ASD and Intellectual Disability

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Autism spectrum disorder frequently co-occurs with other neurodevelopmental conditions (Wing and Potter 2002; [1]). ASD prevalence increase was associated with declines in other diagnostic categories, indicating that a diagnostic substitution had happened (Shattuck 2006). One of the most common co-occurrence is with intellectual disability, which has been renamed in the ICD-11 as disorders of intellectual developmental (DID).

8.1 Intellectual Disability: Disorders of Intellectual Development

Intellectual disability (ID) or disorders of intellectual development (DID), according to the most recent terminology [2], is a condition of difficult definition, which affects many people with many different presentations. Its main characteristic consists of a difficulty in reaching objectives, implying one or more of the many cognitive abilities that are still simplified with the term intelligence and measured, even more simplistically, with the IQ (intellectual quotient). This difficulty reduces the ability to learn, not only at a theoretical and scholastic level, but also at a practical and adaptive level. ID onsets in the first years of life and persists across the entire life span, like autism.

The former term for DID was mental retardation (ICD-10 [3]; *DSM-III* [4]), which was first introduced by the American Association on Mental Retardation (AAMR) in its 1961's manual. At the same time, the AAMR proposed objective diagnostic criteria, as well as tests and reference scores for the assessment of intelligence and adaptive skills. The main criterion was an IQ lower than 84,

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corresponding to one standard deviation below the average of the general population. The impairment of adaptive functioning was divided into four severity levels.

Two updates of the AAMR manual were published in 1973 and 1983; in the former, the IQ cutoff was reduced to two standard deviations below the average and the age of onset was extended to 18 years, in the latter, the IQ standard measurement error was added [5]. The *DSM-IV* [6] remained aligned to the AAMR in the definition of mental retardation, while it departed in the upper limit of the severity range, which was kept lower, and in the multiaxial rather than multidimensional classification.

In recent years, the release of the new international classification systems of mental disorders (*DSM-5* [7] and ICD-11 [2]) has boosted the scientific debate on the difficulties to define and to position ID. In fact these aspects have important implications, not only on clinical practice but also on socio-cultural and socio-health policies. There are two main approaches. The first is promoted by the AAMR (at present renamed as American Association on Intellectual Disabilities and Development—AAIDD) and sets its center on disability, characterized by significant impairments of intellectual functioning and adaptive behavior. This approach is aligned with the one followed in the international classification of functioning (ICF; WHO 2001). The second approach is supported mainly by the Section Psychiatry of Intellectual Disability of the World Psychiatric Association (WPA-SPID) and has a multidimensional, polynomial-polysemic character. It explains ID as a condition to be defined differently according to the classificatory context, i.e., as meta-syndromic grouping of intellectual development disorders in the ICD (International Classification of Diseases), as a condition of complex disability in the ICF.

The WPA-SPID suggested for the ICD also to replace the term "mental retardation" with "intellectual development disorders (IDD)" and proposed a definition and diagnostic criteria free from rigid references to IQ (intelligence quotient) reduction (Bertelli et al. 2014; Bertelli et al. 2018), adaptive skills, and age of onset (Salvador-Carulla et al. 2011). According to the WPA-SPID, ID is characterized by a deficit of one or more cognitive functions, prior to the acquisition of skills through learning, such as to interfere significantly, without the appropriate support, with individual functioning, as expressed by limitations in activities and restrictions in participation (Salvador-Carulla et al. 2011).

As mentioned above, the new ICD (ICD-11; [2]) has adopted the term "disorders of intellectual development" with reference to a group of conditions of different etiology originating during the age of development and characterized by intellectual functioning and adaptive behavior significantly lower than the average, at least two standard deviations (approximately below the percentile 2.3), as defined through an individualized assessment with adequately validated and standardized tests. Where these tests are not available, the diagnosis requires greater reliance on clinical judgment based on appropriate assessment of comparable behavioral indicators.

In the *DSM-5*, the fundamental characteristic of ID is a general intellectual functioning significantly (two standard deviations) below the average (criterion A). This characteristic must be associated with deficits in adaptive functioning, with particular reference to the sociocultural standards of personal independence and social

responsibility (criterion B). Without continuous support, adaptive deficits limit functioning in at least one of the daily activities of life, such as communication, social participation or autonomy, in different contexts, such as one's own home, school, work, and community. The onset of intellectual and adaptive deficits must occur during the development period (criterion C), typically in the years prior to school education [7].

Until the publication of *DSM-5* (2013), the severity of ID (formerly 'mental retardation') was defined almost exclusively on the basis of IQ reduction: mild for values between 50–55 and 70 (50–69 in the ICD-10), moderate between 35–40 and 50–55 ("medium," 35–49 in ICD-10), severe between 20–25 and 35–40 (20–34 in ICD-10), and profound for values lower than 25–20 (<20 in ICD-10). In *DSM-5* the severity levels are defined more on the basis of adaptive functioning than on IQ, especially for the cases that fall within the lower part of the range. For this purpose, the domains of reference are represented by conceptualization, social and practical skills.

The prevalence of ID varies across studies between 1% and 2.5%, also based on diagnostic procedures, geographical and sociocultural factors (WHO 2007; van Bakel et al. 2014; McKenzie et al. 2016). The lowest rates were recorded in some northern European countries, such as Finland or the Netherlands, while the highest rates are for low-middle income countries, up to 6–8% (WHO 2007). The average prevalence is just over 1% (Maulik et al. 2011).

The causes of ID are classified in prenatal, perinatal, and postnatal. Among the prenatal causes, the main ones are genetic alterations, either chromosomal (or genomic, e.g., Down syndrome, Turner syndrome, Klinefelter syndrome, and cri du chat syndrome) or genic (or point-like, e.g., Fragile X, galactosemia, lipidosis, and phenylketonuria), maternal infections, maternal exposure to harmful chemical (e.g., lead, mercury, and drugs) or physical agents (e.g., radiation), malnutrition, gestational diabetes, hypoxia, hypoglycemia, or maternal toxemia. Among perinatal causes, some of the most common are labor complications, childbirth traumas, and the respiratory distress of newborn. Postnatal causes are mainly represented by infections, traumas, malnutrition, and poisoning by chemical substances. Also psycho-social factors seem to be able to determine an early cognitive impairment of intelligence, even if of a slight degree. Some of the most relevant psycho-social factors are the psychologically, socially, culturally, or economically poor environment, the severe alterations of intra-family relations, social isolation, and the forced inhibition of the natural tendency to exploratory behavior.

All scientific associations agree that ID represents a condition of high vulnerability, with mental disorders, physical illnesses, risk of abuse, risk of abandonment, and dissatisfied care needs significantly higher than those of the general population (Bertelli et al. 2009; Salvador-Carulla e and Bertelli 2008). These vulnerabilities seem to extend to persons with borderline intellectual functioning (BIF), who have an IQ below the average (between one and two standard deviations), but not enough to be comprised within the upper limit of ID. According to research findings, one-eighth of the population has BIF and shows, compared to people with higher IQ, greater social disadvantage, higher rates of psychiatric disorders, substance abuse

and consequently greater use of psychopharmacological therapies and health services, including emergency services (Hassiotis et al. 2008; Wieland et al. 2014).

8.2 Co-occurrence and Differentiation of ASD and ID

Both ID and ASD represent meta-syndromic groups, including many different clinical (syndromic) conditions (Salvador-Carulla and Bertelli 2008), which combine cognitive and relational impairment. The two conditions often co-occur and are difficult to distinguish, especially as long as the cognitive impairment increases.

Thirty to forty percent of persons with ID have pervasive autistic features (Morgan et al. 2002; La Malfa et al. 2004; Cooper et al. 2007), as well as about 80% of persons with ASD has lower intellectual functioning compared to the general population ([8, 9]; Fombonne 2003; Hoekstra et al. 2009; Baio et al. 2018; Edelson 2006; Baird et al. 2006; Noterdaeme and Wriedt 2010; Bryson and Smith 1998). Many of the symptoms which characterize ID are quite common also in ASD, such as deficits of cognitive, social, and adaptive skills, as well as stereotypies, problem behaviors, and repetitive behaviors (Lee et al. 2008; Wilkins and Matson 2009). Reversely, many features of ASD are often seen also in ID, such as socialization-communication impairment and restricted-repetitive behaviors or interests (Briegel et al. 2009; Gillberg 2010; Horovitz and Matson 2010; Leung et al. 2010; Matson et al. 2009a, b; Smith and Matson 2010a, b, c; Lee et al. 2008; [9]).

Etiologically both syndromes are considered to result from an interaction of genetic and environmental factors with negative impact on the brain development. The subsequent impairment of logical-learning functions (ID), social-communicative functions (ASD), or both might depend on the position and the extension of this disruption of neural circuits. Recent evidence on alterations of proteins regulating synapses' growth and structure seems to confirm that ID and ASD are part of a single group of neurodevelopmental disorders (Owen et al. 2011; Owen 2012; Waltereit 2013).

The combination of ASD and ID presents many challenges and deficits across a range of behaviors and skills that are not seen in ID or ASD alone [10]. Severe IQ has been found to be associated with a higher severity of ASD and a higher rate of PB [11, 12]. The presence and severity of stereotypies tend to be related to severity of ASD [13] but not to severity of ID [1].

Differential diagnosis between ID and ASD as well as identification of co-occurrence are particularly challenging for those psychiatrists who did not receive specific training on the presentation of PD in persons with neurodevelopmental disorders (Bradley et al. 2011b; Hurley et al. 2003; Lunsky et al. 2008; [14]). Several tools are available to support clinicians in the assessment, such as PDD-MRS (Scale of Pervasive Developmental Disorder in Mentally Retarded Persons; Kraijer and de Bildt 2005), DiBAS-R (Diagnostic Behavioral Assessment for ASD—Revised; Sappok et al. 2014), ASD-DA (Autism Spectrum Disorder—Diagnosis Scale for Intellectually Disabled Adults; Matson et al. 2008), SCQ-AID (Social

Communication Questionnaire for Adults with ID; Derks et al. 2017), and SPAIDD-ASD (Systematic Psychopathological Assessment for persons with Intellectual and Developmental Disabilities—version for Autism Spectrum Disorder; Fruscoloni et al. 2018) for screening, and GARS-2 (Gilliam Autism Rating Scale-2nd Edition; Gilliam 2006), ADI-R (Autism Diagnostic Interview—Revised; Lord et al. 1994), and ADOS (Autism Diagnostic Observation Schedule; Lord et al. 1989) to complete patient evaluation. The Diagnostic Interview for Social and Communication Disorders (The DISCO) also provides a comprehensive assessment ASD across the range of IQ (Maljaars et al. 2012), as well as functioning ability and subtypes of autism (Wing et al. 2002); it also seems to be useful in differentiating between ADS, DID, and schizophrenia spectrum disorders (Unenge Hallerbäck et al. 2012). ADOS and ADI-R have shown some limits when used with persons with DID, especially with those with lower IQ and/or sensory impairment (Sappok et al. 2013; deVaan et al. 2016).

There is an increased risk of underestimating ASD in persons with ID when schizophrenia is diagnosed (Palucka et al. 2009; Savage et al. 2007; Bradley et al. 2011b). About 40% of the items used to screen for psychosis in ID commonly receive a high score when ASD is present (Helverschou et al. 2008).

The introduction of the spectrum model to the diagnosis of autism, which has been consolidated in the *DSM-5* [7], has resulted in the inclusion of subjects with subthreshold symptoms and blurred pictures. Future classification should pay more attention not to excessively increase the inclusive capacities of criteria and create all-encompassing diagnostic categories. They should also consider how a reevaluation of a dimensional approach to some core symptoms would allow a clearer definition of the disorders. The overlap between autism spectrum and other neurodevelopmental disorders has some social therapeutic and economic implications. ASD is more socially accepted and less stigmatizing than ID and receives higher individual, particularly rehabilitative, and family support. Unlike ID, ASD is considered a treatable disorder, and many mental health services are increasingly providing specific interventions. Moreover, autism gets a greater number of grants and economic benefits. A diagnosis of ID does not always offer this advantage.

8.3 Prevalence of Psychiatric Disorders in Persons with ID and ASD

As Boucher et al. [10] reported, people with both ID and ASD present several symptoms and deficits which are not seen in ID and ASD alone, and a different frequency of comorbid disorders. Research showed an inverse relationship between IQ and severity of ASD, with the rate of PB in ASD getting lower as long as IQ increases [11, 12]. Conversely, severity of ASD symptoms—and not that of ID—resulted directly associated with the rates of stereotypies [1, 13].

Although still limited and controversial, the literature on the prevalence of Psychiatric Disorders (PD) in persons with both ID and ASD indicates a higher rate in comparison with those with ID or ASD alone. Greater agreement has been

identified on higher rates of PB, stereotypies and rituals, communication difficulties, and social impairment in comparison to ID alone [9, 15]. Furthermore, the co-occurrence of ASD with ID has been associated with a higher probability to be hospitalized and to receive a psychopharmacological treatment [16–18].

Lunsky and collaborators found that more than half of adults with ID and ASD have a co-occurring PD (26.1% mood disorder, 26.1% psychotic disorder, and 4.3% personality disorder). However, when compared with those with only ID, they did not show statistically significant differences except for the probability to receive a diagnosis of a psychotic disorder, which was lower in the ID+ASD group [14]. Also Melville et al. [19] found no significant rate of increase in the case of co-occurrence of ASD, but a higher number of PB. In addition, individuals with PB and ASD were less likely to receive a diagnosis of schizophrenia, whereas the latter increased if PB were absent [15]. In all cases the presence of PB had a negative impact on the overall functioning and quality of life [8, 15, 17, 20–25].

Cooper and van der Speck [26] found a lower prevalence of PD in people with ID+ASD compared to those with ID alone, but a more frequent diagnosis of schizophrenia.

The presence of ID in persons with ASD seems to negatively impact on the possibility to have an adjunctive diagnosis of PD. In a 10-year longitudinal study, Selten and collaborators found that the co-occurrence of ID in persons with ASD reversed the trend of a higher rate of diagnoses of bipolar and psychotic disorders than the general population [27].

Specific diagnostic procedure and tools seem to represent a significant determinant for the reliability of prevalence findings in persons with ID+ASD. These often include too many subjective symptoms which are not easy to identify in this group of patients and should be substituted by behavioral and observable equivalents (see Chap. 5). Different studies have found an increasing prevalence of PD as long as the specificity of their assessment tools rose. By using the PAS-ADD (Psychiatric Assessment Schedules for Adults with Developmental Disabilities), Thalen found an overall rate of 69.6% vs. 8.6% in persons with ID alone [28], and through the DASH-II (Diagnostic Assessment for the Severely Handicapped-II), Matson and Cervantes found statistically significant differences in eight out of the 12 subscales of the tools, on anxiety, mania, schizophrenia, stereotypies/tics, self-injurious behavior, eating disorders, sexual disorders, and impulse control [29].

Among specific PD, mood disorders [28, 30], anxiety disorders [21, 28, 31], somatic symptoms disorders, and impulse control disorders [20, 32–34] have been reported as the most frequent.

Higher rates of inattention, hyperactivity, and impulsive behaviors have been observed in teens with both autism and ID in comparison with those without ASD [35]. In addition, people with both conditions appear more vulnerable to sleep problems, organic syndrome, stereotypies, and tics [20].

The co-occurrence of PD has been found to be higher in males, youths, and persons with mild-to-moderate ID [14, 15, 17], although Thalen found the rate of psychoses and anxiety disorder to trend inversely to the severity of ID [28].

Some high rates of PD in persons with ID and ASD, such as that of bipolar disorder, seem to be related to behavioral dysregulation, as expressed by restlessness, agitation, or distraction, and may reflect the symptom overlap between PD, ASD, and ID rather than a true co-occurrence of PD. This is particularly probable in individuals with more severe PB [31].

8.4 Peculiarities and Challenges in Diagnosing Co-occurrent Psychiatric Disorders in ASD and ID

As mentioned above, the low-adaptive intellectual disability (or disorders of intellectual development) and the low-functioning autism spectrum disorder represent the fraction of neurodevelopmental disorders that show the greatest degree of disability, in communication, conceptualization, interpersonal relationships, and common activities of life.

These difficulties characterize at various levels the presentation of PD, making them much more complex and difficult to identify than in the general population ([8]; Lainhart 1999; Reaven and Hepburn 2003; Bertelli 2016). The symptomatology can in fact be chaotic, mixed, intermittent, atypical, masked, variable from poorly defined to extremely rigid (Reiss and Szyszko 1993; [36, 37]). These alterations also concern the nuclear elements of some syndromes, such as delusional perception or suicidal ideation, which may not be immediately identifiable, especially in persons with low communication skill (Mikkelsen and McKenna 1999). To promote a correct approach to this complexity, various conceptual references have been proposed. One of the most relevant is that of "diagnostic over-shadowing" (Sovner 1986), which refers to the difficulty for clinicians to distinguish between symptoms of PD and the manifestations of basic conditions.

Other concepts to consider are those of "intellectual distortion," related to the impact of cognitive, communicative, physical, and social dysfunction on the perception and communication of mental suffering (Sovner and DesNoyers Hurley 1986), "evolutionary inappropriateness," or the mismatch between the level of individual development expected for the chronological age and the level of actual individual development (Cooper and Salvador-Carulla 2009), and the "psychosocial masking," referable to the peculiarities of cultural, environmental, and interpersonal influences (Sovner 1986). Even the neurovegetative vulnerability associated with cognitive impairment, or the greater tendency to express mental distress through organic dysfunctions, somatic symptoms, or dystonias of the nervous system, can connote the clinical presentation of PD (Costello and Bouras 2006). In people with neurodevelopmental disorders, there are also more general difficulties in the very conceptualization of the mental disorder. Here in fact the impairment of functioning and the subjective distress arising from the presence of psychiatric symptoms, which constitute in the general population the fundamental criteria for the formulation of a judgment of pathology, are difficult to identify, as they are already altered by the basic condition.

In particular, perceived distress is already remarkably high, due to a complexity of biological, psychological, and socio-environmental factors, such as reduced opportunities for participation in community life, greater exposure to traumatic experiences or lower coping skills (Sovner 1986; Martorell et al. 2009). The difficulty therefore lies in understanding whether the alterations that the clinician is observing depend directly on cognitive deficits, on the presence of a co-occurring psychiatric disorder or both. An adequate assessment of psychiatric symptomatology in this type of patient should be based on the organized observation of significant variations in basic behavior, especially in the most serious cases. The presence of visual hallucinations can be detected, for example, starting from changes in gestures that are not appropriate to the context, such as fixing a point where there seems to be nothing to see, moving around as if to defend oneself against imaginary attacks, covering one's eyes or ears with one's hands in the absence of objectively annoying sounds (Bertelli 2016). A further factor of complexity in the manifestation and in the interpretation of the psychopathological frameworks is represented by PB. PB appear as one of the most frequently encountered criticalities in people with ID and LF-ASD, with a prevalence ranging between 5% and 60% (Smith et al. 1996; Smiley 2005) and very low remission rates (Cooper et al. 2009; Totsika et al. 2008, 2009).

Their incidence seems to increase in people with more marked reduction in IQ, with greater difficulties in communication or social skills and in the absence of stable supports (Felce et al. 2009). The hypotheses put forward to explain their nature and development include a wide range of factors belonging to different fields, often combined together. In some cases it has been suggested that their function was essentially communicative, in others that they represented expressions of protest, attempts to attract attention, manifestations of fear or sadness. Some PB can be identified as specific psychiatric symptoms; in these cases, we speak of "behavioral equivalents" (Hurley 2006). The relationship between these behavioral alterations and some PD has already been suggested and investigated in many studies (Emerson et al. 1999; Felce et al. 2009; Hemmings et al. 2006; Kishore et al. 2005; Moss et al. 2000; Rojan et al. 2004). Some researchers are less likely to consider PB as behavioral equivalents of a psychiatric disorder, defining them alternatively as indicators of aspecific emotional stress (Tsiouris et al. 2003; Rojan and Meier 2009).

Against these discrepancies, a careful evaluation of the onset, of the course, of the possible extinction of the PB, and of the co-presence of other possible symptoms, appears to be of fundamental importance to define whether it can be interpreted or not as a symptom equivalent (Charlot 2005). Peculiarities of the evaluation of errors in the diagnostic process may also be due to deficits in communication skills or lack of language, often present in people with ID and/or ASD (Bertelli 2016). They can indeed present great difficulties in expressing themselves verbally, striving for compliance and attributing atypical meanings to communicative contexts. Furthermore, the limited introspective abilities are often found to determine a series of difficulties in defining life experiences and states of suffering or disturbance. Some peculiar characteristics of PD, such as the sense of desperation or uselessness, suicidal ideation, or delusional

perception, require a high level of expressive language, abstract thought, memory, and self-awareness; it is therefore easy to understand how they are difficult to communicate, particularly in the most serious cases (Costello and Bouras 2006; Bertelli et al. 2015).

Conducting direct interviews with people with ID and/or ASD is made equally problematic by their frequent difficulty in understanding requests (Heal and Sigelman 1995). This aspect is much rarer, if not entirely absent, in people with mild ID or borderline intellectual functioning (BIF), who have shown themselves able to describe their own behaviors and internal states (Moss et al. 1996; Bramston and Fogarty 2000; Deb et al. 2001). However, even in these cases, some aspects related to the impairment of cognitive functioning, such as suggestibility, acquiescence, attention deficits, problems with temporal sequencing, or distractibility, can cause considerable difficulty in providing a detailed account of one's experiences. In light of these difficulties, preparing an adequate assessment setting is of fundamental importance. Particular attention must be paid to aspects such as the length and flexibility of the sessions, to be conducted preferably in the person's everyday life environment; the language used must be simple, without metaphors and idiomatic expressions, and it is advisable to offer alternative answers (Bertelli 2016).

A very important role in the assessment is that played by family members and caregivers, valuable informants in the diagnostic process, and in general in clinical practice. However, even these sources of information can be limited, contradictory, and heterogeneous. The literature indicates that the assessment by proxies is conditioned by a series of factors, which include the informants' personal characteristics, their level of knowledge of the person, and their degree of affective involvement (Pickard and Knight 2005; Petry et al. 2009). The specificity of the symptomatological processions and the relative chronological evolutions require equally specialized skills, in both the evaluation and the intervention phases, but family members and frontline personnel often do not have the adequate tools to distinguish the observed behaviors and to give them a possible psychopathological meaning (Mikkelsen and McKenna 1999; Costello and Bouras 2006). Furthermore, the widespread belief that all the problems of people with ID and/or LF-ASD are inevitable and immutable (Costello and Bouras 2006; Reiss and Szyszko 1983) often leads informants to deny the presence of psychiatric symptoms or to consider them only as their subjective interpretation, thus altering the collection of anamnestic information. A recent review of the literature has highlighted a lack of studies on the correspondence of evaluations carried out by different proxies (Bertelli et al. 2015). Some authors have found a low correspondence, often characterized by the tendency of informants to highlight greater problematic from a behavioral and psychic point of view. Integrating data from different sources seems to be the most effective way to determine any significant behavioral changes, interpret them as symptom equivalents, and increase the validity of psychiatric evaluation. In particular, the scientific community agrees that the best way to assess the presence of psychiatric disorders in people with ID and/or ASD is to use a system that includes self- and hetero-evaluations (Bertelli et al. 2015).

Another reason for the persistent lack of evidence in assessing and diagnosing mental health problems in people with ID and/or ASD is the substantial inadequacy of current diagnostic systems for the general population. In common use manuals, in fact some criteria are formulated on the verbal level and therefore difficult to apply to people with ID and/or ASD, which rather express symptoms through behaviors. Of equally difficult application are the clinical specifications and extensions that often accompany the diagnostic categories, as there is almost always no precise information on the psychopathological situation of the person being evaluated (Cooper and Salvador-Carulla 2009). Moreover, despite the aforementioned frequency of PB in people with cognitive deficits, the manuals do not consider them classifiable symptoms. In order to address the critical issues related to the use of standard diagnostic criteria, in recent years changes have been proposed to be implemented in the classifications used for the general population (Cain et al. 2003; Marston et al. 1997; Ross and Oliver 2003; Szymanski and King 1999).

Specifically, the objective was to exemplify and convert preexisting criteria into behavioral equivalents (Charlot 2005; RCPsych 2001). From this attempt the two manuals Diagnostic Criteria for Learning Disability (DC-LD; RCPsych 2001) and Diagnostic Manual—Intellectual Disability (DM-ID; Fletcher et al. 2007), were produced, respectively, by the Royal College of Psychiatrists and the National Association for Dual Diagnosis. They consist essentially of adaptations and integrations of the tenth edition of the International Classification of Diseases (ICD-10; [3]) and of the revision of the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSMIV-TR; APA 2000), created for the general population. Recently, the second edition of the DM-ID (DM-ID 2; Fletcher et al. 2016) was published, corresponding to the adaptation of the DSM-5 [7].

Although further improvements are needed, the two manuals have proved to be very useful in clinical practice. In the field trials conducted in the United States of America for the first edition of the DM-ID, approximately 36% of clinicians indicated that the adapted criteria had enabled them to make much more valid diagnoses than they could have made using DSM-IV-TR and about 60% found very useful specifications for avoiding inaccurate diagnoses, such as those defined as “not otherwise specifiable.” The group of disorders with the highest number of changes of diagnosis in favor of disorders belonging to other groups was that of psychotic disorders, while the group with most changes within the same group was that of mood disorders [38]. In addition to all the major diagnoses that are found in the DSM-5, the DM-ID 2 includes two additional chapters, which deal with assessment and diagnostic procedures as well as the behavioral phenotypes that are associated with genetic disorders, which is intended to aid in the understanding of how a disorder’s genotype affects its behavioral expression.

The DC-LD provides diagnostic criteria for PD adapted for adults with moderate to severe learning disabilities; if you work with people with mild disabilities, it can also be used in combination with ICD-10 and DSM.

8.5 Assessment Tools for Co-occurrent Psychiatric Disorders in ASD and ID

Similarly to what emerged for the diagnostic criteria, also the application to people with ID and/or ASD of the assessment scales developed for the general population has shown considerable validity problems [36]. In the last 30 years, the scientific community of this field has shown a growing interest in this issue, and various studies have been conducted that aimed to develop specific tools, analyze their psychometric properties, and investigate their clinical utility. However, those supported by a consistent database are still few.

The most common tools currently used are those of general screening, designed to provide information on all the diagnoses compatible with the symptoms and behavioral equivalents found in a person, but there are also tools for specific psychopathological areas. There are few standardized diagnostic interviews, which are complex, time-consuming, and less useful for multidisciplinary collaboration. With the same psychometric qualities, the tools must be chosen on the basis of the specific purpose, the characteristics of the person to be evaluated, the training required, the administration time, and the resources available.

As mentioned above, the standardized interviews for psychopathological diagnosis in ID and ASD are few and addressed exclusively to people with good communication and introspective skills (Heal and Sigelman 1995). The best known is the Psychiatric Assessment Schedule for Adults with Developmental Disabilities (PAS-ADD), developed by Stephen Moss and collaborators (Moss 2011; Moss, Ibbotson and Prosser 1994; Moss et al. 1993) for adults with ID, which uses the ICD-10 diagnostic categories and criteria. It derives from the Schedules for Clinical Assessment in Neuropsychiatry (SCAN), semi-structured clinical interviews produced by the World Health Organization in 1994, starting from the Present State Examination (PSE; Wing, Cooper and Sartorius 1974), and used by specially trained clinicians as a support for the diagnosis of PD in adults.

PAS-ADD was designed to be used by doctors and includes 145 questions that originally referred to seven subscales corresponding to the main acute PD. Personality disorders and many less frequent PD are not detected. Direct questions on autism spectrum disorders and ADHD are not included, but it is possible to reach these diagnoses thanks to the presence of specific sections in the supplementary instruments. The PAS-ADD is available in two versions: one for cases in which it is possible to directly interview the person with ID, the other for cases in which information is provided by a proxy, that is, by an individual who is familiar with the person under evaluation.

The authors compared the scores obtained with the two versions of the instrument and found a low correspondence (41%). To increase the diagnostic sensitivity, Moss and collaborators have therefore suggested to always administer both versions of the instrument. The psychometric properties of PAS-ADD were examined by Costello, Moss, Prosser, and Hatton (1997). The concordance between

assessors of the person-directed version was measured by a session in which different clinicians filled out many questionnaires in a rigorously autonomous manner after following as many interviews recorded on videotape. The concordance was low for both individual items and diagnostic groups (kappa = 0.65 and 0.66, respectively). The factor analysis gave good results, identifying a factor for each of the subscales, and also the concordance with the clinical diagnoses was high, equal to about 76%. No information on internal consistency and test-retest was provided. The experience of many researchers and clinicians suggests that PAS-ADD is more useful for screening for mental health problems in general than for identifying a specific psychiatric disorder. Compared to the Mini and Checklist versions, the PAS-ADD should be preferred in cases where you are faced with a person with ID who has language skills, you want to get a precise ICD-10 or DSM-IV (TR) diagnosis and/or you suspect a psychotic disorder, as the instrument is particularly sensitive to diagnoses in this area. A decade ago PAS-ADD has also been adapted to use with children and adolescents, with the name of Child and Adolescent Psychiatric Assessment Schedule (ChA-PAS; Moss, Friedlander and Lee 2013).

A more recent production interview is the Psychopathology Checklists for Adults with Intellectual Disability (P-AID; Hove and Havik 2008). It is a battery of instruments to be used with informants, designed to identify ten different PD and eight types of PB according to the DC-LD (Royal College of Psychiatrists, 2001). The P-AID showed acceptable internal consistency, reliability, and inter-rater, 8 units orthogonal to the factor analysis, while the sensitivity and specificity are still to be investigated (Hove and Havik 2008). Compared to PAS-ADD, it has the advantage of including a detailed assessment of the main PB, but the disadvantage of not being able to be used directly with the person with ID or LF-ASD.

Another semi-structured interview is the Schedule for the Assessment of Psychiatric Problems Associated with Autism (and Other Developmental Disorders) (SAPPA; [39]). This was also developed in the United Kingdom and includes items derived from the Research Diagnostic Criteria of Spitzer, Endicott and Robins (1978). The SAPPA is based on interviews with the client and/or an informant and helps in identifying each autistic individual's unique baseline of behaviors as well as changes from it, which may represent one or more symptoms of a new onset psychiatric disorder. SAPPA differentiates between those disturbances that were long-standing and those that were episodic and assesses if these disturbances met clinical criteria for PD.

The criteria employed to evaluate an episode of behavior change include (1) psychotic symptoms (delusions, hallucinations, catatonia, etc.); (2) a change in behavior outside the range of normal variation for the individual; and (3) definite diminution in level of social functioning as shown by at least two of the following: loss of interest in play/favourite activities, loss of self-care, loss of social involvement, loss of initiative, and need for change in supervision and/or placement [39].

Episodes of changed behavior are explored further to obtain systematic standardized information on symptoms. A symptom is deemed clinically significant if (1) it is outside the range of normal behavior for that individual; (2) it intrudes into, or

disrupts, the individual's ordinary activities; (3) it is of a degree that is not readily controlled by the individual or caregivers; and (4) it is sufficiently pervasive to extend into at least two activities.

In addition, the onset and the duration of each episode is determined in the context of other circumstances (e.g., life events such as loss, bereavement, medication changes, or medical concerns such as seizures) occurring in the person's life. The symptoms during an episode that meet diagnostic criteria and the pattern of the episodes are used to establish a psychiatric diagnosis. Episodic PD identified using the SAPPA interview include mood, anxiety, and psychotic disorders. A full SAPPA evaluation requires a face-to-face clinical interview with the client and/or the caregivers (informants) for non-verbal clients. In the first part of the interview, inquiry is also made as to the family history of PD. The second part of the SAPPA interview deals with behaviors and disorders that do not follow an episodic course (e.g., some self-injurious, hyperkinetic, obsessive, compulsive, and other anxiety-type behaviors, tics, stereotypies, and other nonspecific challenging behaviors) [30].

The tool was used in a number of studies (Bolton et al. 2011; [21, 30, 40, 41]), predominantly with people with ASD and for research purpose, often with some modifications. An attempt to adapt to use in clinical practice was recently performed by Battaglia, Detrick, and Fermandez [42]. A study on the validity and other psychometric characteristics of the instrument has never been performed.

To date, the most used scales for psychopathological screening in people with ID and LF-ASD are the Psychopathology Instrument for Mentally Retarded Adults (PIMRA) (Kazdin et al. 1983; Matson et al. 1984, 2012), the Psychiatric Assessment Schedule for Adults with Developmental Disabilities Checklist (PAS-ADD) (Moss 1993), and the Diagnostic Assessment for the Severely Handicapped (DASH) (Matson et al. 1991). Although some high-quality studies support its effectiveness, these tools seem to have some limits in sensitivity, especially in reference to schizophrenic spectrum disorders, reproducibility between different evaluators and consideration of clinical anamnestic information [37].

Further limits of these and the other currently available tools are the applicability to all levels of intellectual impairment, above all to the most serious ones, the interdisciplinary usability and the possibility of managing, with the same system of symptomatological equivalence, each phase of the clinical intervention, i.e., general psychopathological screening, specific categorical diagnosis, dimensional diagnosis, and monitoring of symptoms over time. An attempt to overcome all these limits is represented by the Systematic Psychopathological Assessment for persons with Intellectual and Developmental Disabilities (SPAIDD), a comprehensive tool battery including a "G" version for the "General" screening [43], specific tools for psychopathological area (mood disorders, psychotic disorders, anxiety disorders, autism spectrum disorder, etc.), a module for psychopathological dimensional orientation and a module for symptoms' monitoring (follow-up). All the tools use the same set of adapted symptoms, are based on behaviors or other observable aspects and therefore applicable also to persons with severe impairment of communication skills and conceptualization of intrapsychic suffering. All the SPAIDD tools have

been built on the DSM diagnostic criteria and constantly updated to its evolutions. The specific tools for psychopathological area also evaluate the chronology of symptoms, supporting clinicians in the differential diagnosis and in prognostic judgment. All SPAIDD instruments are subjected to in-depth assessments of psychometric characteristics. Particular attention is paid to the validity of the facade, in order to improve the motivation of the informants to use the test.

The SPAIDD-G has undergone numerous evaluations of its psychometric properties [36, 37]. The last one was performed recently on a sample of 395 persons, selected from a wider sample of 944 on the basis of the completeness of data (cases with more than one item without score were excluded). The age range of this sample was 16 and 91 years (M = 51.5; DS = 15.4) and the male-female ratio 73/27. Forty-five percent had a comorbid psychiatric diagnosis (additional to that of ID). The Kuder-Richardson coefficient (KR20) was 0.84 for the full scale and ranged from 0.14 to 0.81 for the 18 subscales. The subscales with a lower internal consistency were "identity disorder" and "sexual disorder," as expected for the low number of items, while those with higher values were "psychotic disorder," "mood disorder—depression," and substance-related disorder.

The inter-rater reliability, estimated through the calculation of Cohen's *K* coefficient, was never less than 0.76, confirming an error variance linked to the scoring criteria and the subjectivity of the rater as a whole not significant. All the raters involved in the validation studies indicated that the tool is clear and easy to use. This judgment was strengthened after the introduction of the description and the exemplification of the items. The SPAIDD-G was judged of great utility by most of the professionals who used it, even in the absence of specific training, immediately understandable and quick to fill out, about 32 min (range 25–42). In the direct comparison with the DASH-II, the SPAIDD-G showed higher face validity, easiness of use, applicability, and syndromic sensitivity. It also required a significantly lower compilation time [43]. The tool is going to be validated in English and German.

8.6 Psycho-pharmacological Therapies

People with ID and LF-ASD receive far more psychoactive drugs than the general population, both in the number of prescribed drugs and in the average prescribed dosage, with rates ranging between 32% and 89%, particularly in adolescents and adults (Bachmann et al. 2014; Merikangas et al. 2013; Steinhausen and Bisgaard 2014; de Kuijper et al. 2010; Doan et al. 2013; Holden and Gitlesen 2004; Stolker et al. 2002; Deb et al. 2015). Drugs are often prescribed to manage PB, without previous assessments of their psychopathological nature and therefore without specific indication. The extensive use also reflects the pressure exerted on clinicians by family members and other assistants of the person with ID to "do something" to quickly alleviate the undefined individual suffering and the negative behavioral changes, which often cause in turn severe distress and destabilization throughout the family and the whole relationship network.

Once prescribed, drugs tend to maintain for a long time, becoming an integral part of the long-term intervention program. On the contrary, an attempt should be made at each stage of monitoring to revisit and reevaluate the formulation and the pharmacotherapeutic plan, aiming at using the lowest possible dose for the minimum duration. Non-medication-based management strategies and the withdrawal of medication should always be considered at regular intervals [44]. Some of the main reasons of long-term treatment are carers' concern of relapse and inaccurate report of efficacy. After months or years of treatment, suspension attempts are reported to be successful only in a limited number of cases (Ahmed et al. 2000).

The most frequently prescribed drugs are antipsychotics, followed by antidepressants (SSRIs and tricyclics), mood stabilizers, and benzodiazepines.

The literature on the psychopharmacological intervention for people with ID and LF-ASD does not offer relevant support to clinicians: studies on the rationale for use, dosages, and safety are few and show great heterogeneity of results, methods, and outcome criteria (Baasland and Engedal 2009; Tyrer et al. 2014). The main hurdles for research are represented by the heterogeneity of the reference population, the indefiniteness of the intervention aims, and the ethical issues, particularly the inability of consensus in participating in randomized controlled trials (RCT) (Feldman et al. 2014). Moreover, the above-mentioned difficulties in identifying PD in persons with communication impairment has aggravated the lack of specific research on drugs with a more general lack of investigations on epidemiology, evaluation tools and procedures, specific clinical presentation, and therefore the definition of therapeutic goals. The lack of research has determined in turn a very low availability of drugs indicated for use with persons with ID and has polarized the prescriptions on the few molecules already approved. At present psychopharmacology for persons with ID and LF-ASD is stuck in a vicious circle; the acts aimed at protecting people with neurodevelopmental disability from inadequate treatments obstacle the development and implementation of appropriate ones.

Only 2% of pharmacological studies include people with ID, and more than 90% are designed to determine their automatic exclusion (Feldman et al. 2014). This trend seems set to continue in the coming years.

SSRI, such as fluoxetine, fluvoxamine, sertraline, citalopram, escitalopram, and paroxetine, are the most prescribed antidepressants due to their greater safety profile than tricyclic antidepressants (TCA), even if studies' results on their efficacy are contradictory and provide evidence of intermediate level (Aman et al. 2000; Deb et al. 2015; Ji and Findling 2016). TCA have also been widely used, both for the treatment of symptoms related to ID or ASD themselves and for the associated psychiatric and behavioral disorders. Clomipramine is the most studied drug of this class, with many reports of efficacy on repetitive behaviors, whether they are attributable to stereotypes or obsessive-compulsive symptoms, co-occurrent to the neurodevelopmental disorder (Gordon et al. 1993; Hurwitz et al. 2012).

Venlafaxine, a selective serotonin and norepinephrine reuptake inhibitor, has shown some beneficial effects in the treatment of hyperactivity, self-injury, and repetitive behaviors in children, adolescents, and adults with ASD. However, studies are very limited (Hollander et al. 2000; Carminati et al. 2006).

Trazodone, a heterocyclic antidepressant, seems to be effective in reducing aggression and self-injurious behavior, but there are only case reports (Gedye 1991).

Benzodiazepines (BDZ) have been found to be scarcely useful in the management of PB and in some cases seem to have even led to significant aggravations (Kalachnik et al. 2002). Their long-term use may increase the risk of tolerance and dependence (with withdrawal symptoms), as well as adjunctive cognitive difficulties, which have frequently been documented in older adults (Puustinen et al. 2012).

BDZ are indicated for catatonia, even at high doses in acute phases. Catatonia represents a potentially fatal psychiatric and medical urgency that is more frequent in persons with ID and ASD than in the general population, especially in late adolescence and in those with more severe disability (Gillberg and Steffenburg 1987; Wing and Shah 2000; Palm, Forsthoff et al. 2011; Ghaziuddin, Dhossche et al. 2012; Torr and D'Abrera 2014; Winarni, Schneider et al. 2015).

The use of antipsychotics (AP) in persons with ID and LF-ASD requires some specific precautions in addition to the usual rule of "go slow and stay low" valid for any psychotropic drug in this population. These precautions are connected to the particular vulnerability to side effects and to frequent comorbidities. Catatonic syndromes and seizures are frequent. In some genetic syndromes, such as Down Syndrome, the central nervous system is subject to early aging and consequent anticipation of the risk increase of cerebrovascular adverse events of some AP (olanzapine, risperidone, aripiprazole and quetiapine), identified in the general population. The use of second-generation antipsychotics (SGA) has also been associated with an increase of cardiovascular morbidity and mortality in elderly persons with ID of different kinds (de Winter, van den Berge et al. 2016; Vigod et al. 2016).

Among the first-generation antipsychotics (FGA), the most used are chlorpromazine and haloperidol. Although some efficacy in the management of PB, especially aggressiveness, FGA should not be considered first-choice therapy, due to limited tolerability (Anderson et al. 1984; La Malfa et al. 2006). For the same reason, they should be used at low dosage and for the minimum possible time. Haloperidol is indicated as an adjunctive therapy in the short term for the management of psychomotor agitation, excitement, and impulsive and violent behaviors (Bhaumik, Branford et al. 2015). Few observational and small open-label studies have shown some efficacy on hyperactivity, aggression, stereotypy, emotional lability, and anger (Naruse et al. 1982; Campbell M 1999). One of the most important studies performed on children with aggressive behaviors showed no differences between risperidone, haloperidol, and placebo (Tyrer et al. 2008).

SGA have been widely introduced in clinical practice. They present a better tolerability profile and a greater number of RCT than FGA. However, studies have been conducted almost exclusively in people with ASD. In addition to risperidone and aripiprazole, there are data on olanzapine, quetiapine, paliperidone, ziprasidone, and asenapine (Advokat et al. 2000). Compared to FGA, SGAs have diversified receptor profiles that seem to impact less on the cognitive and neuromuscular vulnerability of people with ID (de Leon et al. 2009). Some authors claim that they would also have advantages in terms of efficacy, safety, and adherence to treatment, in children, adolescents, and adults (Deb and Unwin 2007).

Despite the lack of solid evidence-based indications specific for ID, anticonvulsants are widely used in clinical practice. In fact, about 20% of people with ID suffer from some kind of epilepsy, a greater number have a history of seizures and electroencephalographic alterations (Robertson, Hatton et al. 2015). Furthermore, some anticonvulsants are currently used as mood stabilizers both in the treatment of acute mania and in the prophylaxis of bipolar disorder. In people with ID, anticonvulsants are used for the control of PB even when a precise psychiatric diagnosis has not been formulated, especially in patients with lower functioning. In many cases, epilepsy co-occur together with PB and PD, indicating some kind of causal link, although evidence upon this is controversial (Arshad, Winterhalder et al. 2011). Also clinical experience indicates a wide range of outcomes: sometimes a good control of epilepsy is associated with the improvement of the general functioning and with the attenuation of any neuropsychiatric and behavioral alteration, in other cases an effective treatment of seizures is followed by worsening of PB and PD. The choice of the anticonvulsant agent seems to play a role in these different results (Deb, Chaplin et al. 2008). Thus, the prescription of anticonvulsants to treat mood disorders and related PB should be made with caution and after a thorough assessment of the neurological comorbidities.

Psychostimulants are the first-choice drugs in children with attention deficit and hyperactivity disorder (ADHD), with a response rate of 70–80% (Greenhill, Swanson et al. 2001). Symptoms of hyperactivity, impulsivity, and inattention are frequently found in the context of other neurodevelopmental disorders including ID and ASD, with rates between 6% and 80% (Frazier, Biederman et al. 2001; Capone, Goyal et al. 2006; Dykens 2007; Rommelse, Franke et al. 2010). In persons with ID and ASD, the co-occurrence of ADHD or ADHD-like symptoms can negatively impact on the outcomes of behavioral interventions and on overall individual quality of life.

Some clinicians hesitate to use methylphenidate in persons with ID for the risk of lowering the seizure threshold in patients who are already more vulnerable than the standard population. A recent study compared the data of more than 18,000 people treated with stimulants with those of almost 55,000 untreated, highlighting that stimulants do not increase the number of hospitalizations related to seizures, even when epilepsy is associated with infantile cerebral palsy, congenital anomalies of the central nervous system, or ID (Liu, Carney et al. 2017).

Atomoxetine appears to be more effective in adults than in children, which is probably due to the different maturation of the dopaminergic and noradrenergic systems in the prefrontal cortex. The drug presents a kinetic of action completely different from the stimulants, developing its therapeutic effect in a period comprised between 1 and 2 months. RCT and open-label studies conducted in children with ASD and ADHD have given unreliable results regarding efficacy on ADHD nuclear symptoms, irritability, verbal and motor stereotypes, PB, and social withdrawal; safety and tolerability were pretty good across studies, with the most common side effects being represented by gastrointestinal alteration, fatigue, palpitations, hyporexia, irritability, and sleep problems (Jou, Handen et al. 2005; Arnold, Aman et al. 2006; Posey, Wiegand et al. 2006; Troost, Steenhuis et al. 2006; Charnsil 2011; Zeiner, Gjevik et al. 2011;

Harfterkamp, van de Loo-Neus et al. 2012). A recent review of the literature has underlined that the quality of the studies in this area is modest, and the results are not very generalizable to the whole autism spectrum (Ghanizadeh 2013). In persons with LF-ASD, atomoxetine seems to be less effective, especially in children, and to determine a higher rate of side effects (Cheng, Chen et al. 2007; Ghanizadeh 2013; Fernandez-Jaen et al. 2010; Kilincaslan et al. 2016).

References

1. Matson JL, Kozlowski AM. The increasing prevalence of autism spectrum disorders. Res Autism Spectr Disord. 2011;5(1):418–25.
2. World Health Organization. ICD-11 international classification of diseases (11th rev.). 2018. https://icd.who.int/ (l.v. 10/3/2019).
3. World Health Organisation. International classification of diseases and related health problems (10th rev., ICD-10). Geneva: World Health Organisation; 1992.
4. APA—American Psychiatric Association. Diagnostic and statistical manual of mental disorders (3rd edition) (DSM-III). Washington, DC: American Psychiatric Association; 1980.
5. Greenspan S, Switzky HN. Forty-four years of AAMR manuals. In: Switzky HN, Greenspan S, editors. What is mental retardation?: ideas for an evolving disability in the 21st century. Washington, DC: AAMR; 2006.
6. APA—American Psychiatric Association. Diagnostic and statistical manual of mental disorders (4th edition; DSM-IV). Washington, DC: American Psychiatric Association; 1994.
7. APA—American Psychiatric Association. Diagnostic and statistical manual of mental disorders (5th edition; DSM-5). Washington, DC: American Psychiatric Association; 2013.
8. Ghaziuddin M. Mental health aspects of autism and Asperger syndrome. London: Jessica Kingsley Publishers; 2005.
9. Matson JL, Shoemaker M. Intellectual disability and its relationship to autism spectrum disorders. Res Dev Disabil. 2009;30(6):1107–14.
10. Boucher J, Bigham S, Mayes A, Muskett T. Recognition and language in low functioning autism. J Autism Dev Disord. 2008;38:1259–69.
11. Murphy O, Healy O, Leader G. Risk factors for challenging behaviors among 157 children with autism spectrum disorders in Ireland. Res Autism Spectr Disord. 2009;3:474–82.
12. O'Brien G, Pearson J. Autism and learning disability. Autism. 2004;8(2):125–40.
13. Goldmon S, Wang C, Salgado MW, Greene PE, Kim M, Rapin I. Motor stereotypies in children with autism and other developmental disorders. Dev Med Child Neurol. 2009;51:30–8.
14. Lunsky Y, Gracey C, Bradley E. Adults with autism spectrum disorders using psychiatric hospitals in Ontario: clinical profile and service needs. Res Autism Spectr Disord. 2009;3(4):1006–13.
15. McCarthy J, Hemmings C, Kravariti E, Dworzynski K, Holt G, Bouras N, Tsakanikos E. Challenging behavior and co-morbid psychopathology in adults with intellectual disability and autism spectrum disorders. Res Dev Disabil. 2010;31(2):362–6.
16. Cowley A, Newton J, Sturmey P, Bouras N, Holt G. Psychiatric inpatient admissions of adults with intellectual disabilities: predictive factors. Am J Ment Retard. 2005;110(3):216–25.
17. Tsakanikos E, Costello H, Holt G, Bouras N, Sturmey P, Newton T. Psychopathology in adults with autism and intellectual disability. J Autism Dev Disord. 2006;36:1123–9.
18. Tsakanikos E, Sturmey P, Costello H, Holt G, Bouras N. Referral trends in mental health services for adults with intellectual disability and autism spectrum disorders. Autism. 2007;11:9–17.
19. Melville CA, Cooper SA, Morrison J, Smiley E, Allan L, Jackson A, et al. The prevalence and incidence of mental ill-health in adults with autism and intellectual disabilities. J Autism Dev Disord. 2008;38:1676–88.

20. Bradley EA, Summers JA, Wood HL, Bryson SE. Comparing rates of psychiatric and behavior disorders in adolescents and young adults with severe intellectual disability with and without autism. J Autism Dev Disord. 2004;34:151–61.
21. Hutton J, Goode S, Murphy M, Couteur AL, Rutter M. New-onset psychiatric disorders in individuals with autism. Autism. 2008;12(4):373–90.
22. La Malfa G, Lassi S, Salvini R, Giganti C, Bertelli M, Albertini G. The relationship between autism and psychiatric disorders in intellectually disabled adults. Res Autism Spectr Disord. 2007;1(3):218–28.
23. LoVullo SV, Matson JL. Comorbid psychopathology in adults with autism spectrum disorders and intellectual disabilities. Res Dev Disabil. 2009;30(6):1288–96.
24. Matson JL, Nebel-Schwalm MS. Comorbid psychopathology with autism spectrum disorders in children: an overview. Res Dev Disabil. 2007;28:341–52.
25. Mouridsen SE, Rich B, Isager T, Nedergaard NJ. Psychiatric disorders in individuals diagnosed with infantile autism as children: a case study. J Psychiatr Pract. 2008;14:5–12.
26. Cooper SA, van der Speck R. Epidemiology of mental ill health in adults with intellectual disabilities. Curr Opin Psychiatry. 2009;22:431–6.
27. Selten JP, Lundberg M, Rai D, Magnusson C. Risks for nonaffective psychotic disorder and bipolar disorder in young people with autism spectrum disorder: a population-based study. JAMA Psychiatry. 2015;72(5):483–9.
28. Thalen M. Comorbidity in adolescents and adults with intellectual disability (ID). Masterthesis Orthopedagogiek; 2011.
29. Cervantes PE, Matson JL. Comorbid symptomology in adults with autism spectrum disorder and intellectual disability. J Autism Dev Disord. 2015;45(2):3961–70.
30. Bradley E, Bolton P. Episodic psychiatric disorders in teenagers with learning disabilities with and without autism. Br J Psychiatry. 2006;189(4):361–6.
31. Bakken TL, Helverschou SB, Eilertsen DE, Heggelund T, Myrbakk E, Martinsen H. Psychiatric disorders in adolescents and adults with autism and intellectual disability: a representative study in one county in Norway. Res Dev Disabil. 2010;31(6):1669–77.
32. Gadow KD, Devincent CJ, Pomeroy J, Azizian A. Comparison of DSM-IV symptoms in elementary school-age children with PDD versus clinic and community samples. Autism. 2005;9:392–415.
33. Hill J, Furniss F. Patterns of emotional and behavioural disturbance associated with autistic traits in young people with severe intellectual disabilities and challenging behaviours. Res Dev Disabil. 2006;27:517–28.
34. McCarthy J. Children with autism spectrum disorders and intellectual disability. Curr Opin Psychiatry. 2007;20:472–6.
35. Bradley EA, Issacs BJ. Inattention, hyperactivity, and impulsivity in teenagers with intellectual disabilities, with and without autism. Can J Psychiatr. 2006;55:598–606.
36. Bertelli M, Scuticchio D, Ferrandi A, Ciavatta C, La Malfa G, Mango F, Porcelli C, Monchieri S. Psychopathology of people with intellectual disability: a multicentre study of a new instrument, the SPAID-G. Ital J Psychopathol. 2010;16(1):53–63.
37. Bertelli M, Scuticchio D, Ferrandi A, Lassi S, Mango F, Ciavatta C, Porcelli C, Bianco A, Monchieri S. Reliability and validity of the SPAID-G checklist for detecting psychiatric disorders in adults with intellectual disability. Res Dev Disabil. 2012;33(2):382–90.
38. Fletcher R, Havercamp S, Ruedrich S, Benson B, Barnhill J, Cooper S-A, Stavrakaki C. Clinical usefulness of the diagnostic manual-intellectual disability for mental disorders in persons with intellectual disability: results from a brief field survey. J Clin Psychiatry. 2009;70(7):967–74.
39. Bolton PF, Rutter M. Schedule for assessment of psychiatric problems associated with autism (and other developmental disorders) (SAPPA): informant version. Cambridge; London: University of Cambridge; Institute of Psychiatry; 1994.
40. Hutton J. Cognitive decline and new problems arising in association with autism. Doctor of Clinical Psychology Thesis, Institute of Psychiatry, University of London; 1998.

41. Raznahan A, Joinson C, O'Callaghan F, Osborne JP, Bolton PF. Psychopathology in tuberous sclerosis: an overview and findings in a population based sample of adults with tuberous sclerosis. J Intellect Disabil Res. 2006;50:561–9.
42. Battaglia M, Detrick S, Fernandez A. Multidisciplinary treatment for adults with autism spectrum disorder and co-occurring mental health disorders: adapting clinical research tools to everyday clinical practice. J Ment Health Res Intellect Disabil. 2016;9(4):232–49.
43. Bertelli M. SPAIDD-G, systematic psychopathological assessment for persons with intellectual and developmental disabilities—general screening, manual. Giunti Psychometrics; 2019. In Press.
44. Deb S, Kwok H, Bertelli M, Salvador-Carulla L, Bradley E, Torr J, Barnhill J, Guideline Development Group of the WPA Section on Psychiatry of Intellectual Disability. International guide to prescribing psychotropic medication for the management of problem behaviours in adults with intellectual disabilities. World Psychiatry. 2009;8(3):181–6.