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Psychiatric comorbidity in young adults with a clinical diagnosis of Asperger syndrome

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ABSTRACT

In children with autism spectrum disorders, previous studies have shown high rates of psychiatric comorbidity. To date, studies on adults have been scarce. The aim of the present study was to investigate psychiatric comorbidity in young adults with Asperger syndrome. Participants were 26 men and 28 women (mean age 27 years) with a clinical diagnosis of Asperger syndrome. Psychiatric comorbidity was assessed by the Structured Clinical Interview for DSM-IV Axis I Disorders. IQ was measured using the Wechsler Adult Intelligence Scale, Third Edition. Autism spectrum diagnoses were confirmed using the DIagnostic Interview for Social and Communication Disorders. In our study group, 70% had experienced at least one episode of major depression, and 50% had suffered from recurrent depressive episodes. Anxiety disorders were seen in about 50%. Psychotic disorders and substance-induced disorders were uncommon. In conclusion, young adults with autism spectrum disorders are at high risk for mood and anxiety disorders. To identify these conditions and offer treatment, elevated vigilance is needed in clinical practice.

1. Introduction

Autism-spectrums disorders (ASDs), classified as pervasive developmental disorders (PDDs) in the DSM-IV (APA, 2000), are relatively common social communication disorders that affect about 0.6–1% of the general population (Baird et al., 2006; Fernell & Gillberg, 2010). ASDs share a core triad of abnormalities: (1) qualitative impairments in reciprocal social interactions, (2) qualitative impairments in verbal and non-verbal communication, and (3) restricted social imagination with repetitive and stereotyped patterns of interests and behaviour. The DSM-IV includes autistic disorder (AD) (pervasive deficits in all three domains), Asperger syndrome (AS) (pervasive deficits in social interaction and behaviours in the presence of superficially normal expressive verbal development) and pervasive developmental disorder not otherwise specified (PDD-NOS) (not meeting full criteria for either AD or AS, but with pervasive deficit in social interaction). High-functioning autism (HFA) is a diagnostic term sometimes used to describe individuals with AD with low normal or normal intelligence, but it is a misnomer, particularly because in HFA, "the autism" is not high-functioning, even though the individual may, occasionally, have high intellectual functioning. Researchers comparing AS and HFA have found no important differences, implying that the boundaries within the autism spectrum are not clear (Howlin, 2003). However, some researchers still consider a

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separation of AS from autism to be clearly motivated, particularly on the basis of discriminative results on neurobiological parameters (Yu, Cheung, Chua, & McAlonan, 2011).

After the inclusion of AS in DSM-IV in 1994, and with better knowledge and awareness about ASD among professionals and the general population, the recognition and clinical diagnosis of individuals with AS/HFA have increased considerably in recent years (Baird et al., 2006). In Sweden, diagnostic assessment of children with ASDs and other neurodevelopmental problems has been available in child psychiatric health care since the beginning of the 1990s. In adult psychiatric health care, however, diagnostic evaluation of developmental disorders has not come to the forefront until the last five years.

There is growing evidence that people with ASDs are at high risk of associated psychiatric disorder, particularly depression and anxiety (Ghaziuddin, 2002; Skokauskas & Gallagher, 2010; Stewart, Barnard, Pearson, Hasan, & O'Brien, 2006; Sverd, 2003; Wing, 1981). However, research has been conducted mostly on children and adolescents (Mattila et al., 2010; Simonoff et al., 2008), and on adults with associated learning disability (LoVullo & Matson, 2009). Very few investigations on adults with ASD and normal intellectual ability have been carried out. Current depression was suggested to be present in a large minority of adults with AS/HFA using the self-report Beck Depression Inventory (Cederlund, Hagberg, & Gillberg, 2010; Hill, Berthoz, & Frith, 2004). By using Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I), Hofvander et al. (2009) showed that about 50% in their study group had a lifetime diagnosis of mood disorder. Another Swedish study found 15% of a tertiary referral group of patients with ASD had bipolar or psychotic disorder (Stahlberg, Soderstrom, Rastam, & Gillberg, 2004). Moderately high rates of other axis-I disorders assessed with SCID-I have also been reported in an investigation on insomnia in 20 individuals with AS, however some exclusion criteria (e.g. no medication) had probably influenced the results (Tani et al., 2003). Sterling et al. found depressive symptoms in about 40% of their clinically referred group of 46 cases with ASD, using a psychiatric history interview similar to the SCID-I, but the recruitment of subjects was not clearly stated (Sterling, Dawson, Estes, & Greenson, 2008). To sum up, very few investigations on clinically relevant systematically examined psychiatric comorbidity in adults with ASD and normal intellectual ability have been undertaken. We have been unable to locate even one such study specifically referring to individuals with clinically diagnosed Asperger syndrome. The selection of participants and measurements has varied considerably across the small number of published studies, making head-to-head comparisons impossible. All the published studies relate to clinic referral studies. No previous study, except the one by Cederlund et al. (2010) has attempted to demonstrate the basis for any generalisability of the results obtained.

The purpose of the present study was to systematically examine psychiatric axis-I-comorbidity in adult individuals, both men and women, with a clinically established diagnosis of AS. The aim was to include a reasonably large sample from a defined geographic area, and one that could be well-defined regarding ASD diagnostics, intellectual ability and clinical representativity.

2. Methods

2.1. Study group

Fifty-four adults (26 men, 28 women, mean age 27.0, SD 3.9 years) with a clinical diagnosis of AS were included in the study. The individuals also included participated in a comparative study of social cognition and neurocognitive functioning in AS and schizophrenia. Data from this study will be presented separately.

The 54 participants with AS were recruited from two different sources: (1) current or previous patients at the Department of Adult Habilitation (DAH) in Karlstad, Värmland county, which is an out-patient clinic for individuals aged 19 years plus with a diagnosis of ASD, (2) previous patients at the Neuropsychiatric Clinic for Children and Adolescents (NCCA) in Karlstad, which is an outpatient clinic for children and adolescents under age 19 years for evaluation of ASD or other neurodevelopmental problems. Both the DAH and NCCA are regional centres within the public health services, free of charge and with a catchment area that includes the whole county of Värmland (population c. 280 000). DAH has a broad range of professional support: some patients have major needs and long-term treatment contacts, whereas others come for a single visit for general information. Its focus is on neurodevelopmental disorders and not on psychiatric treatment. In the county, there exists no other clinic for adults with ASD, and the majority of adults who have ever been given a clinical diagnosis of AS in the area are known at DAH. Moreover, most children and adolescents diagnosed with AS in the county are evaluated at NCCA. Thus, when intending to systematically reach clinically diagnosed individuals regardless of age at AS diagnosis, the two clinics are the most adequate to approach in this particular geographic area. We originally intended to include 30 men and 30 women from the total cohort of individuals with AS registered at one or both of these clinics.

At DAH and NCCA, all patients with a registered clinical diagnosis of AS, born between 1972 and 1986, and still living in the county of Värmland at the end of 2005, were considered *eligible* for the study. Recruitment and assessment of participants was done in order of age, starting with the oldest individuals. Assessments (see below) were performed during 2006–2010. Eligible individuals were sent a participation inquiry including a complete description of the study, a response sheet and a stamped envelope. Additional oral information about the study was provided for those who requested it. If no response had been received after 4–6 weeks, a reminder was sent.

Forty-eight of the 155 eligible individuals (31%) did not respond at all, 46 (30%) actively declined participation and 61 (39%) agreed to participate. After complete description of the study to the participants, written informed consent was obtained. Seven of the 61 individuals left the study before assessment was completed, leaving 54 (35% of the total eligible

Table 1
Characteristics of 155 young adults with Asperger syndrome eligible for study participation.

Characteristic	Total ($N = 155$)		Non-participants (non-responders) ($N = 48$)		Non-participants (declined/interrupted) ($N = 53$)		Study participants (complete) ($N = 54$)		p[a]
Mean age, years (SD)	26.6	(3.7)	26.4	(3.3)	26.3	(3.7)	27.0	(3.9)	–
Male:female (ratio)	94:61	(1.5:1)	36:12	(3:1)	32:21	(1.5:1)	26:28	(0.93:1)	<0.05
	N	(%)	*N*	(%)	*N*	(%)	*N*	(%)	p[a]
Age at diagnosis of AS[b]									NS
≤10 years	12	8	1	2	4	8	7	13	
11–18 years	72	46	28	58	25	47	19	35	
>18 years	69	45	18	37	23	43	28	52	
Recruitment source									<0.05
DAH and NCCA[c]	36	23	9	19	13	25	14	26	
DAH, never NCCA[d]	97	63	25	52	36	68	36	67	
NCCA, never DAH[e]	22	14	14	29	4	8	4	7	

[a] Pearson chi-squared test; NS = nonsignificant.
[b] Information missing for 2 individuals.
[c] Current or previous patient at Department of Adult Habilitation (DAH) and previous patient at Neuropsychiatric Clinic for Children and Adolescents (NCCA).
[d] Current or previous patient at DAH, never known at NCCA.
[e] Previous patient at NCCA, never known at DAH.

group, 50% of those who responded) for in-depth assessment. For demographic characteristics of all eligible individuals, see Table 1. There were no significant differences as regards age at diagnosis of AS or age at being approached for participation in the study across those who did not respond, those who refused to participate, and the group that participated in the final study. However, the three groups differed as regards gender, more males failing to respond to the participation inquiry. Some of the gender differences were also accounted for by our original design which comprised the aim of including 30 women. The three subgroups of eligible individuals also differed in respect of recruitment source: a larger proportion of the non-responders had attended only the child and adolescent clinic. The representativeness of the final sample is addressed in Section 4.

2.2. Measures

2.2.1. SCID

Axis-I psychiatric morbidity was assessed by the first author using the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) (First & Gibbon, 2004). Specific symptoms such as recurrent hallucinations were noted separately during the SCID-I interview.

2.2.2. Additional diagnostic data

Clinically registered diagnoses of attention-deficit/hyperactivity disorder (AD/HD) and Tourette syndrome (not included in the SCID) were not re-assessed systematically within the present study, but the diagnoses of these conditions were drawn from medical records and confirmed by patient report.

2.2.3. WAIS-III

Global intellectual ability was measured using the full-scale Swedish version of the Wechsler Adult Intelligence Scale, Third Edition (WAIS-III) (Wechsler, 1997). For four participants (one man and three women), an assessment with WAIS-III was not carried out. All these four individuals were in the normal range of IQ according to IQ-assessments carried out prior to the present study.

2.2.4. DISCO-11

The AS/ASD diagnosis was confirmed in a vast majority of the cases ($n = 44$) by the second author using the Eleventh version of the DIagnostic Interview for Social and COmmunication Disorders (DISCO-11) (Wing, Leekam, Libby, Gould, & Larcombe, 2002) with a collateral informant. The DISCO-11 is a semi-structured interview that covers a wide range of developmental domains, and with excellent psychometric properties including validity for clinical autism spectrum disorder diagnosis. An algorithm is designed for different diagnostic categories. DISCO-11 interview with a parent/both parents was completed for 45 subjects. Four subjects did not agree to parental interview. Parents of three subjects did not accept to take part and another two have not been possible to assess due to practical circumstances. A diagnosis within the autism spectrum was confirmed in 44 of the 45 DISCO-11-assessed one cases. In the case where criteria for ASD were not fulfilled, the parents described their son as very quiet and shy during childhood but did not consider it a problem. There was however, no doubt that he now had a clear clinical presentation consistent with the diagnosis of Asperger syndrome

Table 2
Demographic characteristics of 54 young adults with Asperger syndrome.

Characteristic	Total ($N = 54$)		Women ($N = 28$)		Men ($N = 26$)	
	Mean	SD	Mean	SD	Mean	SD
Total IQ[a]	102	12	102	12	102	13
Verbal IQ[a]	102	13	102	13	102	12
Performance IQ[a]	103	13	103	11	102	15
	N	%	*N*	%	*N*	%
Maximum educational level						
Special school	3	6	1	4	2	8
Compulsory school (regular program)	4	7	3	11	1	4
High school studies without final exam	17	31	9	32	8	31
High school final exam	23	43	12	43	11	42
University (with or without degree)	7	13	3	11	4	15
Source of income						
Dependent on social services	6	11	5	18	1	4
Disability pension	32	59	16	57	16	62
Combination of disability pension and social services	3	6	2	7	1	4
Combination of disability pension and part-time employment	4	7	1	4	3	11
Study grant	2	4	1	4	1	4
Supported employment	4	7	1	4	3	11
Regular employment	3	6	2	7	1	4
Daily occupation						
No daily occupation	22	41	15	54	7	27
Sheltered occupational activity	15	28	6	21	9	35
Employment (supported or regular)	11	20	4	14	7	27
Studies (different levels)	6	11	3	11	3	11

[a] IQ missing for 3 women and 1 man.

2.3. Ethics

The study was approved by the Medical Ethical Review Board at Uppsala.

3. Results

3.1. Socio-demographic data

Mean age at original AS diagnosis was 19.0 years (SD 7.6). Seven individuals (13%) had received their AS diagnosis when they were 10 years or younger, 19 (35%) between the ages of 11 and 18 years, and 28 (52%) when they were 19 years or older.

Four participants (7%) were previous patients at NCCA and never known at DAH, 14 (26%) were known at both NCCA and DAH, and 36 subjects (67%), were current or previous patients at DAH, never known at NCCA.

Demographic characteristics are shown in Table 2. No differences in between men and women were seen.

3.2. Psychiatric comorbidity

Thirty-eight of the 54 participants (70%) had experienced at least one episode of major depression, and 27 of these (50% of the total group) had had recurrent major depressions. Five participants (9% of the total group) met criteria for bipolar II disorder, whereas none met criteria for bipolar I disorder.

Thirty individuals (56%) met criteria for at least one anxiety disorder, and 11 of these fulfilled diagnostic criteria for two or more anxiety disorder diagnoses. Twelve (22%) had social anxiety disorder (SAD), 12 (22%) had generalized anxiety disorder (GAD), seven (13%) had panic disorder, eight (15%) had agoraphobia and four participants (7%) had obsessive–compulsive disorder (OCD).

Two individuals met criteria for psychosis (one brief psychotic episode, and one psychotic syndrome NOS). Seven participants (13%) had experienced recurrent (primarily auditory) hallucinations without other signs of psychosis. No participant met criteria for schizophrenia, schizoaffective disorder or substance induced psychotic disorder.

Two participants (4%) had bulimia nervosa, and none had anorexia nervosa.

Six participants (11%) had had a previous substance dependence disorder (one woman and one man with a combination of alcohol and drug dependence, two men with alcohol dependence and two men with drug dependence).

Sixteen participants (30%) had been given a diagnosis of AD/HD before the study. One individual (2%) had been diagnosed with Tourette syndrome.

No gender differences were seen in terms of psychiatric comorbidity. The distribution of diagnoses is given in Table 3.

Occurrence of life-time mood or anxiety disorder did not differ significantly between individuals who were dependent on disability pension/social services and individuals with employment (regular or supported, full-time or part-time) or study grant.

Table 3
Psychiatric comorbidity in 54 young adults with Asperger syndrome.

	Total ($N = 54$)		Women ($N = 28$)		Men ($N = 26$)	
	N	%	*N*	%	*N*	%
Disorders based on SCID-I						
Mood disorders						
Life-time major depression	38	70	20	71	18	69
Major depression, single episode	11	20	7	25	4	15
Major depression, recurrent episodes	27	50	13	46	14	54
Bipolar I	–	–	–	–	–	–
Bipolar II	5	9	3	11	2	8
Anxiety disorders						
Any anxiety disorder	30	56	16	57	14	54
Generalized anxiety disorder	12	22	7	25	5	19
Social anxiety disorder	12	22	5	18	7	27
Panic disorder	7	13	5	18	2	8
Agoraphobia	8	15	4	14	4	15
Obsessive–compulsive syndrome	4	7	1	4	3	12
Life-time psychotic disorders						
Brief psychotic disorder	1	2	1	4	–	–
Psychotic syndrome NOS	1	2	–	–	1	4
Schizophrenic disorder	–	–	–	–	–	–
Schizoaffective disorder	–	–	–	–	–	–
Substance-induced psychotic disorder	–	–	–	–	–	–
Recurrent hallucinations	7	13	4	14	3	11
Life-time eating disorders						
Anorexia nervosa	–	–	–	–	–	–
Bulimia nervosa	2	4	2	7	–	–
Life-time substance dependence disorders						
Any substance dependence	6	7	1	4	5	19
Alcohol dependence	4	7	1	4	3	12
Drug dependence	4	7	1	4	3	12
Other disorders						
ADHD	16	30	8	29	8	31
Tourette syndrome	1	2	–	–	1	4

4. Discussion

4.1. Psychiatric comorbidity

The present study found a strikingly high rate of lifetime major depression in young adults with AS. Despite the relatively young mean age of the individuals in the sample (27 years), a full 70% of the group had experienced at least one major episode of depression. Some individuals had had only a single depressive episode, quite often during negative life circumstances (school problems, bullying), and some of these may not relapse in the future. However, half of all participants in the study had already suffered recurrent depressive episodes and this group is clearly at risk for long-standing/chronic psychiatric illness. Our results are in line with earlier assumptions on depression rates in adults with ASD and normal intellectual ability, even though no previous study has made the same systematic approach both regarding measurements and study population (Skokauskas & Gallagher, 2010). Although the limited number of prior investigations have shown a similar occurrence of mood disorder, some patient populations have probably been more biased towards psychiatric illness (Hofvander et al., 2009), and others may have been skewed in the opposite direction due to recruitment procedure (Hill et al., 2004) or exclusion criteria (Sterling et al., 2008). Our study indicates that about two thirds of a young adult population with AS have experienced major depression one, usually more times in their lives. Based on this and our very long term clinical experience of working with hundreds of individuals with AS we believe that this is a finding that is generalisable to other patients with AS in early adult life.

Hypomanic symptoms are liable to be unrecognized without a semi-structured psychiatric interview. Out of the five participants diagnosed with bipolar II in our study, only one had an already previously established clinical diagnosis of bipolar disorder and a mood stabilizing treatment. Despite the fact that some researchers believe bipolar I disorder to be overrepresented in AS, no participant in the present study group had a diagnosis of bipolar I (Raja & Azzoni, 2008). However, one individual (a woman) was diagnosed with bipolar I when she had her first episode of mania six months *after* participating in the present study. Two factors that might have contributed to the low rate of bipolar I in our sample, are (a) the young age of the group and (b) the recruitment process, through which individuals with more serious comorbid psychiatric problems may have been withdrawn.

Very high rates of anxiety disorders were also found in our sample, the most prevalent being GAD and SAD. No previous studies with focus on occurrence of anxiety disorders in adults with AS have been published, but rates varying from 30% to 65% have been reported as associated findings (Hofvander et al., 2009; Sterling et al., 2008; Tani et al., 2003). According to

strict DSM-IV-TR criteria, a diagnosis of GAD is precluded if a PDD is present, a fact that may well have contributed to the lack of studies on coexisting anxiety disorders in ASD. Since generalized anxiety seems to be a common distress response in individuals with AS, although not belonging to the core features, we believe this exclusion criterion is inappropriate.

About a fifth of the participants met criteria for SAD. Even though impairment in social interaction-communication is among the core symptoms in AS, there is considerable variation in the way in which this core difficulty affects social behaviour. Some people with AS are uninterested in and indifferent to other people's opinions, but there are also those who are socially interested but yet unconcerned about how they are seen by others ("active but odd") (Wing, 1997). Furthermore, for some individuals with AS, their disability in interpreting social cues leads to a major concern about what impression they make on others and even a disabling fear for social situations, thus fulfilling criteria for SAD.

OCD is controversial as a co-morbid diagnosis in AS given that rituals and rigid adherence to routines are among the criteria for a diagnosis of AS. DSM-IV criteria for OCD include egodystonicity, whereas many individuals with AS experience their rituals as egosyntonic. Nevertheless, several researchers have pointed out the fact that OCD including egodystonicity may well occur in individuals with AS (Bejerot, Nylander, & Lindstrom, 2001; Cath, Ran, Smit, van Balkom, & Comijs, 2008). In our study, participants who were markedly distressed by their compulsive rituals and/or obsessive thoughts received a diagnosis of OCD. In contrast, participants with egosyntonic ritual behaviours, presenting no subjective suffering, were not given an OCD diagnosis. This, along with differences in study populations, is a probable explanation to our finding (7%) compared to prior studies, in which OCD occurrence have varied between 20% and 35% (Hofvander et al., 2009; Russell, Mataix-Cols, Anson, & Murphy, 2005; Sterling et al., 2008).

A low rate of clear psychotic disorders was found in our study group. Some previous investigations have reported rates of 12–20% (Hofvander et al., 2009; Stahlberg et al., 2004; Tantam, 1991). On the other hand, a follow-up study by Howlin (Howlin, 1997) and a few cross-sectional studies (Ghaziuddin, Tsai, & Ghaziuddin, 1992; Leyfer et al., 2006) have demonstrated no or very few cases of psychotic disorders in ASD samples. Undoubtedly, selection bias may be one important explanation for this variation as well as inclusion criteria concerning PDD-NOS and mental retardation. Moreover, when comparing studies on comorbidity of psychosis, it is crucial to consider the age range of the study sample, as psychosis usually develops between ages 18 and 25 years. Interestingly, 13% of our participants reported recurrent auditory hallucinations, without fulfilling any other criteria for a psychotic disorder. Even though hallucinations had been present for several years, none of these individuals had sought treatment for this reason, probably because the symptoms had not caused major distress. In the general population, psychotic symptoms are estimated to be present in about 5%, although prevalence may well be influenced by socio-economic factors and the occurrence of substance use (van Os, Linscott, Myin-Germeys, Delespaul, & Krabbendam, 2009).

Even though the rate of substance abuse was relatively small in the group as a whole, most of the variance was accounted for by individuals with AS who also had a diagnosis of ADHD. This is clinically important given the now widespread belief that ASDs are unassociated with substance abuse. This may be true for those who have "only" ASD, but clearly is not for those with ASD who have comorbid ADHD.

4.2. Age at AS diagnosis

AS is a heterogeneous concept. To be sure, the core difficulties can be severe and obvious or subtle and less apparent. Early recognition of AS is seen as important in order to understand the child's difficulties, adjustment of the child's total situation and to support development in all domains, everything with a view to improving outcome. One can hypothesize that such early interventions may decrease the risk for secondary psychiatric symptoms such as depression or anxiety. However, the interpretation of data is complicated by the fact that individuals who are recognized at a young age are usually those with core difficulties that are more severe and more obvious. On the one hand, severe core difficulties may lead to a high risk for psychiatric comorbidity *per se.* On the other hand, severe core difficulties also probably increase the chance of an early diagnosis and perhaps early interventions that could contribute to prevent secondary psychiatric comorbidity. More subtle core difficulties are likely to lead to a delayed diagnosis. Referral for a diagnostic evaluation may not even be discussed until secondary problems have become unmanageable. In our study, as many as half of the participants had received their AS diagnosis at or after 19 years of age, most likely, as a consequence of the recent increasing awareness about ASD in adult psychiatric services. Adult individuals seeking a neurodevelopmental diagnostic evaluation, have a reason for doing so. The starting point for an assessment is very often academic or professional failure in combination with psychiatric symptoms. Undoubtedly, this may have increased the rates of depression and anxiety in our study. However, individuals diagnosed in childhood did show as high comorbidity rates as participants with an adult diagnosis. Moreover, a recent study indicates that individuals with more subtle social impairments may actually be more likely to develop depressive symptoms (Sterling et al., 2008). In conclusion, further understanding of the impact of core disabilities and age of diagnosis on risk for psychiatric comorbidity is needed. Most importantly, we need research on what interventions/preventions would be the most beneficial.

4.3. Generalisability of the findings

Just like the very few previous studies on comorbidity in adults with AS, our study is clinically based. Nevertheless, our study is the only one in the field that attempted to recruit cases from a representative group of clinically diagnosed

individuals with AS. In previous research, recruitment of participants has been either from (1) consecutively referred patients to tertiary centres (Hofvander et al., 2009; Russell et al., 2005; Stahlberg et al., 2004; Tani et al., 2003), (2) by advertising within interest organisations/facilities for people with AS (Hill et al., 2004) or (3) not clearly stated (Sterling et al., 2008; Tantam, 1991). In contrast, we did approach the entire patient population with an established AS diagnosis within a certain age range and in a defined geographic area ($n = 155$). Additionally, we have presented some background demographic variables (age, sex, age at diagnosis, referral source) from the whole eligible group. The two recruitment sources, DAH and NCCA, are the most appropriate in the area, and we believe that the number of individuals missed out for eligibility is very small. However, those who are likely to be missed are (1) individuals assessed in childhood at the Child Psychiatry Clinic (not NCCA) who do not request support in adulthood and (2) individuals assessed in adulthood at the Psychiatry Outpatient Clinic, not requesting further support. Individuals missed out for eligibility can be assumed to be either more capable (in *no need* for professional support after a diagnosis is established) or more disabled (*refusing* professional support due to severe drug abuse or to psychiatric disorder). Nevertheless, we conclude that missing out on some individuals for eligibility has not markedly influenced our results.

A more serious concern relates to the low participation rate and the high proportion of non-responders. What may distinguish the non-responders from the total eligible population? A significantly higher proportion of non-responders were previous patients at NCCA and not known at DAH, meaning that that they had never established a clinical follow-up in adulthood. Speculatively, on the basis of research in general population samples, non-responders may be more likely to have low cognitive functioning (especially low executive functioning) and/or more severe psychosocial problems, including homelessness, imprisonment, and substance abuse. In addition, psychiatric comorbidity *per se* may be an explanation for not responding. For these reasons, we believe that our results may well underestimate the true rate of *severe* psychiatric comorbidity (e.g. psychotic disorders, severe substance abuse) in the population (Stormark, Heiervang, Heimann, Lundervold, & Gillberg, 2008).

To some extent, the same line of reasoning as for non-responders is plausible for the group who actively declined study participation: individuals not willing to participate due to low executive functioning, suspiciousness towards health care, psychiatric illness. On the other hand, among those who actively declined, there may well be individuals refusing participation due to good outcome, including lack of time because of full-time employment, and/or lack of interest because of no need/acceptance for a previous neurodevelopmental diagnosis. Taking these different considerations into account, we believe that our results do not substantially overestimate psychiatric comorbidity rates in AS. Clearly, one may question how representative the result is, given the relatively low participation rate and the small sample. However, voluntary participation and informed consent are fundamental principles in clinical research, even in observational studies, and there is no alternative way to address these questions. True rates of comorbidity require total population studies, which are undoubtedly highly desirable, nevertheless hardly possible within the field of adult psychiatry, due to time-consuming diagnostic processes and individuals who may be reluctant to research participation because of their actual symptoms/disabilities. New knowledge in clinical psychiatry has to rely on clinically based studies with all their limitations.

There are no instruments specifically for the assessment of psychiatric morbidity in adults with autism spectrum disorders with normal IQ. In this population, there is a risk of both underrating and overestimating psychiatric symptoms. There are difficulties in classifying some symptoms in relation to the core disorder. In our study group, all participants were verbal and of normal intelligence. Nevertheless, the core difficulties of AS, restricted social communication and social interaction, may affect a psychiatric diagnostic evaluation. Semi-structured interviewer-rated method, such as the SCID-I, performed by a clinician experienced in the field of autism, could be expected to be more valid than highly structured respondent-based methods (e.g. web-based self-rated questionnaires).

4.4. Gender aspects

In the total eligible population, the male:female ratio was 1.5:1, which is at odds with most previous reports on sex distribution in AS (Fombonne, 2005). One explanation may be an early awareness of the existence of "female" ASD among staff at NCCA, which has facilitated recognition and diagnostic assessment and consequently affected the sex distribution rate in our total population (Kopp, Berg Kelly, & Gillberg, 2010). Another contributing factor may be increased health care-seeking behaviour among women. Moreover, women were (1) more likely to respond to the participation enquiry and (2) more willing to participate in the study. A marked overrepresentation of males is seen in the non-responder group and, therefore, there is greater uncertainty concerning generalisability of our results when it comes to the men. We assume that the above line of reasoning about non-responders is valid also when interpreting the results in view of gender differences: it is highly possible that non-responding individuals (most commonly men) represent a more disabled subgroup compared to the total population and, consequently, an underestimation of comorbidity rates in the AS men of this sample is probable (Stormark et al., 2008).

4.5. Clinical implications

Despite good verbal ability and normal intelligence in most cases with a clinical diagnosis of AS, the core difficulties in social interaction and communication seriously affect the person with regard to mental health and psychosocial functioning. A high level of alertness for additional psychiatric disorders is needed when an assessment for a neurodevelopmental

disorder is made. Preparedness for offering psychiatric treatment is essential. Likewise, when treating patients with a long-term history of depression and/or anxiety, an increased vigilance for neurodevelopmental disorders (such as AS) is highly recommended.

Disclosures

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