use disorders: a review of major perspectives and findings. *Clin Psychol Rev* 20:149–171
- Leray E, Camara A, Drapier D, Riou F, Bougeant N, Pelissolo A, Lloyd KR, Bellamy V, Roelandt JL, Millet B (2011) Prevalence, characteristics and comorbidities of anxiety disorders in France: results from the “Mental Health in General Population” survey (MHGP). *Eur Psychiatry* 26:339–345
- Lingford-Hughes A, Potokar J, Nutt D (2002) Treating anxiety complicated by substance misuse. *Adv Psychiatr Treat* 8:107–116
- Magidson JF, Liu SM, Lejuez CW, Blanco C (2012) Comparison of the course of substance use disorders among individuals with and without generalized anxiety disorder in a nationally representative sample. *J Psychiatr Res* 46:659–666
- Marquenie LA, Schadé A, van Balkom AJ, Comijs HC, de Graaf R, Vollebergh W, van Dyck R, van den Brink W (2007) Origin of the comorbidity of anxiety disorders and alcohol dependence: findings of a general population study. *Eur Addict Res* 13:39–49

- Martins SS, Gorelick DA (2011) Conditional substance abuse and dependence by diagnosis of mood or anxiety disorder or schizophrenia in the U.S. population. *Drug Alcohol Depend* 119:28–36
- McLellan AT, Cacciola JC, Alterman AI, Rikoon SH, Carise D (2006) The addiction severity index at 25: origins, contributions and transitions. *Am J Addict* 15:113–124
- Moreira FA, Wotjak CT (2010) Cannabinoids and anxiety. *Curr Top Behav Neurosci* 2:429–450
- Mueser KT, Drake RE, Wallach MA (1998) Dual diagnosis: a review of etiological theories. *Addict Behav* 23:717–734
- Nepon J, Belik SL, Bolton J, Sareen J (2010) The relationship between anxiety disorders and suicide attempts: findings from the National Epidemiologic Survey on Alcohol and Related Conditions. *Depress Anxiety* 27:791–798
- Pandey SC (2003) Anxiety and alcohol abuse disorders: a common role for CREB and its target, the neuropeptide Y gene. *Trends Pharmacol Sci* 24:456–460
- Pasche S (2012) Exploring the comorbidity of anxiety and substance use disorders. *Curr Psychiatry Rep* 14:176–181
- Petrakis IL, Poling J, Levinson C, Nich C, Carroll K, Rounsaville B, VA New England VISN I MIRECC Study Group (2005) Naltrexone and disulfiram in patients with alcohol dependence and comorbid psychiatric disorders. *Biol Psychiatry* 57:1128–1137
- 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
- Robins LN, Wing J, Wittchen HU, Helzer JE, Babor TF, Burke J, Farmer A, Jablenski A, Pickens R, Regier DA et al (1988) The composite international diagnostic interview. An epidemiologic instrument suitable for use in conjunction with different diagnostic systems and in different cultures. *Arch Gen Psychiatry* 45:1069–1077
- 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
- Saunders JB, Aasland OG, Babor TF, de la Fuente JR, Grant M (1993) Development of the Alcohol Use Disorders Identification Test (AUDIT): WHO collaborative project on early detection of persons with harmful alcohol consumption—II. *Addiction* 88:791–804
- Sheehan DV, Lecrubier Y, Sheehan KH, Amorim P, Janavs J, Weiller E, Hergueta T, Baker R, Dunbar GC (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(Suppl 20):22–33
- Silberman Y, Bajo M, Chappell AM, Christian DT, Cruz M, Diaz MR, Kash T, Lack AK, Messing RO, Siggins GR, Winder D, Roberto M, McCool BA, Weiner JL (2009) Neurobiological mechanisms contributing to alcohol-stress-anxiety interactions. *Alcohol* 43:509–519
- Smith JP, Book SW (2008) Anxiety and substance use disorders: a review. *Psychiatry Times* 25:19–23
- Smith JP, Randall CL (2012) Anxiety and alcohol use disorders: comorbidity and treatment considerations. *Alcohol Res* 34:414–431
- van Laar M, van Dorsselaer S, Monshouwer K, de Graaf R (2007) Does cannabis use predict the first incidence of mood and anxiety disorders in the adult population? *Addiction* 102:1251–1260
- Watkins KE, Hunter SB, Burnam MA, Pincus HA, Nicholson G (2005) Review of treatment recommendations for persons with a co-occurring affective or anxiety and substance use disorder. *Psychiatr Serv* 56:913–926
- Whiteford HA, Degenhardt L, Rehm J, Baxter AJ, Ferrari AJ, Erskine HE, Charlson FJ, Norman RE, Flaxman AD, Johns N, Burstein R, Murray CJ, Vos T (2013) Global burden of disease attributable to mental and substance use disorders: findings from the Global Burden of Disease Study 2010. *Lancet* 382:1575–1586