Identification of anxiety and other psychiatric disorders in individuals with autism and intellectual disability

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Abstract

Individuals with autism and intellectual disability (ID) are assumed to have higher vulnerability for developing psychiatric disorders than the general population. However, psychiatric disorders are frequently overlooked in this group and psychiatric symptoms attributed to the disability itself. Efforts to increase the identification of psychiatric disorders in this group of individuals are therefore needed. When problem behaviours are recognized as manifestations of a comorbid psychiatric disorder, rather than attributed to the disorder of autism or ID, it is likely that more appropriate treatment will be provided.

One problem related to identifying psychiatric disorders in individuals with autism is the considerable conceptual overlap between autism and psychiatric disorders. There is considerably symptom overlap and similar behaviours may be indicators of both autism and a psychiatric disorder. Differentiating conceptually between these disorders is, however, a prerequisite for developing more accurate and reliable diagnoses. The complexities of identifying mental health disorders are further increased due to the fact that individuals with autism and ID have reduced capacity for introspection and problems communicating their personal state. In addition, they may display idiosyncratic or atypical psychiatric symptoms.

The present thesis addresses the conceptual overlap between autism and psychiatric disorders, and the delineation between them. The conceptual boundaries between autism and psychiatric disorders are explored, and the results applied as a basis for further explorations. The aim is to contribute to an improved conceptual understanding of both autism and psychiatric disorders and the relationship between them. A better conceptual understanding of the phenomena may reduce the difficulties related to identifying psychiatric disorders in individuals with autism and ID, facilitate increased awareness among professionals, and improve the quality of the mental health care for this group.

The project contains four parts: Part one is a conceptual analysis and an empirical investigation to identify symptoms of psychiatric disorders which may be differentiated from the core characteristics of autism. Part two is a pilot study and the first validation of a new screening checklist: the Psychopathology in Autism Checklist (PAC). The aim is to examine

whether the PAC differentiates between sub-groups of individuals with autism and ID with and without psychiatric comorbidity, and between subgroups with different psychiatric disorders comorbid to autism and ID. Part three is a screening study of a representative sample, including all individuals diagnosed with autism and ID in Nordland County in the northern part of Norway. The aim is to estimate the prevalence of individuals with autism and ID identified by the PAC as in need of referral to psychiatric examination. This study also includes a comparison with a representative sample of persons with ID only. Part four addresses the assessment of anxiety in more detail. Anxiety seems to occur frequently in individuals with autism, but is difficult to recognize in individuals with both autism and ID. The study explores the recognition of specific anxiety symptoms in a representative and a clinical sample of individuals with autism and ID, using the anxiety subscale of the PAC. The study also includes a comparison of anxiety assessment with the PAC and a comprehensive clinical assessment.

The conceptual analysis demonstrate that it is possible to differentiate conceptually between symptom descriptions of autism and of the four psychiatric disorders (psychosis, depression, anxiety, and obsessive compulsive disorder, OCD), as well as between the four psychiatric disorders. A set of symptoms was identified in the investigation, which were rated as specific to a psychiatric disorder and not characteristic of autism as it appears in individuals with intellectual disability. These symptoms were regarded as indicators of psychiatric disorders in this group.

The Psychopathology in Autism Checklist (PAC) was constructed on the basis of the results from the conceptual analysis. It is a carer-completed checklist designed to identify adults with autism and ID in need of psychiatric services. The checklist contains five subscales: psychosis (10 items), depression (7 items), anxiety disorder (6 items), OCD (7 items), and general adjustment problems (12 items).

The results of the pilot study indicate acceptable psychometric properties, and that the PAC discriminates between adults with autism and ID with and without psychiatric disorders, and partially between individuals diagnosed with different psychiatric disorders, especially psychosis and obsessive compulsive disorder (OCD). High levels of general adjustment problems and moderate levels of anxiety were demonstrated in all psychiatric subgroups.

In the screening study, psychiatric disorders and severe general adjustment problems were found to be high in more than 50 percent of the autism group and approximately 20 percent of the ID-only group. The statistical interaction between autism and psychiatric disorder was significant. The largest difference between the autism and the ID-only group was

in the prevalence of anxiety, indicating that anxiety problems are an important characteristic of the adult autism population. In both groups, the majority of the individuals identified with a psychiatric disorder, were afflicted with more than one psychiatric disorder. Individuals with more severe psychiatric disorders had higher degrees of diagnostic overlap. Having an intellectual disability thus seem to imply a risk for developing adjustment problems, and it seems particularly difficult for individuals with ID who also have autism to master every-day challenges.

In the anxiety study, the scores on items that are supposed to assess the cognitive aspects of anxiety were higher than the scores on the items assessing physiological arousal. This suggests that physiological arousal may not be as readily observable as assumed in individuals with autism and ID, and points to a need for increased clinical awareness toward such symptoms. The low number of idiosyncratic symptoms reported in the clinical assessment indicates that anxiety may be recognized by symptoms generally similar to those reported for individuals without autism. The finding that nearly forty percent of a representative sample of people with autism was assessed with anxiety problems, support the assumption that anxiety occur frequently in this population. The differences found between the clinical assessment and the checklist scores indicate that both anxiety signs and signs of general adjustment problems may have to be included in order to identify individuals with anxiety problems by checklists. However, for diagnostic purposes and for monitoring treatment, individual anxiety assessment seems indicated.

The differentiation of symptoms related to autism and to psychiatric disorders demonstrated in the present thesis may elucidate the understanding of the delineation between them. The assumed high levels of psychiatric comorbidity among adolescents and adults with autism and ID have been supported by the findings in the present thesis, although the levels are lower than in some of the highest reports.

The PAC is not a diagnostic instrument, and an accurate diagnostic evaluation requires additional information from informants with thorough knowledge about the individual and the individual's changes in behaviour and mood over time. In particular the difficulties related to recognizing anxiety signs in people with autism and ID indicate the need for cooperation with key informants. The PAC may, however, contribute to the identification of people within this population who are at risk for having mental health problems and thereby to their access to specialized mental health services.

List of papers

Paper I

Helverschou, S.B., Bakken, T.L. & Martinsen, H.(2008). Identifying symptoms of psychiatric disorders in people with autism and intellectual disability: An empirical conceptual analysis. *Mental Health Aspects of Developmental Disabilities,* 11, 105–115.

Paper II

Helverschou, S.B., Bakken, T.L. & Martinsen, H.(2009). The Psychopathology in Autism Checklist (PAC): a pilot study. *Research in Autism Spectrum Disorders,* 3, 179–195.

Paper III

Bakken, T. L., Helverschou, S. B., Eilertsen, D. E., Hegglund, T., Myrbakk, E., & Martinsen, H. (2010). Psychiatric disorders in adolescents and adults with autism and intellectual disability: A representative study in one county in Norway. *Research in Developmental Disabilities,* doi: 10.1016/j.ridd.2010.04.009

Paper IV

Helverschou, S.B. & Martinsen, H. (2010). Anxiety in people diagnosed with autism and intellectual disability: Recognition and phenomenology. *Research in Autism Spectrum Disorders*, doi:10.1016/ j.rasd.2010.05.003

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Introduction

The present thesis addresses the conceptual overlap between autism and psychiatric disorders. Identification of psychiatric disorders in individuals with autism and intellectual disability (ID) represents a complex process and involves several challenges. It is especially difficult to distinguish between features representing autism and symptoms of psychiatric disorders. However, the understanding of the interrelationship between autism and psychiatric disorders has been changing during the last decades. In recent years, comorbidity and overlap with other disorders have become a major focus for research on autism, including the presence of psychiatric disorders (Clarke et al., 1999; Ghaziuddin, Alessi, & Greden, 1995; Gillberg & Billstedt, 2000; Howlin, 2000; Lainhart, 1999; Matson & Nebel-Schwalm, 2007; Reaven & Hepbrun, 2003; Tsai, 1996).

Autism, intellectual disability and psychiatric disorders

Autism is a neurodevelopmental disorder characterized by a triad of impairments affecting the development of social interaction, communication and imagination (ICD-10, World Health Organization, 1992, 1993; DSM- IV, American Psychiatric Association, 1994). Due to the persistent impact it makes on central functions such as the ability to communicate and understand social interaction, and developmental risk it represent, autism is termed a pervasive developmental disorder (Wing & Gould, 1979).

While autism earlier was considered the best validated diagnosis within child psychiatry (Volkmar & Rutter, 1995; Volkmar et al., 2004), it is now more common to talk about autism spectrum disorders (ASD), emphasizing the tremendous variation present in both severities of symptoms and intellectual capacity (Lord & Spence, 2006; Wing, 1996). In the present thesis, when not referring to a specific sub-diagnosis within the autism spectrum, the term "autism" is used synonymously with the DSM-IV category "autistic spectrum disorder" (American Psychiatric Association, 1994) and the ICD-10 category "pervasive developmental disorders" (World Health Organization, 1993).

In autism, language and communication deficits vary from delayed or absent language development, poor functional language use, to apparently adequate language. At least a quarter of all children with ASD fail to develop meaningful language (Ghaziuddin, 2005), and among individuals with childhood autism, about one-half are non-verbal (Lord & Paul, 1997). Communication difficulties like literal comprehension, echolalia, idiosyncratic words and phrases, pronouns reversals, and problems related to dialog skills and use of language in varied situations, are frequently seen in individuals who have developed language (Lord, 1985; Wing, 1996; Walenski, Tager-Flusberg & Ullman, 2006).

Among the deficiencies and cognitive impairments associated to autism, are their use of eye contact, gaze exchange, and focus for attention (Klin et al., 2002, Mundy, 2003), emotional reciprocity and interpretation of others peoples thoughts, feelings and reactions, (Baron Cohen, 1995; Baron-Cohen, Tager-Flusberg & Cohen, 2000), complex information processing, cognitive flexibility, planning and coherent understanding (Happé & Frith, 1996; Pennington & Ozonoff, 1996; Volkmar et al., 2004). The combination of communication deviances and difficulties in comprehension and interpretation is particularly of significance to the deficits in social interaction that characterize autism. Although individuals with autism are able to form relationships, the quality of their reciprocal social interaction is different, lacking flexibility and spontaneity in charing experiences and interests with others (Trevarten et al., 1996). The result is often a lack of friends and social withdrawal. Repetitive and stereotypic behaviour and limited interests and imagination are the third main clinical feature of autism. One-tracked minds and ways of behaviour, unusual attachment to objects and themes, and rigid and over involvement in interests are common (Ghaziuddin, 2005). Further characteristics are peculiar repetitive pattern of movement, fixation on simple routines such as lining up objects, and strong reactions towards small changes and new situations (Kanner, 1943, 1944).

There is a general agreement that autism is a congenital disorder with a significant genetic component, with increased risk for siblings to develop autism and autism-like conditions (Ghaziuddin, 2005; Polleux & Lauder, 2004; Volkmar et al., 2004; Zafeiriou, Ververi & Vargiami, 2007). Twin studies indicate, however, that genotype information alone is insufficient for predicting phenotype severity (Losh et al., 2008). Thus, autism is assumed to be the result of an interaction between genetic vulnerability and prenatal environmental factors. With prevalence rates recently reported between 0.6 and one percent in child and adolescents populations, autism is more common than previously thought (Baird, et al., 2006; Fombonne, 2003). Whether the increase is real or due to expansion of diagnostic criteria, and

improvement in identification practice, or whether environmental factors are involved, is an ongoing discussion (Volkmar et al., 2004).

Intellectual disability

Intellectual disability (ID) occurs frequently in individuals with infantile autism, in about 75 to 80 percent, but the rates are significantly lower in the whole autism spectrum, between 10 and 25 percent (Fombonne, 1999, 2003, 2005; Ghaziuddin, 2000). People with ID represent a heterogeneous group with several etiologies (Burack, Hodapp & Zigler, 1998), characterized by impairment of skills manifested during the developmental period, skills which contribute to the overall level of intelligence, i.e., cognitive, language, motor, and social abilities (ICD-10, World Health Organization, 1992). The diagnosis is based on the overall assessment of intellectual functioning, and degrees of intellectual disability are usually assessed with standardized intelligence tests in combination with scales assessing social adaptation.

Comorbidity

Many individuals with autism have somatic and behavioural problems not accounted for by the diagnosis of autism (Gillberg, 1998; Moss & Howlin, 2009; Rutter et al., 1994; Zafeiriou, et al., 2007). Examples are epilepsy (Fombonne, 2003), Attention Deficit Hyperactivity Disorder (ADHD) (Kadesjø, Gilberg & Hagberg, 1999; Leyfert, et al., 2006), tics disorder and Tourette syndrome (Baron-Cohen et al., 2000, Ehlers & Gilberg, 1993). Moreover, review articles indicate increased rates of autism in at least 30 different genetic syndromes (Polleux & Lauder, 2004; Zafeiriou, et al., 2006). Autism is also more frequent in Fragile X, Tuberous Sclerosis, Angelman syndrome, Down syndrome, deafness, and blindness than expected (Gillberg, 1998; Moss & Howlin, 2009; Rutter et al., 1994). Thus, in autism, comorbidity seems to be the rule rather than the exception (Gillberg & Billstedt, 2000).

Comorbidity refers to the occurrence of two or more disorders in the same persons (Matson & Nebel-Schwalm, 2007). The co-occurring conditions may or may not be causally related (Ghaziuddin, Ghaziuddin & Greden, 2002). However, the term implies the co-occurrence of two independent conditions or disorders which may be differentiated from each other (Caron & Rutter, 1991). In the present thesis, the terms "comorbidity" and "co-occurring disorders" are used synonymously.

Psychiatric disorders

According to the World Health Organization (2001) and the American Psychiatric Association (2000) a psychological or behavioural condition or disorder is considered a psychiatric disorder when it causes a significant degree of distress and impairment in the person's performance of everyday activity. To differentiate between psychiatric disorders, criteria are used for diagnosis of identifiable clusters of symptoms, signs and behaviour such as the Diagnostic Statistical Manual of Mental Disorders (American Psychiatric Association, 1994, 2000) and International Classification of Diseases (World Health Organization, 1992, 1993). The criteria are based on a descriptive and atheoretical model of psychiatric disorders and the nomenclature represents consensus by a group of professionals at the time of the publication (Othmer, Othmer & Othmer, 2005; Zimmerman & Spitzer, 2005).

Anxiousness and anxiety

Anxiousness and anxiety represent a continuum from insecurity, via anxiousness and restlessness, to anxiety and panic. Anxiousness is characterized by weaker reactions than anxiety, and includes shyness, embarrassment and inhibition, and is a reaction most people experience (Crozier & Alden, 2001). The prevalence of social anxiousness has been reported between 50 and 60 percent, and more recent surveys suggest an increase in the incidence (Crozier & Alden, 2001). Anxiety disorders are among the most common psychiatric disorders with life time incidence estimates in USA of 30 percent among women and 20 percent among men (Kessler et al., 1994). Similar estimates have been suggested in Norway (Statens helsetilsyn, 2000). Due to the differences in severeness and frequency, it is important to separate anxiousness from anxiety disorders.

Both fear and anxiety are characterized by bodily preparedness and physiological arousal. What differentiates between the conditions is whether the reactions may be linked to a known object or not. When people experience fear, they know what they are afraid of, while anxiety is characterized by an arousal the individual is unable to explain (Martinsen, Lanesskog & Duckert, 1979). Symptoms of anxiety fall into two main categories: cognitive and somatic (ICD-10; DSM-IV; Doctor, Kahn & Adamec, 2008). The somatic symptoms are signs of physiological arousal, and subjective and emotional feelings of uneasiness and

discomfort are the cognitive aspect of anxiety (Statens helsetilsyn, 2000). The cognitive aspect of anxiety have been regarded as difficult to recognize in individuals with autism and ID, and probably explain why fears, phobias and anxiety among people with autism have been largely ignored in the literature (Green et al., 2000; Lainhart, 1999; Luscre & Center, 1996; Matson & Nebel- Schwalm, 2007; Schopler & Mesibov, 1994; Tantam, 2000).

Adjustment problems

Autism is a disability which demands special and usually life-lasting environmental adjustment (Martinsen & Tellevik, 2001). In general, disability is understood as the result of the interaction between conditions related to the individual and conditions related to the environment in which the person lives, i.e., the interaction between the individual's impairment and the barriers created by society (be social, environmental and attitudinal) (European Disability Forum, 1996; World Health Organization, 2007). Disability occurs when there is a gap between the individual's abilities and the environmental requirements (Lie, 1996), and an impairment may be caused by disease, trauma or other health condition. The requirements of the society are usually based on the developmental trajectories of the general population, and when a typical level of functioning is not reachable, problems with participating in the society may occur, which indicate planning of special services, adjustments or treatment (World Health Organization, 2001).

      The symptoms that characterize individuals with autism are associated with a number of problems and considered as general risk factors when they occur in the general population. The qualitative impairments in communication and reciprocal social interaction, and the restricted, repetitive repertoire of behaviours which are central to the diagnosis of autism, are associated with mental health problems (Reese et al., 2005). The sensitivities to sensory stimuli, such as noise, light and smell, commonly experienced by individuals with autism (Dawson & Watling, 2000; Kern et al., 2006) have been associated with behavioural problems (Reese et al., 2005). Thus, autism seems to imply a significant vulnerability for developing adjustment problems and psychiatric disorders (Clarke et al., 1999).

      Lainhart (1999) emphasizes four vulnerability factors related to autism: 1) deviancies in social interaction and communication; 2) difficulties in comprehension and interpretation, and intelligence levels below the normal range; 3) medical comorbidity such as epilepsy; and 4) life experiences with autism. For example, environmental change may cause loss of a

significant carer or friend, and due to the social and communicational difficulties, it is hard for people with autism to establish a similar relationship. The vulnerability associated with autism and the higher probability of problems for people with both autism and ID are illustrated by reports of higher rates of problem behaviour in this group than in individuals with ID only (Collacot et al., 1998; Holden & Gitlesen, 2006; McClintock, Hall & Oliver, 2003; Tyrer et al., 2006).

Most individuals with autism have problems mastering everyday activities, and such problems may be perceived as signs of psychiatric disorders. Likewise, psychiatric disorders are also characterized by a significant degree of distress and impairment in the person's performance of everyday activity. Thus, it is necessary to differentiate between problems related to autism and problems caused by inadequately environmental adjustment (Martinsen and Tellevik, 2001). In individuals with autism and a comorbid psychiatric disorder, it is also necessary to distinguish problems related to autism and adjustment problems from signs of a psychiatric disorder, i.e., to differentiate between characteristics of autism, adjustments problems, and psychiatric disorders.

Identification of psychiatric disorders

In individuals with developmental disability (ID), psychiatric disorders are often overshadowed by the ID and therefore not recognized (Bortwich-Duffy, 1994; Glenn, Bihm & Lammers, 2003; Jacobsen, 1999; Jopp & Keys, 2001; Matson et al., 2000; Moss, 1999; Moss et al., 1996). In adults with both ID and autism, psychiatric disorders may be even less often identified (Ghaziuddin, 2005, 2009; Howlin, 2002; Lainhart, 1999; Matson & Boisjoli, 2008; Wing, 1996). The tendency to overlook psychiatric disorders represent a significant problem, since individuals with autism and ID are assumed to have higher vulnerability for developing psychiatric disorders than the general population (Bradley et al., 2004; Brereton, Tonge & Einfeld, 2006; Clarke et al., 1999, Ghaziuddin & Greden, 1995; Ghaziuddin et al., 1992, 1998; Howlin, 1997; 2000; Howlin et al., 2004; Leyfer et al., 2006; Simonoff et al., 2008).

There are especially two fundamental problems related to the complex process of identifying mental health disorders in individuals with autism and ID: (1) the individuals' reduced capacity of introspection and their problems in communicating personal state (Ghaziuddin, 2005; Howlin, 1997; Lainhart, 1999); and (2) the conceptual overlap between

autism and psychiatric disorders (Clarke et al., 1989, 1999; Ghaziuddin & Greden, 1998; Ghaziuddin, Tsai & Ghaziuddin, 1992; Ghaziuddin et al., 1995, Kobayashi and Murata, 1998; Lainhart, 1999; Long, Wood & Holmes, 2000; McDougle, Kresch & Posey, 2000; Reaven & Hepburn, 2003; Volkmar & Cohen, 1991; Wing, 1996).

The difficulties of identifying psychiatric disorders in individuals with autism and ID are further increased by the presence of idiosyncratic or atypical psychiatric symptoms (Lainhart, 1999; Myers & Winters, 2002; Stavrakiki, 1999). Idiosyncratic and atypical psychiatric symptoms like self injury and aggressive behaviour have been reported as signs of depression in case studies (Ghaziuddin, 2005; Myers & Winters, 2002). Typical autism symptoms like repetitive and ritualistic behaviour also seem to increase in individuals with autism who have anxiety problems (Tantam, 2000). Increased intensity of ruminations has been described in individuals with autism who develop other psychiatric disorders (Tantam, 2000; Wing, 1996).

A psychiatric diagnosis is based on comprehensive information about signs, symptoms, and problems, and the duration and frequency of the problems. The diagnosis usually is based on descriptions of the person's own experiences and problems obtained in an interview or in combination with self-rating checklists (Othmer et al., 2005). Thus, diagnostic classificatory systems (e.g., DSM-IV, American Psychiatric Association, 1994; ICD-10, World Health Organization, 1992, 1993) rely heavily on descriptions of the subjective experience of the individuals who are being diagnosed. The reliability of ordinary psychiatric diagnostic provided for individuals with ID has therefore been questioned (Einfeld & Aman, 1995).

Most individuals with ID have difficulties describing their subjective experiences and problems, and hence in reporting information needed to identify a psychiatric disorder. In individuals with ID, psychiatric disorders may have to be identified by observable behaviours and recognition of the possible impact of ID in modifying the symptoms of psychiatric illness such as in DC-LD (Royal College of Psychiatrists, 2001) and in DM-ID (Fletcher et al., 2007). In individuals with both autism and ID, the diagnostic process is further complicated by the combination of the comprehension and communication difficulties related to autism and the problems in self-report related to ID. Thus, diagnosing psychiatric and behaviour disorders in persons with autism and ID poses formidable challenges, and indicate the use of other sources, e.g., informants or observation.

Confounding between autism and psychiatric disorders

Many authors have pointed to the considerable overlap between autism and psychiatric constructs and their associated disorders, resulting in symptom overlap and problems distinguishing both conceptually and empirically between autism and psychiatric disorders. Similar behaviours may be indicators of both autism and a psychiatric disorder, and the considerable overlap in symptoms between autism and psychiatric disorders may explain both why a complex autistic condition may be diagnosed as a psychiatric disorder, and why psychiatric disorders in individuals with autism often are attributed to the autism diagnosis and not identified as a separate psychiatric disorder (Clarke et al., 1989, 1999; Ghaziuddin et al., 1995, 1992; Kobayashi & Murata, 1998; Lainhart, 1999; Long et al., 2000; McDougle et al., 2000; Reaven & Hepburn, 2003; Volkmar & Cohen, 1991; Wing, 1996).

Psychosis

The symptom overlap between autism and psychosis is especially comprehensive. Shared characteristics are problems in social interaction, and especially social withdrawal (Konstantareas & Hewitt, 2001). Individuals with both disorders also seem to experience misunderstandings, confusion, and misinterpretations, although how these experiences are understood depend with the disorder in question. The conceptual overlap between autism and schizophrenia is apparent in the selection of the term "autism" derived from descriptions of socially withdrawn individuals with schizophrenia (Kanner, 1943). Childhood schizophrenia and autism have been seen as overlapping conditions (Eisenberg & Kanner, 1958), and the terms have sometimes been used interchangeably (Wolf, 2004). In the very first descriptions autism was considered a biologically rooted disorder (Kanner, 1943), but this view changed, and for many years autism was understood as an emotional disorder, termed childhood psychosis, and categorised as a psychiatric disorder similar to schizophrenia in ICD-8 (World Health Organization, 1967) and ICD-9 (World Health Organization, 1978). The criteria for diagnosing autism and the understanding of the pathogenesis have, however, changed during the last decades. The conditions are now viewed as distinct, and Autism Spectrum Disorders (ASD) are referred to as developmental disorders (American Psychiatric Association, 1994; World Health Organization, 1992).

Shared interpersonal and cognitive impairments in autism and schizophrenia have historically contributed to a controversy with regard to whether autism is a vulnerability factor for later psychosis (Clarke et al., 1989; Petty et al., 1984). However, this hypothesis has not

received empirical support (Mouridsen, Rich & Isager, 1999; Volkmar & Cohen, 1991). Despite the large variation and somewhat inconsistent findings related to the prevalence of psychiatric disorders in individuals with autism, neither Asperger syndrome nor autism is associated with increased risk of schizophrenia in adult life, and the probability for developing schizophrenia seem to be similar to the risk in the general population (0.6 %) (Cederlund, et al., 2008; Ghaziuddin et al., 1992, 1995; Howlin, 1997, 2000; Howlin et al., 2004; Lainhart, 1999; Schopler & Mesibov, 1994; Tantam, 2000). For example, a large study found a similar prevalence of schizophrenia in people with autism as in the general population (Volkmar & Cohen, 1991), and in a 22-year follow-up study, none of the 38 people with autism developed schizophrenia or other psychotic disorders (Mouridsen et al., 1999). Further, in a follow-up study of 140 males with Asperger syndrome and autistic disorder, only a small group had been diagnosed with psychosis by an independent psychiatrist, and none of them with schizophrenia (Cederlund et al., 2008). However, higher rates of schizophrenia have been reported, for example, in a register study of 118 individuals diagnosed with infantile autism as children (Mouridsen et al., 2008). In a comparison with 336 individuals with ID only, 48.3 percent of the group with autism had been in contact with a psychiatric hospital during the observation period, while this was the case for only 6.0 percent of the group with ID only. In the autism group, the most prevalent psychiatric disorder in addition to autism was schizophrenia. The authors explain the high rates of schizophrenia with the service provision in Denmark. They argue that many individuals with autism live in specialized institutions where psychiatric consultants are easily accessible, so that contact with psychiatric hospitals tends to occur only in the most severe cases. In a register study, there is also reason to suppose diagnostic uncertainties and a biased sample. On the other hand, psychotic depression was the most common psychiatric diagnosis reported in a review of 112 case studies on psychiatric disorders in individuals with autism, reported in about 25 percent of the cases (Howlin, 2002). This may indicate that the majority of individuals with autism who become psychotic develop an affective type of psychosis.

The overlap of symptoms between autism and psychotic disorders, as well as the problems related to interpreting the clinical features of autism, may have led to complex autistic conditions being misdiagnosed as psychoses (Wing, 1996). Symptoms of autism and negative symptoms of schizophrenia may have been confused (Clarke et al., 1999; Lainhart, 1999), for example lack of social interaction may be interpreted both as a feature of autism and as a symptom of schizophrenia (Konstantareos & Hewitt, 2001). Likewise, odd and unusual features in people with autism and idiosyncratic preoccupations have been mistaken

for delusions or other positive signs of schizophrenia, and language problems like literal comprehension in individuals with autism have been confused with thought disorder (Clarke et al., 1999; Lainhart, 1999). Among 130 adult psychiatric patients suspected with ASD, who were referred to a tertiary service, eighty-four (64.6 %) were identified with ASD, indicating that many individuals with ASD remain undiagnosed until adulthood (Rydén & Bejerot, 2008). In a representative sample of 1323 adult psychiatric outpatients, at least 19 individuals (1.4) percent were found to have ASD, and most of them had wrongly been given a diagnosis of schizophrenia (Nylander & Gillberg, 2001). Thus, the confounding between autism and psychosis is related to both the identification of autism in individuals supposed to have psychoses, as well as the identification of psychosis as a comorbid disorder to autism.

Obsessive compulsive disorder

The confounding between OCD and autism has been comprehensive both conceptually and symptomatically since the first descriptions of autism (Kanner, 1943, 1944; Lainhart, 1999; Shahill et al., 2006). Rituals, repetitive and stereotypic behaviour, and limited interests and imagination represent one of the three core symptom clusters which define autism (ICD-10, World Health Organization, 1993; DSM- IV, American Psychiatric Association, 1994). In the first descriptions of autism, obsessiveness - "obsessive insistence of sameness" – was the described as common in the individuals (Kanner, 1943/1968, p. 130). They showed persistence of structure and predictability and had strong reactions in new situations. Such problems often result in one-tracked minds and ways of behaving, unusual attachment to objects and themes, and rigid interests and over involvement. Some individuals have peculiar and repetitive pattern of movement, and many react strongly to small environmental changes and new situations. Thus, individuals with autism are usually understood as rigid and inflexible.

The compulsion-driven quality that characterises OCD goes beyond the core features of autism, but the differentiation between OCD and autism has still been considered especially complicated (Ghaziuddin, 2005; Lainhart, 1999; Shahill et al., 2006). The compulsions associated with autism are not "egodystonic", that is, they do not seem to occur against the person's will (Ghaziuddin, 2005; Lainhart, 1999). Clinically, the difference between the two conditions has been described as the difference between not bothersome or even pleasurably repetitive and ritualistic behaviour related to autism versus uncontrollable and unpleasant compulsions related to OCD (Shahill et al., 2006). The repetitive behaviour in OCD functions

to reduce anxiety, and when prevented from continuing the repetitions severe distress is displayed.

Anxiety

The common diagnostic overshadowing and the tendency to attribute anxiety symptoms such as distress symptoms to the autism condition per se, illustrate the apparent confounding between autism and anxiety (Lainhart, 1999; MacNeil, Lopes, & Minnes, 2009; Tsai, 2006). Nervousness and anxiety symptoms were included in the first descriptions of autism, where anxiety related to changes in routines or furniture arrangements were described as "an anxiously obsessive desire for the maintenance of sameness" and panic attacks as results of such changes (Kanner, 1943/1968, p. 130). Anxiety and autism seems to be intertwined to such a degree that it has been suggested that anxiety is an integral component of autism (Weisbrot et al., 2005). It has been argued that generalized anxiety is so common in individuals with autism that it should not be diagnosed as a separate disorder (Bellini, 2006; Gillot & Stranden, 2007; Ghaziuddin, 2005; Goldstein et al., 1994; Lainhart, 1999; Steingard, et al., 1997). Question has also been raised whether autism is a stress disorder (Morgan, 2006), despite the fact that anxiety symptoms are not included in the symptoms that characterize autism. The difficulties in differentiating between symptoms related to autism and to anxiety may be illustrated by the fact that frequent and repetitive questioning may be interpreted as anxiety signs, verbal rituals or communication deviances (Ghaziuddin et al., 1995).

Individuals with autism seem to be especially vulnerable to develop anxiety related to life problems associated with autism (Gillott & Stranden, 2007). The cognitive comprehension difficulties that characterize individuals with autism may lead to confusion and coping difficulties, their negative reactions to environmental change often result in bodily preparedness and distress, and difficulties in arousal regulation may lead to reduced capacity for coping with stress (Bellini, 2006; Goldstein et al., 1994; Steingard, et al., 1997). Some of the features that characterize autism, like rituals and repetitive behaviour, have also been considered as related to anxiety or as strategies for coping with anxiety (Ghaziuddin et al., 1995; Howlin, 1997). Thus, anxiety in individuals with autism has been understood as an effect of having autism as well as a cause of some of the characteristics of autism (Gillott, Furniss & Walter, 2001). Moreover, treatment procedures typically recommended for

individuals with autism, such as the creation of structure and predictability, include strategies similar to those recommended to prevent and reduce anxiety (Helverschou, 2006).

The high prevalence of anxiety symptoms and disorders which have been reported in the last decade may have contributed to a growing awareness of the presence of anxiety in individuals with autism (Green et al., 2000; Lainhart, 1999; Luscre & Center, 1996; Matson & Nebel- Schwalm, 2007; Schopler & Mesibov, 1994; Tantam, 2000). A review of 13 studies on anxiety in autism conducted between 1995 and 2008 suggests that children and adolescents with ASD show higher levels of anxiety than normative and community samples (MacNeil, et al, 2009). Compared to clinically anxious comparison groups, similar levels of anxiety have been demonstrated, while higher levels of anxiety have been demonstrated in ASD samples than in samples of people with conduct disorder and language disorder, and different patterns of anxiety have been demonstrated in samples with Down syndrome and mixed (non-ASD) clinical samples (Evans et al., 2005; Gillott et al., 2001; Green et al., 2000). Reports of such high prevalence rates emphasize the important implications of identifying anxiety problems in addition to the diagnosis of autism for the conceptualisation and treatment of these individuals (Gillott, Furniss & Walter, 2001; Green et al., 2000; Kim et al., 2003; Luscre & Center, 1996; MacNeil, Lopes & Minnes, 2009; Matson & Nebel- Schwalm, 2007; White et al., 2009).

The prevalence estimates of anxiety in individuals with autism vary, however, extensively (Kim et al., 2000). Reported rates vary for example between seven and 84 percent (Lainhart 1999; MacNeil, et al, 2009; White et al., 2009). It is generally samples of individuals with Asperger syndrome or high functioning autism that has been studied. Thus, it does not seem clear how anxiety may be recognized and diagnosed in individuals with autism, and especially in the lower functioning individuals who have larger problems reporting about their experiences and symptoms.

Comparisons across ASD subtypes have yielded conflicting results, but the majority of the studies suggest that the more cognitive able children and adolescents with Asperger syndrome and pervasive developmental disorder not otherwise specified may experience more anxiety symptoms than individuals with autistic disorder and ID (Gillott, Furniss & Walter, 2001; Kim et al., 2000; Sukhodolsky et al., 2008; MacNeil, et al., 2009). These findings may indicate that anxiety problems are related to cognitive ability and autism spectrum disorder subgroup (White et al., 2009). However, the special difficulties encountered when recognizing anxiety in individuals with autism and ID (Green et al., 2000; Lainhart, 1999; Luscre & Center, 1996; Matson & Nebel- Schwalm, 2007; Schopler & Mesibov, 1994; Tantam, 2000), and the lack of specific methods for assessing anxiety in this population (MacNeil et al.,

2009), may have resulted in failure in recognizing anxiety and underreports in the mental lower functioning individuals.

Depression

Depression is the only major psychiatric disorder that never seem to have been directly linked to autism. Studies have, however, demonstrated that professionals tend to overlook symptoms of this disorder in individuals with autism (Gillberg & Billstedt, 2000). Mood changes, which are among the main symptoms of depression, have been especially difficult to observe in this group (Perry et al., 2001). Thus, symptoms of depression seem to have been overshadowed by autism, probably due to the fact that the same symptoms may be indicators of both disorders. Regulation symptoms, for example sleeping and eating problems may be interpreted as related to autism or as symptoms of depression (Perry et al., 2001).

The prevalence of depression in individuals with autism is assumed to be high. Studies of clinical samples, mainly children and intellectually higher functioning individuals, suggest that between 50 and 70 percent of individuals with autism suffer from additional psychiatric disorders (Ghaziuddin & Zafar, 2008), and depression is the most frequent disorder, often combined with anxiety disorders (Ghaziuddin et al., 1992, 1995; Ghaziuddin & Greden, 1998; Howlin, 1997, 2000; Howlin et al., 2004; Lainhart, 1999; Schopler & Mesibov, 1994; Tantam, 2000). Recent studies of community samples of adults with autism and ID, give support to previous findings of depression as the most frequent comorbid psychiatric disorder in autism (Hutton, Goode & Murphy, 2008), but the prevalence rates vary between 5.2 and 30 percent (Melville et al., 2008; Morgan, Roy & Chance, 2003). Thus, differences in how depression is identified among individuals with autism and ID seem implied.

Instruments for assessment

Several checklists and instruments have been developed to assist the process of assessment of psychiatric disorders. Instruments developed for the general population have been used to measure behavioural problems and aspects of psychiatric comorbidity in individuals with ID including autism, but mainly instruments especially designed for the use in individuals with ID have contributed to the study of psychiatric comorbidity in autism and ID. The eight most commonly used screening instruments are presented in Table 1. Several of these instruments are designed for screening for psychopathology in individuals with ID. They address autism as one of the disorders to be identified and have not yet been examined for reliability and validity in identifying psychiatric comorbidity in individuals with autism (Leyfer et al., 2006).

Only one of the screening instruments presented in Table 1 is developed especially for use with individuals with autism. The Autism Spectrum Disorder-Comorbidity for Adults (ASD-CA; Matson & Boisjoli, 2008) is one of two recently published instruments designed for identifying psychiatric disorders in this population. It contains items judged by the authors as characteristic of the most probable psychiatric disorders in the ASD population, and is constructed to screen for comorbid psychopathology in adults with ASD and ID. The ASD-CA was recently published and only psychometric properties of have been reported. Thus, more research is needed to validate its clinical use.

The Autism Co-Morbidity Interview - Present and Lifetime version (ACI-PL, Leyfer et al., 2006) is a semi structured interview with parents to be made by experienced clinicians. It addresses ADHD, depression, OCD, schizophrenia, and specific phobia, and is supposed to identify comorbid psychiatric diagnoses in children with ASD. The diagnostic instrument is organised in disorder specific sections and includes screening and more specific questions in each section. The ACI-PL has been piloted in a sample of relatively high-functioning children with autism, but has been tested for validity and reliability for only three DSM diagnoses. The authors conclude, however, that they have probably not fully succeeded in differentiating between symptoms related to the core features of autism and symptoms of comorbid psychiatric disorders (Leyfer et al., 2006, Minshew, 2006).

Table 1. Screening instruments assessing psychiatric symptoms in individuals with ID and /or autism

INSTRUMENT	DISORDERS / SYMPTOMS ADDRESSED *	GROUP	FORM	ITEMS
The Mini Psychiatric Assessment Schedule for Adults with a Developmental Disability; Mini PAS-ADD Prosser et al., 1998	Anxiety, depression, hypomania / mania, OCD, pervasive developmental disorder, psychosis, unspecified disorder	Individuals with ID	Structured interview	86
The Diagnostic Assessment for the Severely Retarded; DASH II Matson et al., 1991	Anxiety, autism, eating disorder, eliminating disorder, impulse control, mania, mood, organic syndromes, schizophrenia, self injurious behaviour, sleep disorder, stereotypes, sexual disorder	Adults with severe and profound ID	Structured interview	84
The Psychopathology Instrument for Mentally Retarded Adults; PIMRA Matson, 1988	Adjustment disorders, affective disorders anxiety, personality disorders, psychosexual disorders, psychosomatic disorders, schizophrenia,	Individuals with ID	Carer completed checklist	56
The Assessment of Dual Diagnosis; ADD Matson & Bamburg, 1998	Anxiety, conduct disorder, dementia, depression, mania, eating disorder, personality disorder, pervasive developmental disorder, PTSD, somatoform disorders, substance abuse, schizophrenia, sexual disorder	Adults with mild and moderate ID	Carer completed checklist	79
Reiss Screen for Maladaptive Behaviour Reiss, 1987	Aggressive behaviour, avoidant personality disorder, autism, dependent personality disorder, depression, maladaptive behaviour, paranoia, psychosis	Individuals with ID	Carer completed checklist	38
Aberrant Behaviour Checklist; ABC Aman & Singh, 1986	Behaviour problems: Irritability, inappropriate speech, lethargy, hyperactivity, stereotypy	Individuals with ID	Carer completed checklist	58
The Developmental Behaviour Checklist for Adults; DBC-A Mohr, Tonge & Einfeldt, 2005	A checklist developed using a descriptive empirical approach and provide a comprehensive list of symptoms of psychopathology	Adults with ID	Carer completed checklist	106
The Autism Spectrum Disorder-Comorbidity for Adults; The ASD-CA Matson & Boisjoli, 2008	ADHD, conduct disorder, depression, eating disorder, OCD, phobia, tic disorder	Adults with ASD and ID	Structured interview	84

* Presented in alphabetical order

The problems related to identifying psychiatric disorders in individuals with autism and the lack of available assessment instruments and diagnostic criteria are reflected in the significant variability in prevalence rates of psychiatric disorders reported for this population. For example, in a review of 29 studies, prevalence rates of depression ranged from 4.4 percent to 57.6 percent, of mania from 0 to 21 percent, of anxiety disorders from seven to 84 percent, and of obsessive compulsive disorder (OCD) from 16 to 81 percent (Lainhart, 1999). A summary of six follow-up studies on high functioning individuals with autism reported prevalence of psychiatric diagnoses from nine to 89 percent, and depression, often associated with anxiety, was the most common psychiatric disorder (Howlin, et al., 2004). Several researchers have pointed to a need for standardized instruments or criteria for diagnosing psychiatric disorders in individuals with autism (Ghaziuddin, 2000; Howlin et al., 2004; Lainhart, 1999; Matson & Nebel-Schwalm, 2007; Tsai, 1996), and especially are tools for assessing psychiatric symptoms in low functioning individuals with autism needed (Ghaziuddin, 2009). In order to develop more accurate and reliable diagnoses, it is, however, necessary to differentiate conceptually between autism and psychiatric disorders. This is the focus of the first part of the present thesis.

Present project

The present thesis represents a new approach and an attempt toward solving the fundamental and practical problems related to the identification of individuals with autism and ID who have psychiatric disorders. The conceptual overlap and the difficulties related to differentiation between autism and psychiatric disorders make the identification of individuals with psychiatric disorders in this population complex. In order to develop more accurate and reliable diagnoses it is necessary to differentiate conceptually between these disorders. The delineation between autism and psychiatric disorders may contribute to an improved understanding of both autism and psychiatric disorders, and the relationship between them. It is also suggested that such identification may aid sub-grouping of individuals with autism according to comorbidity in neurobiological research (Leyfer et al. 2006; Ming et al., 2008).

The thesis explores the conceptual boundaries between autism and psychiatric disorders and applies the results as the basis for further exploration. In the development of a screening checklist for the identification of individuals with autism and ID with psychiatric disorders, the obstacles related to symptom overlap between autism and psychiatric disorders, as well as possible atypical psychiatric symptoms and the individuals' impaired ability to report about their problems, are taken into consideration.

The thesis is based on the assumption that people with ID manifest the full range of mental heath conditions shown in the general population (Moss, 1999), and that conceptually psychiatric disorders in these individuals are the same as individuals who are not intellectually disabled, although they might be manifested somewhat differently (Lainhart, 1999). Thus, when applied to individuals with autism and intellectual disability, the concepts of different psychiatric disorders are used as they are defined in diagnostic manuals, i.e. ICD-10 and DSM IV. Identifying psychiatric disorders in individuals who not are able to report about their symptoms is difficult, and differentiation between different types of diagnoses is problematic (Glenn et al., 2003). Thus, in the present thesis, identification of four major disorders is addressed; anxiety disorder, depression, psychoses, and obsessive-compulsive disorder (OCD). There is a particular focus on anxiety disorders.

Design

The study contains four parts. Part one is a theoretical and empirical analysis of the concepts, and examines whether symptoms of psychiatric disorders may be differentiated from the core characteristics of autism. Part two reports the results from the first validation of a new screening checklist, the Psychopathology in Autism Checklist (PAC). The PAC is constructed based on the results from the analysis of the concepts. The aim of the pilot and validation study in part two, is to test whether the PAC differentiates between individuals with autism and ID *with and without* psychiatric comorbidity. The study also addresses whether the PAC differentiates between individuals with different psychiatric disorders, i.e., psychosis, depression, anxiety, and OCD comorbid to autism and ID. Part three is a screening of a representative sample, including all individuals diagnosed with autism and ID in Nordland County in Northern Norway. Based on the results of the validation study, cut-off values were defined that distinguished mentally ill from individuals who were not suffering any mental illness. In part three, the aim is to assess the prevalence of individuals with autism and ID identified by the PAC as in need of referral for psychiatric examination. This study also includes a comparison with a representative sample of persons with ID only. In part four, the recognition of anxiety symptoms are explored, including comparison between anxiety assessment by the PAC and a comprehensive clinical assessment.

Aims of the thesis

The general objectives of the thesis are to contribute to an improved conceptual understanding of autism and psychiatric disorders, and the delineation between them. A better understanding may reduce the difficulties of identifying psychiatric disorders in individuals with autism and ID, and the findings may facilitate increased awareness among professionals, and lead to improved quality of mental health care for this group.

Specific objectives:
- To identify indicators of psychiatric disorders which do not overlap with the core characteristics of autism (Paper I).
- To investigate whether the PAC differentiates between subgroups of individuals with autism and ID with and without psychiatric comorbidity, and between subgroups with autism, ID and different psychiatric disorders (Paper II).

- To estimate the prevalence of individuals with autism and ID in a geographical area identified in need of referral to psychiatric examination (Paper III).
- To explore how anxiety symptoms are recognized and in what ways anxiety is manifested in individuals with autism and ID (Paper IV).

Ethical considerations

In all parts of the present thesis, the assessment of the participants was performed by clinicians in the ordinary service provision in the specialized health services and municipalities. As these were assessment studies, treatment was not included as part of the studies. However, participants with high scores on the assessment instruments were reported to the clinicians in charge of service provision, and further psychiatric assessment advised. All assessments obtained in the studies were accessible to the clinicians in charge and included in each participant's case notes. The research team was available for the clinicians in charge for discussion anonymously on questions and advice related to diagnosis or treatment.

Informed consent was obtained from all the participants, their families or other representatives. All data were de-identified and processed without name, identity number or other directly recognizable type of information. The project has been approved by the Regional Committee for Medical and Health Research Ethics.

Statistical analyses

Data were analyzed using the Statistical Package for Social Science (SPSS, version 13.0 and version 15.0), and mainly analyzed descriptively by analyses of average scores and frequencies. Due to the small sample sizes and the fact that the participants were not assumed to have been drawn from a normally distributed population, differences between groups in the pilot study and the clinical anxiety assessment were estimated using nonparametric statistics (Kruskal-Wallis Test and Robust Rank-Order Test, Siegel & Castellan, 1988) (Paper II and IV). In the screening study, t-test and Pearson's Chi-Square test were used to estimate differences between groups, Cochran's q-test as an overall test, and ANOVA to test

interaction effects (Paper III). The internal consistency of the subscales in the checklist was computed by Cronbach's alpha (Paper II) and the inter-rater agreement was analysed by Cohen's Kappa (Paper II and III).

Summary of papers

I: Identifying symptoms of psychiatric disorders in people with autism and intellectual disability: An empirical conceptual analysis

Aim of the study

The aim of the study was to explore whether it is possible to differentiate between symptoms of psychiatric disorders and symptoms that characterize autism, and to identify indicators of psychiatric disorders which do not overlap with autism.

Methods

A panel study design was applied to investigate which symptoms clinicians use to discriminate between autism and four major psychiatric disorders – psychosis, depression, anxiety disorder and OCD. Both psychiatric disorders and autism can only be assessed indirectly by indicators. A panel of experts was used to review the indicators of the concepts, for representativeness. This method is recommended for the study on content validity (Morgan, Gliner & Harmon, 2001), since content validity mainly involves systematic examination by experts to determine whether different indicators cover a representative sample of the concept (Cook & Campbell, 1979; Crocker & Algina, 1986).

The conceptual analysis explored which symptoms experienced clinicians regard as indicators of psychiatric disorders and not of autism and which symptoms they regard as indicators of autism. Analysis also explored whether the phenomenological core of the concepts representing the different psychiatric disorders is maintained in the symptoms not representing autism.

Indicators of psychiatric disorders and autism
Symptom clusters or domains representing the core symptomatology for each of the four psychiatric disorders and for autism were operationalised for the selection of indicators representing the concepts as they are defined in diagnostic manuals (i.e. ICD-10, DSM IV).

Psychosis was operationalised with symptoms within the following three domains: "positive symptoms", "negative symptoms" and "disorganisation". The domains of "mood", "cognition", "psychomotor" and "somatic" represented depression. Anxiety disorder was operationalised by symptoms within the domains of "physiological arousal", "avoidance" and "cognition", and OCD with symptoms within the domains of "rituals", "repetitive behaviour" and "obsessions". Symptom descriptions were copied from several psychiatric diagnostic checklists, and items describing symptoms for each domain were selected in accordance with the principles of comprehensiveness, behavioural equivalence, and over-inclusiveness. The total item pool for investigation encompassed 254 items: Among indicators of psychosis 43 items were selected, 70 items were selected among indicators of OCD, 39 items among indicators of anxiety disorder, 32 items among indicators of depression, and 70 items among indicators of autism.

The evaluation procedure

A panel of nine interdisciplinary and experienced clinicians (i.e. 2 psychiatrists, 4 psychologists and specialists in clinical psychology, 2 psychiatric nurses (MAHSc), and 1 pedagogue (MaEd.), and all with at least 20 years experience in the field of autism and /or psychiatry) recruited from the specialised health services. The clinicians independently rated the 254 randomly ordered items on a six-point scale. Each clinician gave each item a score for each disorder according to how well the item represented each of the four psychiatric disorders and autism. Based on the nine raters' average ratings for each item for each of the five disorders, the items were categorised according to how well they were evaluated to represent each of the disorders.

Main results

According to how well the items were evaluated as representing each of the disorders, they were categorised into five categories. Only 61 items (33%) were rated as specific to a psychiatric disorder and not characteristic of autism as it appears in individuals with intellectual disability. These items represent the same symptom domains used in the item selection, and therefore the phenomenological core of the concepts of the different psychiatric disorders seems to be maintained. These symptoms may be used as indicators of psychiatric disorders in individuals with autism and intellectual disability.

Eighteen items were classified as non-specific, and regarded as representing at least three disorders and not specifically representing the disorder they originally were selected to measure. They may consequently be considered as general indicators of impaired functioning or mental health problems. Seventy-two items were regarded as characteristic of both autism and one of the psychiatric disorders and categorized as overlapping items. These items represent the conceptual overlap between autism and the psychiatric disorders, and may be considered unsuitable for identifying psychiatric disorders in individuals with autism. Only 32 items (13%) were classified as items with large inter-rater variability and assumed to represent differences in the clinicians' considerations of the various symptoms. All the 70 items selected as indicators of autism were rated as characteristic to autism.

Thus, the results demonstrated that it was possible to differentiate conceptually between symptom descriptions of autism and of the four psychiatric disorders, as well as between the four psychiatric disorders, and to identify indicators of psychiatric disorders that do not overlap with autism.

Limitations

The panel of clinicians consisted of nine professionals and even more participants would have been preferable. To our knowledge, a similar study has not been published before, and future replications will be desirable.

II: The Psychopathology in Autism Checklist (PAC): a pilot study.

Aim of the study

The aims of the study were twofold; 1) to develop a checklist, The Psychopathology in Autism Checklist (PAC), based on the result of the conceptual analysis, and 2) to perform the first validation of the checklist. The main research question was whether the PAC differentiates between subgroups of individuals with autism and ID, with and without psychiatric comorbidity and between subgroups with different psychiatric disorders.

The Psychopathology in Autism Checklist (PAC)

The PAC is a carer-completed screening checklist for the identification of individuals with autism and ID in need of psychiatric services. Care staff and family may be the best source for reporting on changes in relation to premorbid or typical pattern of behaviour and mood, and to give information on idiosyncratic or atypical psychiatric symptoms (Bradley et al., 2004; Howlin, 1997; Lainhart, 1999; Matson & Boisjoli, 2008).

In the conceptual analysis (Paper I), 61 items were evaluated as specific to one of the psychiatric disorders and not related to autism as it appears in individuals with ID. Two more items related to anxiety and one related to depression were added afterwards.

In addition, eighteen items were evaluated in the conceptual analysis as related to three of the psychiatric disorders or to both autism and at least two other disorders, and thus considered as not representing the specific disorder they were originally selected to measure. These non-specific items include behaviour often observed both in individuals with autism and ID and in individuals with psychiatric disorders in general, such as irritability, disturbed sleep and challenging behaviour, and may therefore be considered general indicators of impaired functioning or mental health problems. These items were included in a general adjustment subscale to strengthen the possibility of identifying all individuals in need of further psychiatric assessment. This decision was based on reports of idiosyncratic or atypical psychiatric symptoms in individuals with autism and ID, and emphasizes the importance of including indicators of general adjustment problems to identify psychiatric or behaviour problems in individuals with autism (Lainhart, 1999; Reiss, 1988; Stavrakiki, 1999).

The present 42-item version of the checklist is the result of an item specification procedure adapted the use of non-professional informants, a first draft trial on six clients, as well as a final item review performed by a group of expert clinicians (cf. Crocker and Algina, 1986). As a consequence, the majority of the items were reworded. All items in the checklist are based on ICD-10 and DSM-IV criteria and the PAC contains five subscales: ten items related to psychosis, seven to depression, six to anxiety disorder, and seven to OCD. Twelve items are related to general adjustment problems.

Validation study

The assessment of clients with previously identified psychiatric disorders was chosen for the first empirical test, the pilot study of the PAC, because it is a well-known method for validating psychometric instruments (Matson et al., 1991; Moss et al., 1998). The scores of

participants previously identified with co-occurring psychiatric disorders (i.e. psychosis, depression, anxiety disorder, or OCD) were compared with the scores of participants without psychiatric disorders. Validity studies examine the relationship between an instrument and an outside criterion, and validity of an instrument is established for a particular purpose in a particular population. Criterion validity refers to validating the instrument against some form of external criterion (Cook & Campell, 1979; Morgan et al., 2001). The particular purpose of the PAC is to identify individuals with autism and ID suspected to have psychiatric disorders, and the criterion by which the PAC could be examined was thus against individuals with autism and ID already identified with a psychiatric disorder.

Participants

Originally, a sample of 47 adults was selected for the study based on the diagnoses of autism, intellectual disability and a psychiatric disorder. A new diagnostic evaluation was performed to include only participants with fully verified psychiatric diagnoses or absence of psychiatric co-morbidity. The final 35 participants with autism and intellectual disability included nine adults with psychosis, five with depression, six with anxiety disorder, and six with OCD. Nine adults did not have a psychiatric diagnosis.

Procedure

The informants were either family members or care staff who had known the person for at least one year. The ratings took place in or nearby the participants' home, their family home or at the hospital ward. All 35 participants were rated by two independent raters. Each randomly presented item was scored on a scale from 1to 4.

Main results

All psychiatric subgroups obtained significantly higher average scores on all subscales than the non-psychiatric group, indicating that all the subscales seem to discriminate well between individuals with autism and ID with and without psychiatric diagnoses.

There was significant variation with regard to how well the subscales differentiated between the four psychiatric subgroups. Both the psychosis and OCD subscales differentiated well between individuals with, respectively, psychosis and OCD and other psychiatric disorders, but the depression subscale differentiated only between the depression subgroup

and the subgroup with anxiety disorders. High levels of general adjustment problems and moderate levels of anxiety were demonstrated in all participants with psychiatric disorders. Thus, the results indicate that the PAC differentiates between the individuals with and without psychiatric disorders and partly between the individuals with different psychiatric disorders, especially psychosis and OCD.

Limitations

The participants were selected as typical representatives of different subgroups of autism, ID and psychiatric disorders. However, they may be characterized by more severe and chronic symptoms than many others in the same population since they already had been given a psychiatric diagnosis. The psychometric properties, i.e. the subscales' internal consistency computed by Cronbach's α and inter-rater agreement computed by Cohen's Kappa were found acceptable in this first examination of the PAC. Some items obtained, however, low scores in all subgroups and did not differentiate well between them. Further studies are indicated to fully examine these items and the psychometric properties of the PAC.

III: Psychiatric disorders in adolescents and adults with autism and intellectual disability: A representative study in one county in Norway

Aim of the study

The aim was to assess the prevalence of psychiatric disorders in individuals with intellectual disability only (*ID-only*) and with combination of autism and ID (autism).

Methods

Sample

There were two groups of participants. *The autism group* included all diagnosed and registered individuals with autism and intellectual disability from 14 years and up in Nordland County, altogether 62 individuals. *The intellectual disability group*, *the ID only group*, is

considered a representative sample of individuals with ID without autism, and comprised 132 adolescents and adults with intellectual disability, and included the majority of all administratively registered individuals with ID in five municipalities in Nordland County.

Procedure

All participants were screened for psychiatric disorders with The Psychopathology in Autism Checklist, PAC. Each randomly presented item was scored on a scale from 1 to 4. The informants were family members or care staff who knew the participants well. All participants were rated on the PAC by two independent raters.

The PAC is a conceptually analysed and validated screening instrument and screens for psychosis, depression, anxiety and OCD and also incorporates an assessment of general adjustment problems (*GAP)* and severe adjustment problems (*SGAP*). Cut-off criterion that distinguished mentally ill from individuals who were not suffering any mental illness were defined for each subscale based on the results of the validity study of the PAC. To meet criteria for a suspected psychiatric disorder, participants were required to score above cut-off for both severe adjustment problems and general psychopathology. "Diagnostic overlap" was defined as more than one psychiatric disorder concurrent with autism.

Main results

By screening the prevalence of psychiatric disorders and severe adjustment problems was found to be high among adolescents and adults with autism and intellectual disability. Also for those with intellectual disability only, higher prevalence rates were found than could be expected compared with estimates in non-autism and non-ID populations. A psychiatric disorder was screened in 53.2 percent of the autism group and 17.4 percent of the ID-only group. Psychosis was nearly three times as frequent in the participants with autism, depression more than twice as frequent, and anxiety and OCD approximately four times as frequent as in the ID-only group. More than half of the participants with autism and approximately twenty percent of the ID-only group were identified with severe adjustment problems. This seems to reflect that having an intellectual disability implies a high risk of developing adjustment problems, and that it is especially difficult for persons with autism to master every-day challenges. The differences between the autism and ID-only groups with regard to the prevalence of both severe general adjustment problems (SGAP) and psychiatric disorders

were statistically significant. Anxiety was the main symptom that differentiated between the autism and the ID-only group, indicating that anxiety problems are an important characteristic of the adult autism population.

In addition, the majority of the individuals in both study groups were screened to have more than one psychiatric disorder. The overlap between the psychiatric disorders was very high. Among individuals who were found by the screening to have a psychiatric disorder, sixty percent were found to have more than one disorder, with an average number of 2.1 disorders. Particularly high degrees of diagnostic overlap were found for OCD and psychosis. Individuals with the more severe psychiatric disorders had higher degrees of diagnostic overlap than individuals with less severe psychiatric disorders.

Limitations

The present study was a screening study. Due to limited resources, a comprehensive psychiatric assessment of the participants who were screened to have a psychiatric disorder was not performed afterwards. Thus data are lacking on (a) whether they would have received a psychiatric diagnosis, and (b) if so which diagnosis they would have been given if they had been psychiatrically examined by specialists. Moreover, there is no information on the participants with scores below the cut off and whether any of them would have received a psychiatric diagnosis if psychiatrically examined (false negatives). More studies on the properties of the PAC are warranted, especially on external validity and the sensitivity and specificity of the checklist.

Another limitation is that the PAC has not been validated in a population of individuals with ID only. Thus, we do not know whether cut-off values would have been different in such a population. However, the use of the PAC in assessing psychiatric disorders in individuals with ID only seems appropriate. The PAC is constructed to assess psychiatric disorders in individuals who are not able to report their problems, and consists of items without overlap to autism. These items may be considered as indicators of psychiatric disorders in individuals with ID with and without autism.

The diagnoses of autism and level of ID were clinically performed based on diagnostic criteria (ICD-10) in both samples. All participants were adolescents or adults, and diagnostic practice has changed in the specialized health services since they were first diagnosed. Unfortunately, due to limited resources, it was not possible to perform a new diagnostic assessment on autism or ID as part of the present study. The clinicians in the specialized

health services responsible for the diagnosis were, however, specialists in autism, had extensive clinical experience in diagnosing autism and ID, and had a comprehensive diagnostic practice including observations, interviews and the use of standardized instruments.

The design of the present study did not address the differences in distribution of sex, age, and large functional differences in ID between the autism group and the ID-only group. Not assessing the possible effect of these differences might be considered a limitation.

IV: Anxiety in people diagnosed with autism and intellectual disability: Recognition and phenomenology

Aim of the study

The study explores the recognition of anxiety symptoms, and aims to provide suggestions for the assessment of anxiety in individuals with autism and ID. The main research question is whether physiological arousal, which was the assumption, was more easily recognized than the cognitive aspect of anxiety in these individuals. Moreover, in comparing assessment by checklist and reports on anxiety symptoms obtained in a comprehensive diagnostic process, the aim was twofold: 1) to explore whether assessment by a screening checklist is sufficient to identify the individuals with anxiety problems, and 2) to examine in more detail how anxiety is manifested in these individuals.

Method

Two separate samples, a community sample of 62 individuals and a clinical sample of nine individuals, were assessed with anxiety items from a screening checklist, the Psychopathology in Autism Checklist (PAC). Each item's scores were analyzed. In addition, in the clinical sample, checklist results were compared with clinical assessments.

Samples

The community sample included all individuals with autism and ID above the age of 14 years in Nordland County. The sample consisted of 62 participants (45 males and 17 females) (corresponds to the autism group in paper III).

The clinical sample comprised five males and four females who were referred to a clinical project on treatment of co-occurring psychiatric disorders in adults with autism and ID at Ullevål University Hospital. Inclusion criteria were a clinical diagnosis both of autism and ID, and a comorbid psychiatric diagnosis.

Among the nine participants, five fulfilled the criteria for a diagnosis within the schizophrenia spectrum, non-affective psychosis (DSM-IV 295-298), three were diagnosed with bipolar disorders, and three with anxiety disorder (general anxiety disorder, or specific phobia). Two persons were given two different psychiatric diagnoses in addition to autism.

Procedure

The informants were family members or care staff who knew the participant well. All participants were rated on the PAC by two independent raters, and the average scores of the two raters was used in the analysis. Each randomly presented item was scored on a scale from 1 to 4.

Based on the results of the validity study of the PAC, cut-off criteria were defined for each subscale that distinguished mentally ill from individuals who were not suffering any mental illness. Severe general adjustment problems were established as a criterion for psychiatric disorders. To be identified suspected with anxiety problems, the participants had to obtain general adjustment problems scores above cut-off (≥ 2.0) concurrent with anxiety scores above cut-off (≥ 1.8).

The anxiety subscale in the PAC contains six items related to somatic and cognitive symptoms. The items assessing somatic symptoms, i.e. physiological arousal, are termed "specific" items. Due to the difficulty assessing cognitive anxiety through observation or by informants, items assessing the informants' general impression of the probands' distress and well-being are included and termed "general" items.

The systematic anxiety assessment in the clinical sample was scheduled after the PAC ratings and followed a four-step procedure: First, the informants, who were care staff or family members, were provided with general information about anxiety disorders and anxiety symptoms by experienced clinicians in the treatment project. Second, all informants, i.e.,

family members and care staff involved in the target person's care or treatment, were interviewed as a group (i.e., semi-structured interview used in a focus group) about the person's anxiety symptoms, to generate various descriptions of how anxiety could be observed in this particular person. Third, each informant completed a list describing the signs and symptoms of anxiety in the target person. Finally, all the individually obtained information was discussed in the group, supervised by the experienced clinicians. Consensus was established on all regularly observed anxiety symptoms in the target persons. This procedure resulted in a list of symptoms acknowledged by all informants. All symptoms were allocated in four categories; general symptoms, specific symptoms, anxiety reactions, or idiosyncratic symptoms.

Main results

The scores on the general anxiety items in the PAC, which are supposed to assess the cognitive aspect of anxiety, were higher than the scores on the specific items, which assess physiological arousal. The similar pattern was demonstrated in the total community sample, in the anxiety group, and in the clinical sample. Twenty-three participants (37.1 %) in the community sample obtained a general adjustment problem score above cut-off concurrent with an anxiety score above cut-off, and were classified as the anxiety group.

Only seven of nine participants in the clinical sample obtained an anxiety score above cut-off on the PAC, although all nine participants had general adjustment scores above cut-off. Comparison between clinical assessment and assessment by the PAC also revealed diverging reports in four participants. In the clinical anxiety assessment, anxiety symptoms were reported in all the participants in the clinical sample.

The anxiety symptoms reported in the clinical assessment include 36 different symptoms and most of the symptoms described are typically anxiety symptoms, i.e. anxiety symptoms often described in individuals without autism. Only nine idiosyncratic symptoms were reported, i.e. unusual expressions of anxiety.

Thus, the results of the present study indicate that physiological arousal may not be as readily observable as assumed in individuals with autism and ID. The results also indicate that anxiety occurs frequently in this population, and support previous findings that the close association between anxiety and other psychiatric disorders also applies to individuals with autism and ID. Moreover, anxiety may be recognized in this group by similar symptoms as in individuals without autism, but the difficulties in recognizing signs of physiological arousal

indicate the importance of increased clinical awareness toward such symptoms. General impressions of the probands distress and well-being seem to be easier to report on, and anxiety reactions, both usual and idiosyncratic reactions, seem more easily recognized. To be able to identify individuals in need of further psychiatric examinations by using screening checklists, anxiety signs as well as signs of general adjustment problems probably have to be included. However, for diagnostic purposes and for monitoring treatment, individual anxiety assessment conducted by care staff and family who know the individual well in cooperation with professionals with knowledge both of autism and anxiety seems indicated.

Limitations

The most important limitation of the present study is the small number of participants, particularly in the clinical sample. Moreover, the diagnoses of autism and level of ID were clinically performed based on diagnostic criteria (ICD-10) in both samples, and due to limited resources, it was not possible to perform a new diagnostic assessment on autism or ID as part of the present study. The clinicians in the specialized health services responsible for the diagnosis were, however, specialists in autism, had extensive clinical experience in diagnosing autism and ID, and had a comprehensive diagnostic practice including observations, interviews and the use of standardized instruments.

The participants in the community sample with above cut-off scores were not given a psychiatric assessment as a part of the present study. This implies that we do not have information on what diagnoses they would have received if they had been psychiatrically examined by specialists. More studies on the properties of the PAC are warranted, especially on external validity and the sensitivity and specificity of the checklist.

Discussion

The conceptual analysis demonstrates that it is possible to differentiate between symptom descriptions of autism and four major psychiatric disorders, and to identify symptoms which are specific to a psychiatric disorder and not characteristic of autism as it appears in individuals with intellectual disability (Paper I). The findings confirm the view of autism as a well defined and specific disorder (Vokmar & Rutter, 1995; Volkmar et al., 2004), and may contribute to a better delineation between autism and psychiatric disorders. The results of the pilot study of the PAC (Paper II), demonstrate that by using indicators of psychiatric disorders that do not overlap with the core characteristics of autism, it is possible to differentiate between individuals with autism and ID who are diagnosed with a psychiatric disorder and those who are not. The results support an understanding of psychiatric disorders in this group as additional disorders, and suggest that co-occurring psychiatric disorders can be identified by changes or deterioration in the patterns of behaviour typical of autism (Ghaziuddin, 2005; Hutton et al., 2008; Lainhart, 1999). The results also support the foundation of the present thesis that conceptual differentiation between the disorders is a prerequisite for developing more accurate and reliable diagnoses and for developing psychiatric screening tools for individuals with autism and ID.

The delineation between autism and psychiatric disorders

More than half of the individuals with autism and ID in the screening study obtained scores indicating co-occurring psychiatric disorders (Paper III). This indicates a high prevalence of the four psychiatric disorders investigated. Although the prevalence may not be as high as suggested by some reports (e.g., Brereton et al., 2006; Leyfer et al., 2006; Simonoff et al., 2008), the findings give further support to the assumption that individuals with autism are more vulnerable for developing psychiatric disorders than the general population (Bradley et al., 2004; Brereton, Tonge & Einfeld, 2006; Clarke et al., 1999, Ghaziuddin & Greden, 1995;

Ghaziuddin et al., 1992, 1998; Howlin, 1997; 2000; Howlin et al., 2004; Leyfer et al., 2006; Simonoff et al., 2008).

The present results are in line with studies reporting more moderate comorbidity rates (e.g., Bradley et al., 2004). Differences in diagnostic criteria and problems connected with the delineation between autism and psychiatric disorders probably account for the wide variation in reported prevalence rates of psychiatric disorders in individuals with autism (Bradley et al., 2004; Howlin, 2000; Lainhart, 1999). Biased samples, small sample sizes, differences in the disorders targeted and the populations' characteristics, differences in assessment methods used and the clinical experience of interviewers, and whether the measure had been validated and was appropriate for use in the ASD populations, limit the conclusions that can be drawn from the different studies. Nevertheless, certain factors seem implicated in the varying prevalence rates of psychiatric disorders reported among people with autism.

Nine recently published studies are summarized together with the present screening study (Paper III) in Table 2. The studies that report the lowest rates of co-occurring psychiatric disorders seem to have the strictest criteria for identifying a comorbid psychiatric disorder. For example, Hutton and colleagues (2008) report an onset of new psychiatric disorders at follow–up in only 16 percent of adults diagnosed with ASD as children. Another five percent of the individuals were identified with a possible new psychiatric disorder. The authors claim to have used strict criteria to differentiate between autism and psychiatric disorders. To consider a disorder as a comorbid psychiatric disorder, termed "new psychiatric disorder" by the authors, they explicitly demanded the emergence of a condition that represents more than a worsening of already existing autism features and that constituted a clear break from the pre-existing autism. However, by using such strict criteria, the researchers may have failed to recognize all symptoms and overlooked the very specific appearances of psychiatric disorders in individuals with autism. The use of such strict criteria contrasts with the view of researchers who consider the appearance of new maladaptive behaviours and an increase in typical autism symptoms (i.e., more intense ruminations and repetitive and ritualistic behaviour) as indicators of psychiatric disorders in individuals with autism (Ghaziuddin, 2005; Tantam, 2000; Wing, 1996). Due to confounding between anxiety and autism (Morgan et al., 2006; Weisbrot et al, 2005), and the finding by Hutton and colleagues (2008) of only one person with an anxiety disorder, there is reason to suspect that anxiety is not identified by these criteria.

Low rates were also reported in a prospective community-based follow-up study of 120 individuals originally diagnosed with autism and autism-like disorders and mainly with

intellectual disability (Billstedt et al., 2005). Eight individuals were identified with psychosis (6.7 %), one with non-psychotic depression (0.8 %), thirteen individuals (12 %) with catatonia, and another four with possible catatonia. However, the authors reported that 50 percent of the participants had been engaged in moderate or severe degrees of self-injurious behaviour and that 19 percent showed violent behaviour, indicating major problems in at least half of the participants even if the criteria and assessment methods used in the study did not generate a psychiatric diagnosis.

Two studies (Morgan et al., 2003; Mouridsen et al, 2008) based on register data and psychiatric case notes have presented more moderate prevalence rates, i.e. 41 percent (Morgan et al., 2003) and 48.3 percent (Mouridsen et al, 2008). These findings are slightly lower than the findings in the present screening study (Paper III). However, the authors of the register data studies assume that only the most severe cases have been registered, and that the diagnoses are based on an interpretation which has changed. Thus, they believe that not all individuals with psychiatric disorders have been identified by the method used.

Among the studies with high prevalence rates, Leyfer and colleagues (2006) found 72 percent psychiatric comorbidity in a community sample of children with autism. The authors have designed a diagnostic interview for the use in children with autism, the Autism–Comorbidity Interview – Present and Lifetime version (ACI-PL). The ACI-PL requires that a psychiatric symptom must be conceptually the same, qualitatively and quantitatively, as in DSM-IV. This view contrasts with the approach of the present thesis, and may indicate that the ACI-PL not fully have succeeded in differentiating between autism symptoms and symptoms of psychiatric disorders (Minshew, 2006). For example, OCD were identified in 37 percent of the participants, and the most frequent compulsions reported in the autism group involved dysfunctional interaction with other people in a compulsive manner. Dysfunctional interaction and social problems are among the core features of autism. Therefore, the most frequent compulsions which were reported as a symptom of OCD in the study by Leyfer and colleagues (2006) seem to be characteristic of individuals with autism in general. As a result, the ACI-PL probably identify too many with ordinary autism symptomatology. Similarly, high prevalence rates were also reported by Simonoff and colleagues (2008), who identified at least one comorbid psychiatric diagnosis in 70 percent of a population-derived cohort of children with autism spectrum diagnoses by an instrument developed for the general population. By using measurements not adjusted for ASD populations, ordinary autism symptoms are likely to be misinterpreted as psychiatric symptoms.

Table 2. Recent studies on psychiatric disorders in individuals with autism; samples, comparison group, measurement, types of psychiatric disorders addressed, and rates of point prevalence

Study	Autism sample	Control sample	Measurement	Percent of psychiatric disorders in autism and control sample		Prevalence [a] Autism	Non-autism
Morgan, Roy & Chance, 2003	164 adults with autism and ID identified by screening in community sample	400 adults with ID only in community sample	Retrospective collected Review of psychiatric case notes	Psychotic disorder [b]:	6 / 5.25	41	9.75
				Depression:	20 / 2.75		
				Bipolar affective disorder: 11 / 1.75			
				Tourette syndrome:	2		
Bradley et al., 2004	12 persons with autism and ID Population sample IQ < 40 Age range 14-20	12 matched controls with ID only IQ < 40 Age range 14-20	Screening by DASH-II Interview of informants	Anxiety:	42 / 0	50 [c]	25 [d]
				PDD/autism:	83 / 0		
				Mania:	67 / 8	The rate of comorbidity was four times higher in the group with autism than in the non-autism group	
				Depression:	50 / 8		
				Schizophrenia:	8 / 8		
				Stereotypes/tics:	67 / 0		
				Self injury:	58 / 50		
				Eating disorder:	58 / 25		
				Sleep disorder:	50 / 25		
				Sexual disorder:	33 / 8		
				Impulse control:	25 / 0		
				Elimination disorder:	25 / 8		
Brereton et al., 2006	Cohort of 381 young people with autism Age range: 3.8-24 About 75 % with ID	A representative sample of 581 young people with ID Age range: 4-18	Parents / carers report by DBC-P	Average group scores on subscales reported in both samples Significantly higher levels of psychopathology in autism cohort		73.5	
Leyfer et al., 2006	109 children with autism Recruited from community sources age range 5 – 17 67.7 % had IQ >70		Parents interviewed by ACI-PL	Schizophrenia:	0	72	
				Depression:	10		
				Specific phobia:	44		
				OCD:	37		
				ADHD:	31		
				Median number of diagnoses per child 3			
Tsakanikos et al., 2006	147 adults with autism and ID aged ≥ 16 clinical referrals to specialist service IQ < 70 and significant social impairment	605 adults with ID only aged ≥ 16 not matched clinical referrals IQ < 70 and significant social impairment	Comprehensive psychiatric evaluation based on ICD-10 clinical criteria A subgroup was controlled by PAS-ADD assessment	Schizophrenia:	16.4 / 18.5	36.4	53.3
				Personality disorder:	2.9 / 9.0		
				Depressive disorder:	6.4 / 9.0		
				Anxiety:	4.3 / 8.1		
				Adjustment reaction:	5.0 / 6.5		
				Dementia:	1.4 / 4.2		

Study	Sample	Controls	Method	Findings	%	%
Hutton, Goode & Murphy, 2008	135 adults Diagnosed with ASD autism as children aged ≥ 21 at follow-up IQ < 30		Screening identified 39 individuals (29 %) with possible psychiatric disorders. They underwent comprehensive psychiatric assessment through parental interview	Affective disorders most common; OCD second most common disorder with or without catatonia, or just catatonia; One person with bipolar disorder; One person with acute anxiety reaction; Another 5 % with possible new psychiatric disorder	16[e]	
Melville et al., 2008	77 adults with autism and ID were identified by screening in total population of adults with ID	154 individually matched controls with ID only	Comprehensive psychiatric examination. Diagnoses according to DC-LD, ICD-10, and DSM-IV-TR criteria.	Psychotic disorder[b]: 1.3; Affective disorder: 5.2; Anxiety disorder: 3.9; OCD: 0; Pica: 5.2; ADHD: 3.9; specific phobia excluded	48.1	40.3
Mouridsen et al., 2008	118 individuals Diagnosed with autism as children Clinical referrals	336 matched controls Drawn from central person register	Data from psychiatric register. Longitudinal study. Period of 36 years. Individuals treated in psychiatric hospitals	Psychotic disorder: 6.8 / 0.9; Affective disorder: 3.4 / 1.2; Nervous /Stress disorder: 1.7 / 1.8; Personality disorder: 0.8 / 3.0; Tic disorders. 1.7 / 1.8; Alcohol /drug use: 0.8 / 2.4	48.3[f]	6[f]
Simonoff et al., 2008	112 children with autism population-derived cohort 12-14 years old		Parents interviewed CAPA	Anxiety disorders: 29.2; ADHD: 28.2; Oppositional defiant disorder: 28.1; Two or more comorbid disorders: 41	70	
Bakken et al., 2010	132 individuals with autism and ID aged ≥ 14 population sample	62 individuals with ID only aged ≥ 14 representative sample	Parents / carers report by PAC	Psychosis 25.1 / 9.1; Depression 37.1 / 15.2; Anxiety 33.9 / 9.1; OCD 12.9 / 3.3	51.6	20.5

a Percentage of the sample with at least one DSM-IV psychiatric disorder; b Psychotic disorder – includes schizophrenia, schizoaffective disorder, schizophrenia spectrum disorders; c More than five clinically significant disorders; d Two or more comorbid disorders ; e A definite new psychiatric disorder comorbid to autism
f Any contact with psychiatric hospital
DASH-II: The Diagnostic Assessment for the Severely Retarded (Matson, 1995). DBC-P; Developmental Behavior Checklist (Einfeld & Tonge, 1992, 1995).
ACI-P; The Autism Comorbidity Interview – Present and Lifetime Version (Leyfer et al., 2006). CAPA; The Child and Adolescent Psychiatric Assessment (Angold & Costello, 1995).

Two studies (Melville et al., 2008; Tsakanikos et al., 2006), which include comparison of prevalence rates between adults with autism and ID and adults with ID only, both found similar moderate rates of psychiatric disorders in those with autism (48.1 %, Melville et al., 2008; 36.4 %, Tsakanikos et al., 2006). In both studies, the diagnosis of autism was made as part of a general psychiatric assessment, which may have overshadowed other psychiatric diagnoses in this group. This interpretation is suggested by the higher rates of problem behaviour in the autism group than in the ID only group (Melville et al. 2008), and the significant differences between the proportion of patients who received medication in the autism group than in the ID only group (Tsakanikos et al. 2006). The authors also express surprise that schizophrenic spectrum disorders were the most common diagnoses in the autism group. They propose that the different diagnostic practices between the ID only and the autism group, including concurrent identification of autism and psychiatric disorders in the autism group, may explain the low rates of depression and anxiety in the autism group, and that the measures used, probably were insensitive to differences between the groups with or without autism (Melville et al., 2008).

Whether anxiety is included as a comorbid diagnosis or not seems to make a large impact on prevalence rates. In two of the studies reporting the highest rates of psychiatric comorbidity, specific phobias and anxiety were included, and indeed were the most common psychiatric disorder identified. In the study by Leyfer and colleagues (2006) 44 percent were identified with specific phobia, and 42 percent were identified with anxiety disorder by Bradley and colleagues (2006). However, in studies reporting lower rates of psychiatric comorbidity, specific phobias were excluded and anxiety probably overshadowed by symptoms of autism (Melville et al., 2008).

In the present thesis (Paper III), more than half of the population with autism and ID obtained PAC scores indicating a need of further psychiatric assessment. The moderate level of psychiatric comorbidity probably reflects that the PAC does not include ordinary autism symptomatology since overlapping symptoms were excluded from the checklist. On the other hand, the PAC identifies higher rates of psychiatric disorders than some studies, which may indicate that the very specific ways psychiatric disorders is manifested in individuals with autism are identified. These symptoms may have been overlooked clinically and in studies where autism and psychiatric disorders have been identified at the same time (i.e., Melville et al., 2008; Tsakanikos et al., 2006) as well as in the studies that demand "a clear break" from the pre-existing autism (i.e., Hutton et al., 2008). Such criteria do not include deterioration of

already existing autism features or increase in typical autism symptoms as symptoms of psychiatric disorders.

Adjustment problems and psychiatric disorders

The conceptual analysis identified a set of non-specific items regarded as representing at least three disorders and not specific to the disorder they originally were selected to measure (Paper I). These general indicators of impaired functioning or mental health problems were included in the general adjustment problem (GAP) subscale of the PAC to increase the probability of identifying all individuals in need of further psychiatric assessment. Symptoms such as sleeping problems, general passivity, challenging behaviour and general distress, which are among the items in the GAP subscale, are typically associated with most psychiatric disorders in individuals with autism and ID as well as reactions to a difficult life situation (Ghaziuddin, 2005; Lainhart, 1999; Reiss, 1988; Stavrakiki, 1999). The high levels of general adjustment problems found in all participants with psychiatric disorders in the pilot study (Paper II) support the inclusion of the general adjustment problems (GAP) subscale. These findings may also imply a criterion of severe general adjustment problems as the first step in the screening procedure with the PAC. This strategy is supported by the results of the screening study, when more than half of the autism and ID population were identified with severe general adjustment problems and concurrently obtained scores of psychiatric disorders that were equal to the level of the participants with autism, ID and a previously identified psychiatric disorder in the pilot study (Paper III). Moreover, the comparison between anxiety assessment by PAC and clinical assessment demonstrates that the anxiety items in the PAC are not sufficient to identify all individuals with anxiety problems, but have to be combined with severe general adjustment problems, i.e., a GAP score above cut-off (Paper IV).

The strategy of using severe general adjustment problems as a criterion for possible psychiatric disorders in the screening procedure of the PAC corresponds to the criteria for diagnosing psychiatric disorders generally. Psychiatric disorders are conceptualized as a behavioural or psychological syndrome or pattern that is associated with distress (i.e., a painful symptom) or disability (i.e., impairment in one or more important areas of functioning) (DSM IV- TR; Sadock, 2005). Thus, the requirement of a significant degree of distress and impairment in the person's performance in everyday activities, that characterizes psychiatric disorders generally, is also utilized in the PAC screening procedure.

More than half of the participants with autism and approximately twenty percent of the ID-only group were identified with severe adjustment problems in the present screening study (Paper III). This seems to reflect that having an intellectual disability implies a high risk of developing adjustment problems, and that it is especially difficult for people with autism to master every-day challenges. Thus, adjustment problems and difficulties in coping with daily life seem to be directly linked with having autism as well as intellectual disability. Especially the comprehension difficulties and the problems with interpreting the activities of others, that characterize most individuals with autism, can increase stress and give rise to cognitive overload. This is not a phenomenon limited to individuals with autism alone. When individuals without autism or ID experience stress or develop a psychiatric disorder, the adjustment problems seem to increase together with traits that usually are related to autism. For instance, most people become more literal and concrete in their understanding and more vulnerable to noise, interruptions, and other irrelevant influences when they are tired and stressed (Dreyfus, 2001). They also tend to be more preoccupied with doing things in a scheduled order, and to focus more on details. Automatic and nonconscious processes require little cognitive capacity, but all cognitive activity implies allocation, supervision, and regulation of cognitive resources (Sternberg, 2003). Cognitive resources are, however, limited, and when the need for resources becomes too demanding, it may result in cognitive overload and stress. Thus, stress is often caused by cognitive complexity typically involving poor predictability and comprehension of causality (Grimsmo & von Tetzchner, 2007). Whether a situation is stressful or not will depend on the individual's comprehension and interpretation of the situation, and not on objective criteria. People become more conscious about their own behaviour and of characteristics in a situation when they experience the situation as strange, unfamiliar, challenging, difficult or confusing, and poor comprehension of what is happening imply vulnerability to stress. Most people are more sensitive to noise, confusion and interruptions and other irrelevant influence in situations that demand reflection and attention. Thus, when faced with problems of cognitive economy, most individuals may, in unusual circumstances or when they are mentally ill, show reactions similar to those that generally characterize individuals with autism.

Individuals with autism are in double jeopardy. Firstly, they are characterized by a number of problems that are considered as risk factors for mental health problems when they occur in the general population (Dawson & Watling, 2000; Kern et al., 2006; Reese et al., 2005). Secondly, they also tend to become more "autistic", i.e., show an increase in autistic features such as repetitive and ritualistic behaviour, when they develop a psychiatric disorder

(Tantam, 2000). Because individuals with autism experiences many challenges in mastering everyday activities, their attempts to cope with these problems may often be interpreted as adjustment problems or signs of psychiatric disorders.

It may be difficult to interpret a person's symptoms correctly, and to differentiate between problems due to inadequate adjustment and problems due to psychiatric problems. Although the items in the GAP subscale assess a wide range of problems, items assessing self-injury, violent behaviour, and breaking of objects are included, which are behaviour often characterized as problematic or "challenging" (Emerson, Moss and Kiernan, 1999). The significant relationship between behaviour problems and psychiatric disorders in individuals with ID has been clearly demonstrated, and several authors have suggested that behaviour problems may be indicators of psychiatric disorders in this group (Emerson et al., 1999; Moss et al. 2000; Minshew, 2006; Myers and Winters, 2002; Myrbakk & von Tetzchner, 2008). There is, however, no reason to assume that all individuals assessed as having severe general adjustment problems on the PAC have a psychiatric disorder. The inter-relationship between challenging behaviour and psychiatric disorders is complex, and it is unlikely that all behaviour problems in this group are underpinned by psychiatric disorders (Hemmings, 2007). Challenging behaviours are more likely symptoms of underlying psychiatric disorders if environmental change, communication problems, over stimulation and physical health problems can be eliminated as causes (McClintock, Hall & Oliver, 2003; Minshew, 2006). Thus, severe general adjustment problems, in combination with low disorder-specific scores, which were identified in less than five percent in both groups investigated in the screening study (Paper III), may more likely be related to non-psychiatric problems such as somatic or psychosocial problems. The design of the PAC, with a subscale on general adjustment problems as well as subscales for major psychiatric disorders, may contribute to the differentiation between characteristics of autism, signs of adjustment problems and symptoms of psychiatric disorders, and particularly in differentiating between problems related to psychiatric disorders and to other types of problems.

Anxiety and autism

The relationship between anxiety and autism has been demonstrated in the results of all the papers in the present thesis (Paper I, II, III, and IV). Among the psychiatric disorders examined in the conceptual analysis, anxiety disorder had the lowest scores and the highest degree of disagreement among the experienced clinicians (Paper I). Thus, even experienced clinicians seem to be uncertain in their evaluation of whether symptoms are characteristics of anxiety or of autism, illustrating the difficulties related to differentiating between the two disorders (Lainhart, 1999; MacNeil, et al., 2009; Tsai, 2006). These difficulties may be traced back to the first descriptions of autism (Kanner, 1943, 1944), and are in line with the view that anxiety is an integral component of autism (Weisbrot et al., 2005). Nevertheless, the results of the conceptual analysis demonstrated that it is possible to distinguish between the symptoms of the two disorders. The results offer support to an understanding of anxiety as a separate disorder to autism (Bellini, 2006; Gillot & Stranden, 2007; Ghaziuddin, 2005; Goldstein et al., 1994; Lainhart, 1999; Morgan, 2006; Steingard, et al., 1997). The high prevalence of anxiety symptoms and disorders, which have been reported in the last decade, may have contributed to the growing awareness of the importance of identifying anxiety in individuals with autism (Green et al., 2000; Kim et al., 2000; Luscre & Center, 1996; MacNeil, et al, 2009; Matson & Nebel- Schwalm, 2007; Schopler & Mesibov, 1994; Sukhodolsky et al., 2008; Tantam, 2000; White et al., 2009). Increased awareness of anxiety in this group may also be related to reports of individuals who have benefited from having their anxiety problems identified and receiving specific anxiety treatment (Cardaciotto & Herbert, 2004; Chalfant, Rapee & Carroll, 2007; Reaven, et al., 2009; Sofronoff, Attwood & Hinton, 2005; Sze & Wood, 2007; White et al., 2009; Wood et al., 2009).

The difficulties related to recognizing signs of arousal in individuals with autism and ID demonstrated in the anxiety paper (Paper IV), may partly explain why anxiety has been considered difficult to recognize in these individuals (MacNeil et al., 2009; Tsai, 2006), and why anxiety symptoms have been overshadowed by symptoms of autism (Jopp & Keys, 2001; Lainhart, 1999). Furthermore, the results indicate that anxiety disorder may be identified in individuals with autism and ID with the same or similar symptoms as in non-autistic individuals. However, the difficulties in recognizing all symptoms indicate the need for several assessment methods, combining the use of checklists, direct observation, information from family or other key informants, and physiological measures (Groden, Baron, & Groden, 2006; MacNeil et al., 2009).

There is reason to assume that there are similarities in the development of anxiety and of autism. In normally developing children, there seems to be an interaction between biologically rooted individual characteristics in early temperament and factors related to the children's interplay with their social environment which predict later anxiousness and anxiety problems (Alden, 2001). Some children seem to have inborn vulnerability for developing anxiousness and anxiety (Kagan, 1994). According to Kagan (1998), fearfulness and shyness are included in the broader temperament category, of behavioural inhibition, and an inhibited temperament seem to represent vulnerability for developing anxiety problems. Inhibited children tend to develop social anxiety and other anxiety disorders later in life more often than other children (Hirschfeldt et al., 1992; Kagan, 1998; Turner, Beidel & Wolff, 1996). Within a transactional perspective (e.g., Sameroff & Chandler, 1975; Sameroff & Fiese, 2000) similar relationships are likely in children with autism. Autism is generally understood as a congenital disorder with a neurobiological origin. The etiology of autism is assumed to be an interaction between genetic vulnerability and prenatal environmental factors although the biological factors involved have not been identified (Volkmar et al., 2004).

Thus, most of the problems that characterize autism, such as difficulties in communication, comprehension and social interaction, are biologically rooted, influence their interplay with the environment, and represent vulnerability factors. In addition, poor social competence, misunderstanding, confusion and insecurity related to their own achievements may make children with autism more vulnerable to developing anxiousness and anxiety (Bellini, 2006; Bruch, 2001; Gillott & Stranden, 2007; Goldstein et al., 1994; Steingard, et al., 1997). In individuals with autism, anxiety may thus be understood as an effect of having autism and the cause of some of the characteristics of autism, especially rituals and repetitive behavior (Gillott et al., 2001; Ghaziuddin et al., 1995; Howlin, 1997). It is likely that the children with autism, who have an inhibited temperament, as well as those who show strong reactions towards newness and have difficulties in arousal regulation, are especially at risk for developing anxiety problems.

The relationship between anxiety and other psychiatric disorders among individuals with autism and ID found in the present thesis (Paper II, III and IV) suggest that anxiety has a central role in the development of psychiatric disorders in this population. Generally, anxiety scores were found to be on the similar low level for all participants with low levels of adjustment problems or without psychiatric diagnoses, and on the same higher level for those with severe adjustment problems and psychiatric disorders. The highest anxiety scores were obtained in the groups with other co-occurring psychiatric disorders than anxiety disorder

(Paper II and III), and an interaction effect of anxiety was demonstrated (Paper III). These results indicate that anxiety symptoms contribute most to the overlap with other psychiatric disorders. The overlap between symptoms of anxiety and other psychiatric disorders is well acknowledged in general psychiatry (Alden and Crozier, 2001; Gelder, Lopez-Ibor & Andreasen, 2003; Lindenmayer et al., 2002; Regier et al., 1998; Schneier et al., 1989, 1992). The results of the present thesis therefore support assumptions of similar symptom overlap between different psychiatric disorders in persons with autism and ID as in the general population (Dekker & Koht, 2003; Gahziuddin 2005; Kim et al., 2000; Lainhart, 1999; Matson et al., 1991, 2000; Moss et al., 2000; Rutter et al., 1976).

In the present screening study, anxiety showed the largest differences in prevalence between the autism group and the ID-only group (Paper III), suggesting that having anxiety problems are an important characteristic of the adult autism population. The vulnerability to anxiety problems seems to be a characteristic of autism, and is probably involved in the development of psychiatric disorders in this population. Biological, genetic and social influences are all likely contributing factors, but the causes of the higher rate of psychiatric disorders, and especially anxiety disorders, depression and OCD, in autism than in the general population remain unclear (Saulnier & Volkmar, 2007). Some researchers have suggested that the occurrence of psychiatric disorders in autism constitutes an intrinsic feature of an autistic liability, due to the poor association between psychiatric disorders and language skills or level of IQ (Hutton et al., 2008). The difficulties in differentiating between autism and anxiety have been pointed to by several researchers (Lainhart, 1999; MacNeil, et al., 2009; Tsai, 2006), while others view anxiety as an integral part of autism (Weisbrot et al., 2005). The exploration of temperament characteristics as well as reactions to newness may represent an alternative approach and provide a new perspective on these problems.

Comparison between PAC and other checklists

Two new assessment instruments designed to identify individuals with autism and psychiatric disorders; the Autism Co-morbidity Interview - Present and Lifetime version (ACI-PL, Leyfer et al., 2006) and the Autism Spectrum Disorder-Comorbidity for Adults (ASD-CA, Matson & Boisjoli, 2008, Lovullo & Matson, 2009) have been published parallel in time to the PAC. The strategy chosen for the development of the PAC is, however, quite different from how the

other instruments were designed. All three instruments use primary carers or family members as informants, but the instruments reflect different approaches in design as well as with regard to which disorders and patient groups that are targeted.

The ACI-PL is a diagnostic instrument for children, designed to distinguish impairment due to comorbid psychiatric disorders from impairment due to the core features of autism. As previously shown, however, this instrument has not fully succeeded in differentiating between autism symptoms and symptoms of psychiatric disorders (Leyfer et al., 2006; Minshew, 2006), and this may also have resulted in the high prevalence rates of psychiatric disturbance identified by use of the instrument.

Both the PAC and the ASD-CA are developed with the same purpose, namely to screen for comorbid psychopathology in adults with autism and ID. However, the construction of the two checklists differs. Based on definitions of psychiatric disorders in diagnostic manuals, i.e., ICD-10 and DSM IV and the conceptual analysis, the approach chosen in the development of the PAC can be described as a top-down approach, while the strategy chosen in the development of the ASD-CA can be described as a bottom-up approach (e.g., Achenbach, Dumenci & Rescorla, 2003). The ASD-CA contains items judged by the authors as characteristic of the most probable additional disorders in the ASD population. This instrument addresses neuro-psychiatric disorders such as ADHD, as well as "core" psychiatric disorders like anxiety and depression. Psychosis is, however, not explicitly included. Matson, who is also the first author of several checklists for assessing psychiatric disorders in individuals with ID, for example the Diagnostic Assessment for the Severely Retarded (DASH II, Matson et al., 1991), the Psychopathology Instrument for Mentally Retarded Adults (PIMRA, Matson, 1988) and the Assessment of Dual Diagnosis (ADD, Matson & Bamburg, 1998), also participated in constructing the ASD-CA. Matson's wide experience probably guaranties that the ASD-CA include key items of psychiatric disorders in adults with autism and ID. The DASH II, which is among the few instruments especially designed to assess psychiatric disorders in individuals with severe and profound ID, and which has been used in a study on psychiatric disorders in individuals with autism and ID, reported prevalence similar to those found by the PAC (e.g., Bradley et al., 2004). At the present time, cut-off values and psychometric properties have been reported on the ASD-CA, which the authors consider as important steps in the development of the scale, but they argue for the need for more studies to further examine the scale's usefulness (Lovullo & Matson, 2009). More studies on the properties of the PAC are also warranted, especially on external validity and the sensitivity and specificity of the checklist. Since the ASD-CA and the PAC represent

different approaches but with a similar aim, they might prove useful complementary tools. Probably, each of these new and much needed assessments instruments may be useful tools and contribute to the identification of psychiatric disorders in this population being less challenging.

Comments and limitations

The present thesis represents a new approach and a starting point in a neglected area of research. The issue of validation has therefore been addressed in the two first phases of the present thesis (Papers I and II). In the conceptual analysis in the first phase (Paper I), the issue of content validity was addressed. A panel study design was applied to investigate which symptoms clinicians use to discriminate between autism and four major psychiatric disorders – psychosis, depression, anxiety disorder and OCD. Both psychiatric disorders and autism can only be assessed indirectly by indicators. A panel of experts was used to review the indicators of the concepts, i.e. symptom descriptions representing the core symptomatology for each of the four psychiatric disorders and for autism, for representativeness of each disorder. This method is recommended for the study of content validity (Morgan, Gliner & Harmon, 2001), since content validity mainly involves systematic examination by experts to determine whether different indicators cover a representative sample of the concept (Cook & Campbell, 1979; Crocker & Algina, 1986).

In the second phase of the present thesis (Paper II), the issue of validating the PAC was addressed. Validity studies examine the relationship between an instrument and an outside criterion (criterion validity), and the validity of an instrument is established for a particular purpose in a particular population (Cook & Campbell, 1979; Morgan et al., 2001). The specific purpose of the PAC is to be used as a screening instrument and to identify individuals with autism and ID suspected to have psychiatric disorders. The criterion by which the PAC could be examined was thus against individuals with autism and ID already identified with a psychiatric disorder. In the validation study, the assessment of clients with previously identified psychiatric disorders was chosen because it is a well-known method for validating psychometric instruments (Matson et al., 1991; Moss et al., 1998). The scores of participants previously identified with co-occurring psychiatric disorders (i.e. psychosis,

depression, anxiety disorder, or OCD) were compared with the scores of participants without psychiatric disorders.

The definition of the cut-off values used in the screening study in the present thesis (Paper III), was based on the first validation of the PAC (Paper II). The cut-off values were defined to differentiate between individuals with and without mental illness. It would have been preferable to perform a comprehensive psychiatric assessment of the participants in the screening study (Paper III) and the community sample in the anxiety study (Paper IV) after they were screened to have a psychiatric disorder. However, due to limited resources such an external validation procedure was not performed as a part of the studies. Thus data are lacking on (a) whether they would have received a psychiatric diagnosis, and (b) if so which diagnosis they would have been given if they had been psychiatrically examined by specialists. Moreover, there is no information on the participants with scores below the cut off and whether any of them would have received a psychiatric diagnosis if psychiatrically examined (false negatives).

The cut-off values for the four diagnostic groups used in the screening study (Paper III) were defined to differentiate between mentally ill individuals and individuals without mental illness, and the values may be considered as rather strict. The cut-off scores for psychosis, depression, anxiety disorder and OCD were estimated as the lowest value of the range of the scores of the subgroups with co-occurring psychosis, depression, anxiety disorder and OCD, respectively. The cut-off for severe general adjustment problems, SGAP, was estimated as the middle value between the range of scores for the "autism only" group and the scores for the four psychiatric subgroups. This definition was chosen to avoid over reporting probable cases. Such a strict distinction between afflicted and non-afflicted participants was aimed for in keeping with the usual clinical practice of identifying only those with significant problems as psychiatric patients.

The participants in the validation study (Paper II) were selected as typical representatives of different subgroups of people with autism, ID and psychiatric disorders. Given the assumption that many individuals with autism, ID and psychiatric disorders have not had their psychiatric disorder identified, the participants with psychiatric disorders in the study may not be representative of this population in general. The participants in the study had already been given a psychiatric diagnosis and are possibly characterized by more severe and chronic symptoms than many others in the same population. The sample studied may therefore be more severely disabled than a non-selected clinical group. Therefore, applying cut-off criteria based on their ratings may have resulted in too low estimates of rates of

psychiatric disturbance, and may in clinical settings, be too strict and thus fail to identify all individuals in need of referral to psychiatric services (many false negatives). In contrast, setting criteria too low may result in too many referrals (many false positives) and unnecessary worry for the individual in question and their family and carers. Accordingly, from a public health perspective, too many referrals might lead to inefficient use of professional competence and effort and unnecessary increase in costs of service provision. Thus, the selection of an appropriate cut-off value is rather important, and represents an economic as well as social political issue. In deciding the cut-off values for screening purposes, the probable number of individuals who might be identified is a central factor. The question is how many individuals the mental health services can afford to serve and have professional capacity to handle. The general adjustment problems (GAP) subscale was included in the PAC to increase the probability of identifying all individuals in need of further psychiatric assessment. If a disorder has a high base rate, as is the case for depression and anxiety disorders in people with autism and ID, strict criteria for general adjustment problems are indicated, in order to keep the number of individuals at a level which is possible to manage. In contrast, if the base rate is low (as in psychosis and OCD), the criteria for general adjustment problems are of less importance, since the likelihood of case identification is much lower.

Some further limitations of the present thesis warrant care in interpreting the findings and mandates future research. In the conceptual analysis (paper I) the panel of clinicians consisted of nine professionals and even more participants would have been desirable. Since a similar study, to our knowledge, has not been published before, replications are warranted. In the validity study (Paper II), the number of participants was relatively small. By selecting only typical representatives of different subgroups of autism, ID and psychiatric disorders, the participants may be considered as prototypical of each psychiatric subgroup. However, a larger sample would probably have resulted in more individual variation.

The present thesis represents a start. Further studies are warranted fully to examine the properties of the PAC and the scale's usefulness. Especially indicated are studies on external validity and the sensitivity and specificity of the checklist. Further studies are also required to examine whether individuals with below cut-off scores on the general adjustment subscale used in the present screening study, represent false negatives.

Clinical implications

When problem behaviours are recognized as manifestations of a comorbid psychiatric disorder, rather than behaviours attributable to autism per se, more appropriate treatment is possible. In general psychiatry, it has been clearly demonstrated that individuals with psychiatric disorders benefit from specific treatment related to the disorder they suffer from (Lehman & Steinwachs, 1998; Pratt et al., 2007), and there is reason to suppose the same in individuals with autism. Clinical experience suggests that individualized treatments of individuals with autism are associated with greater improvement in functioning, than general interventions (Leyfer et al., 2006). Standard treatments of autism, i.e., environmental adjustments and psychosocial and educational interventions, are assumed to work more efficiently, i.e., associated with greater improvement in functioning, when comorbid disorders are treated in a timely and systematic manner (Simonoff et al, 2008).

The importance of identifying and manage mental health issues in individuals with autism and intellectual disability (ID) is emphasised by the significant impairment and additional burden comorbid psychiatric disorders may impose on the individuals and their families. It has been recognized that factors such as a high level of intelligence and good communication skills, alone are not sufficient for a good outcome (Ghaziuddin & Zafar, 2008), and mental health problems have been shown to be associated with negative long term outcomes for people diagnosed with autism (Billstedt, Gillberg & Gillberg, 2005; Howlin et al., 2004).

The relationship between anxiety and autism and the possible central role of anxiety in the development of psychiatric disorders among individuals with autism, highlight the importance of recognizing anxiety in this population. Recognizing specific signs of arousal can be difficult, and requires cooperation between professionals and care staff or family who know the person well. An educational perspective seems indicated, to teach care staff and professionals to be more aware of anxiety symptoms in this population. General adjustment problems seem more easily recognized, and may in some individuals be expressions of an underlying psychiatric disorder.

From a public health perspective, costs of service provision may reduce with more adequate and efficient treatment. Moreover, rates of comorbid psychiatric disorders in autism are an important consideration in planning the provision of services. To ensure adequate services for adults with autism, ID and mental health problems, increased competence in treating comorbid psychiatric disorders and the development of specialized services are needed. Although, once considered a rare and not recognized disorder with prevalence

estimates between four to six individuals per 10 000 (Sponheim & Skjeldal, 1998; Fombonne, 1999), autism is now a relatively common disorder, with a prevalence of between 0.6 to 1 percent of ASD in child and adolescents populations (Baird, et al., 2006; Fombonne, 2003, 2005). This increased level of prevalence must be taken into consideration in planning the levels of service provision.

The PAC seems to be useful for identifying people within the adult population with autism and ID who are at risk for having mental health problems and who may benefit from more proactive health-care approaches. Thus, the use of the PAC may lead to more suitable treatment for individuals with autism and ID, which may result in general improvement in well being, and hopefully, increased quality of life and reduction of the families' burden of care.

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