

Psychopathology in Children and Adolescents with ASD Without Mental Retardation

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Abstract This study analyzes subclinical psychopathology in children and adolescents with autism spectrum disorders (ASD) without mental retardation with no comorbid disorder, assessed by an extensive general psychopathology interview. The K-SADS-PL was administered to a group of 25 patients with ASD (mean age = 12.80 ± 2.86 years) and 25 healthy controls (mean age 12.52 ± 2.86 years). Significant differences were found between patients with ASD and controls for the domains of: depressive disorder, anxiety separation disorder, agoraphobia and specific phobias, obsessive compulsive disorder (OCD), and attention deficit hyperactivity disorder (ADHD). In patients without a comorbid disorder, we found a profile of subclinical disturbances that suggest high risk for comorbid psychiatric conditions derived from the presence of subthreshold symptomatology.

Keywords Asperger syndrome · Psychopathology · Comorbidity · Adolescent · Developmental disorders

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Introduction

In clinical practice, it has long been recognized that autism spectrum disorders (ASD) are complicated by co-existence and symptomatic overlap with other psychiatric disorders, and a growing number of systematic studies confirm the clinical observations (Gjevik et al. 2011; Meyer et al. 2006; Tantam and Girgis 2009). With respect to patients with ASD without mental retardation, a combined community- and clinic-based study showed that 74 % of a sample of 50 children between 9 and 16 years of age had a comorbid psychiatric disorder evaluated using the Kiddie Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime version (K-SADS-PL) (Mattila et al. 2010). Behavioral disorders, anxiety, and tic disorders were found in 44, 42, and 26 % of the sample, respectively.

Studies using different self-administered screening questionnaires completed by parents and/or patients have shown that there are significantly more psychiatric symptoms in the ASD without mental retardation group than in controls, especially problems related to withdrawal and anxiety/depression, as well as social and attentional problems (Hurtig et al. 2009; Kuusikko et al. 2008). A recent study at our institution, which used the Strengths and Difficulties Questionnaire (SDQ) to evaluate risk for behavioral and emotional problems in Asperger syndrome (AS), revealed significant differences in all assessed areas of psychopathology (Merchán-Naranjo et al. 2010).

A recently published review of clinical studies supports these data (Mazzone et al. 2012), but remarks on the need for longitudinal studies that may help to distinguish those symptoms that are part of the ASD clinical phenotype from those that are the expression of a comorbid disorder. Those comorbid disorders or symptoms represent an additional

handicap for the affected child, requiring considerable attention, intervention, and medical treatment (Gadow et al. 2008), and result in lifelong disability and important burden of disease (Sanchez-Valle et al. 2008).

Subsyndromal psychopathology may be a remarkable complication in patients with ASD without mental retardation, given the precarious social balance in this population, especially during adolescence. However, to our knowledge, no study has assessed the presence of subsyndromal psychopathology in children and adolescents with high-functioning ASD or Asperger Syndrome using a clinician-administered semi-structured interview.

The K-SADS-PL semi-structured clinical interview (Kaufman et al. 1997) is an extensive general psychopathology interview that explores the presence of symptoms of different disorders included in the DSM-IV-TR. It is one of the most commonly administered instruments in mental health care and has been used to report comorbidity.

The objective of this study was to evaluate a group of ASD without mental retardation children and adolescents and a group of matched healthy controls for the presence of subclinical symptoms in the affective, anxious, behavioral, and psychotic domains using a semi-structured clinical interview. We hypothesized that children and adolescent ASD patients with no mental retardation and no complete comorbid disorder have more subsyndromal psychopathology than healthy controls, and that this psychopathology involves different psychopathological domains.

Methods

Participants

Data were recorded from a sample of 25 patients with ASD without mental retardation and 25 controls. ASD patients were recruited via the Spanish Asperger Syndrome Family Association (via advertisements) and from the autism spectrum disorder (ASD) Program at Hospital General Universitario Gregorio Marañón in Madrid, Spain (Parellada et al. 2011).

Patients attending the ASD Program or who answered the Family Association ads were consecutively invited to participate in the study and enrolled if they met the inclusion criteria. The sample formed part of a more extensive study aimed at assessing oxidative metabolism in patients with AS (Parellada et al. 2012). The control group was recruited from high schools in the catchment area of the ASD Program. The groups were matched for age, gender, and socioeconomic status (measured as number of years of parental education).

The study was approved by the Ethics and Clinical Research Committee of Hospital General Universitario

Gregorio Marañón. Before starting, participants and their parents or legal guardians signed an informed consent after receiving an explanation of the study procedures.

Inclusion and Exclusion Criteria

The inclusion criteria were as follows: (1) between 7 and 17 years of age; (2) a diagnosis of ASD without mental retardation; (3) Spanish mother tongue or fluency in Spanish; and (4) informed consent for the study signed by the parent or legal guardian with patient assent. The exclusion criteria were as follows: (1) comorbidity with other Axis I disorders; (2) a history of head injury with loss of consciousness; (3) mental retardation or other significant disorders not related to a pervasive developmental disorder (PDD); (4) pregnancy or breastfeeding at time of study; and (5) substance abuse or dependence. The inclusion and exclusion criteria for the control group were the same, except for the diagnosis of ASD.

Measurements

Demographic and Intelligence Quotient (IQ) Data

Demographic data (age, sex, race, and socioeconomic status) were collected along with IQ of both patients and controls. IQ (estimated with the vocabulary and block design tests of the Wechsler Intelligence Scale) was recorded for controls. Given that estimated IQ is not a reliable measurement in patients with AS (Merchan-Naranjo et al. 2011), the full IQ test was administered in this group.

Clinical Scales

All participants were evaluated by psychiatrists trained in the use of the K-SADS-PL. The administration and correction of that instrument was done blind to the analysis of the data included in this study. This semi-structured interview is designed to assess current and past psychopathology and establishes diagnoses based on DSM-IV-TR criteria. It can diagnose most childhood and adolescent psychiatric disorders (see Table 1). Both parents and children/adolescents were interviewed using the K-SADS-PL, and the interviewer determined the final score for each item based on both sets of answers.

Within each section, there are several items that refer to specific symptoms. Items are scored as 0 (no information), 1 (absent), 2 (subthreshold, if symptoms appear occasionally), or 3 (threshold). We considered any threshold or subthreshold value to be subclinical psychopathology.

The K-SADS-PL has 5 supplements (Affective Disorders, Psychotic Disorders, Anxiety Disorders, Behavioral

Table 1 KSADS-PL domains and items

Disorder	Explored areas
Affective disorders	
Depression	(1) Depressed mood, (2) irritability and anger, (3) anhedonia, lack of interest, apathy, low motivation, or boredom, (4a) recurrent thoughts of death, (4b) suicidal ideation, (4c) suicidal acts–intent, (4d) suicidal acts–medical lethality, (5) self-injurious behaviour
Mania/hypomania	(1) Elevated, elated, or expansive mood, (2) explosive irritability/anger, (3) episodes of unusual energy/activity, (4) decreased need for sleep, (5) hypersexuality
Psychotic disorders	
Psychosis	(1) Hallucinations, (2) delusions
Anxiety disorders	
Panic disorder	(1) Panic attacks
Anxiety separation disorder	(1) Fears calamitous event that will cause separation, (2) fears harm befalling attachment figure, (3) school reluctance/refusal, (4) fears sleeping away from home/sleeping alone, (5) fears being alone at home
Social phobia	(1) Fear of social situations, (2) distress/avoidance
Agoraphobia/specific phobias	(1) Agoraphobia, (2) distress/avoidance
Generalized anxiety disorder	(1) Excessive worries, (2) somatic complaints, (3) marked feeling of tension/unable to relax
Obsessive-compulsive disorder (OCD)	(1) Obsessions, (2) Compulsions
Post-traumatic stress disorder	1) Catastrophic events 2) Avoidant/hyperarousal response against them
Developmental/learning disorders	
Disorders usually first diagnosed in infancy, childhood, or adolescence	
Enuresis	(1) Repeated voiding, (2) evidence of enuresis
Encopresis	(1) Repeated passage of feces, (2) evidence of encopresis
Attention deficit hyperactivity disorder	(1) Difficulty sustaining attention in tasks or play activities, (2) easily distracted, (3) difficulty remaining seated (4) impulsivity
Oppositional defiant disorder	(1) Loses temper, (2) argues a lot with adults, (3) disobeys rules a lot/defies or refuses to comply with adults, (4) bullies, threatens, or intimidates others
Behavioral disorder	(1) Lies, (2) plays truant, (3) initiates physical fights; bullies, threatens, or intimidates others
Tic disorder	(1) Motor tics, (2) phonic tics
Eating disorders	
Anorexia nervosa	(1) Fear of becoming obese, (2) emaciation
Bulimia nervosa	(1) Weight loss methods, (2) eating binges or attacks

Disorders, and Eating Disorders) that are administered only if an item of the corresponding domain is scored 3. The results are corrected and summarized with a final score of 1 (absent), 2 (probable), 3 (partial remission), or 4 (final) for each disorder. Table 1 shows the symptoms included in the K-SADS-PL, by domain.

All diagnoses of ASD were made by psychiatrists at baseline based on the developmental history of each participant and on previous medical, psychoeducational and specialized diagnostic private services reports using DSM-IV-TR and Gillberg criteria (Gillberg and Gillberg 1989). The Autistic Diagnostic Observation Schedule-Generic (ADOS-G) (Lord et al. 2002) interview, which is an observational instrument that provides the basis for a diagnosis of ASD and autism was administered by child psychiatrists who had received ADOS Research Training (MP, CM), whenever there were conflicting results

between the Gillberg and DSM-IV-TR criteria (35 % of patients).

Data Analysis

The sociodemographic data of the two groups were compared using a Chi square test for qualitative variables (gender or race) and a *t* test for continuous independent variables (age, IQ, years of education), once the distribution was shown to be normal by means of a Kolmogorov–Smirnov test. The percentage of subjects in each group (ASD without mental retardation and controls) with at least one item with a threshold or subthreshold value in a given symptomatic domain was compared using a Chi square test. Logistic regression analyses were performed to control for the possible influence of IQ on all variables where significant differences were found between the groups.

A Chi square test was also used to compare the percentage of individuals in each group with absent, threshold, or subthreshold values in each item individually. Given that the values of the individual items follow an ordinal scale (absent, subthreshold, threshold), we are providing the linear-by-linear association statistic to compare the groups. Statistical significance was set at $p < 0.05$. Data were analyzed using SPSS for Windows version 16.0.

Results

Sociodemographic Data

The comparison between the ASD and control groups revealed no significant differences in age (ASD group = 12.80 ± 2.86 years, control group = 12.52 ± 2.86 ; $p = 0.73$), gender (24 males and 1 female in the ASD group vs. 23 males and 2 females in the control group, $p = 1$), race (23 Caucasians in both groups, 2 “other races” in the ASD group, and 2 Hispanics in the control group; $p = 0.13$), or years of parent/guardian education (13.43 ± 3.99 in the ASD group vs. 11.88 ± 4.30 in the control group, $p = 0.20$).

All participants in both groups had IQs within the normal range ($IQ > 85$), per the inclusion criteria. Despite that, we tested for IQ differences between groups and found statistically significant differences ($IQ = 97.88 \pm 27.60$ in the ASD group vs. 114.438 ± 16.099 in the control group; $p = 0.016$).

Psychopathological Domains

The presence of at least one symptom at threshold or subthreshold levels within the different domains of the K-SADS-PL was significantly higher for the group with ASD in the following domains: Depressive Disorder, Anxiety Separation Disorder, Agoraphobia and Specific Phobias, Obsessive Compulsive Disorder (OCD), and Attention Deficit Hyperactive Disorder (ADHD). No statistically significant differences were found in psychopathology in the following areas: Psychosis, Panic Disorder, Social Phobia/Avoidant Disorder, Oppositional Defiant Disorder (ODD), Generalized Anxiety Disorder, Enuresis, Encopresis, Anorexia and Bulimia Nervosa, Behavioral Disorder, and Tic Disorder (see Table 2).

In all cases, the difference was still significant after covarying for sociodemographic factors, IQ included.

Symptoms

Table 3 provides the percentages of subjects with subthreshold or threshold scores on the individual items, per group.

Table 2 Differences between AS group and control group in the presence of at least one subthreshold or threshold item per domain

	One or more/ symptoms (threshold/ subthreshold)		<i>p</i>
	Control N total (%)	Asperger N total (%)	
Depressive disorder	2 (8)	14 (56)	0.001
Psychosis	0	3 (12)	0.23
Panic disorder	1 (4)	5 (20)	0.18
Separation anxiety disorder	0	7 (28)	0.01
Social phobia	7 (28)	10 (40)	0.55
Agoraphobia and specific phobia	1 (4)	9 (36)	0.01
Generalized anxiety disorder	5 (20)	8 (32)	0.52
Obsessive-compulsive disorder	2 (8)	12 (48)	0.004
Enuresis	0 (0)	4 (16)	0.11
Encopresis	0 (0)	3 (12)	0.23
Anorexia nervosa	2 (8)	2 (8)	1.00
Bulimia nervosa	0 (0)	0 (0)	1.00
Attention deficit hyperactivity disorder	3 (12)	17 (68)	<0.001
Oppositional defiant disorder	5 (20)	12 (48)	0.07
Conduct disorder	3 (12)	4 (16)	1.00
Tic disorder	6 (24)	5 (20)	1.00

Two of the five assessed Affective Disorders-Depression items, namely “irritability and anger” and “recurring thoughts of death” (Table 3), were significantly more frequent in the ASD group.

With respect to anxiety disorders, five (of 15) items reached statistical significance (in threshold or subthreshold values). Of the five items that comprise the Separation Anxiety Disorder domain, only school refusal was significantly more frequent in ASD. Similarly, symptoms of anxiety and avoidance in agoraphobia as well as specific phobias were significantly more frequent in ASD patients. Although not significant, there was a greater tendency to experience panic attacks, generalized anxiety disorder, and social phobia symptoms. We therefore devised a new variable that included all anxiety items except for OCD, and found more marked anxiety symptoms in the ASD group than in controls (76 vs. 36 %, respectively, $p < 0.01$). Both obsessive and compulsive symptoms were more frequent in the ASD group.

Almost all symptoms of ADHD (impulsivity was an exception) were more frequently present in the ASD group. Remarkably, 56 % in the ASD group reported having attention problems vs. 4 % in the control group. With respect to oppositional-defiant symptoms, loss of control was more frequent in the ASD group (40 vs. 12 %).

Table 3 Percentage of subjects with presence of sub threshold or threshold symptoms, per group

Disorder group	Anxiety disorders											
	Affective		Separation anxiety		Agoraphobia and specific phobias		OCD		Compulsions		Obsessions	
Disorder	Depression		School refusal		Anxiety		Avoidance		OCD		Obsessions	
Symptom	Irritability and anger		Recurrent thoughts of death		Anxiety		Avoidance		OCD		Obsessions	
	CTR	ASD	CTR	ASD	CTR	ASD	CTR	ASD	CTR	ASD	CTR	ASD
Absent	24 (96.0 %)	13 (52.0 %)	25 (100.0 %)	20 (80.0 %)	24 (96.0 %)	18 (72.0 %)	25 (100.0 %)	18 (72.0 %)	23 (92.0 %)	16 (66.7 %)	24 (96.0 %)	15 (62.5 %)
Sub-threshold	1 (4.0 %)	7 (28.0 %)	0 (0 %)	1 (4.0 %)	1 (4.0 %)	4 (16.0 %)	0 (0 %)	4 (16.0 %)	2 (8.0 %)	5 (20.8 %)	1 (4.0 %)	6 (25.0 %)
Threshold	0 (0 %)	5 (20.0 %)	0 (0 %)	4 (16.0 %)	0 (0 %)	3 (12.0 %)	0 (0 %)	3 (12.0 %)	0 (0 %)	3 (12.5 %)	0 (0 %)	3 (12.5 %)
	$X^2 = 11.658$ ($p = 0.001$)		$X^2 = 5.161$ ($p = 0.050$)		$X^2 = 5.444$ ($p = 0.050$)		$X^2 = 7.000$ ($p = 0.010$)		$X^2 = 5.410$ ($p = 0.021$)		$X^2 = 7.997$ ($p = 0.003$)	
Disorder group	Development											
Disorder	ADHD											
Symptom	Difficulty in keeping attention		Easily distracted		Difficulty staying seated		Loss of control					
	CTR	ASD	CTR	ASD	CTR	ASD	CTR	ASD				
Absent	24 (96.0 %)	11 (44.0 %)	22 (88.0 %)	11 (44.0 %)	24 (96.0 %)	17 (68.0 %)	22 (88.0 %)	15 (60.0 %)				
Sub-threshold	1 (4.0 %)	6 (24.0 %)	3 (12.0 %)	6 (24.0 %)	1 (4.0 %)	3 (12.0 %)	3 (12.0 %)	6 (24.0 %)				
Threshold	0 (0 %)	8 (32.0 %)	0 (0 %)	8 (32.0 %)	0 (0 %)	5 (20.0 %)	0 (0 %)	4 (16.0 %)				
	$X^2 = 15.207$ ($p = 0.0005$)		$X^2 = 12.413$ ($p = 0.0005$)		$X^2 = 7.028$ ($p = 0.01$)		$X^2 = 6.170$ ($p = 0.020$)					

CTR control, ASD autism spectrum disorder, OCD obsessive-compulsive disorder, ADHD attention deficit-hyperactivity disorder, ODD oppositional defiant disorder

Discussion

Our results show a significantly higher rate of subthreshold symptoms in children and adolescents with ASD without mental retardation, but with no comorbid psychiatric disorders, than in controls. More than half of the cases in our ASD sample showed symptoms in several of the evaluated areas as compared with controls. Most remarkably, poor attention and distractibility were present in more than 50 % of cases of ASD, irritability and anger in almost 50 %, and obsessions, compulsions, and loss of control in around 40 %. In other words, our sample of patients with ASD without mental retardation did not meet the criteria for other mental disorders (per the exclusion criteria), but did have significant comorbid psychopathology.

The most remarkable overlap was with symptoms of ADHD. Although the diagnostic classification of PDD currently considers a diagnosis of concomitant ADHD to be an exclusion criterion, this may change in the DSM-5. In our study, 68 % of the ASD patients had one or more symptoms. This is in line with the results of other groups (Hofvander et al. 2009; Mattila et al. 2010), although others have reported even higher rates (Ehlers and Gillberg 1993), supporting the need for a thorough cognitive assessment of such patients in view of possible interventions.

Even in the absence of clinical depression, we observed depressive symptoms more frequently in our ASD patients than in the control sample (odds ratio > 11). As for anxiety, statistical significance was reached for “separation anxiety,” “agoraphobia and specific phobias,” and OCD, but also for anxiety when studied as a unique variable.

Depression and anxiety are common in people with autism, particularly in those with a higher IQ and during the transition from childhood to adulthood (Belinchón et al. 2008; Ghazziuddin and Zafar 2008; Mattila et al. 2010). The tendency for patients with ASD without mental retardation to become depressed or anxious may be partially explained by the fact that they are able to better acknowledge and communicate their feelings than those with low-functioning autism, making those symptoms easier to detect. In addition, their greater awareness of their own difficulties could make them more vulnerable to these symptoms. Furthermore, these patients are considered especially vulnerable to stress, owing to a highly restricted repertoire of coping mechanisms (Grodén et al. 2001). Anxiety could derive from comparisons with their peers and their difficulties coming to terms with a highly incomprehensible world. “School refusal” could also be related to this and also to maladjustment or bullying.

The greater presence of obsessive-compulsive symptoms in the ASD group than in controls must be emphasized. This difference was much more marked than in previous studies (Hofvander et al. 2009; Russell et al.

2005; Ruta et al. 2010), which also found a higher frequency of obsessive and compulsive symptoms in children with PDD than in those without PDD. However, the type of obsessions and behaviors reported in those studies in PDD seem to be different from those in OCD. Our study does not allow for such specific approximations, but again serves as a warning that, even in the absence of a comorbid disorder, the symptoms must be addressed.

We did not find symptoms of psychosis or eating disorders in this study. However, it is likely that the sample size was too small to detect such low-prevalence disorders.

As far as we know, this is the first study to explore the presence of psychopathology in children and adolescents with ASD without mental retardation but with no significant psychiatric comorbidity, using a clinician-administered interview. We must take into account the difficulties that these patients have in understanding and expressing their emotional states and the atypicality of their presentation (Paula-Perez and Martos-Perez 2009), which complicates detection. Some studies have verified the presence of psychiatric symptoms with self-administered screening questionnaires. However, there are few studies that have used a clinician-administered interview (Gjevik et al. 2011; Mattila et al. 2010) such as the K-SADS-PL. The study by Kanne et al. (2009) recorded a lower percentage of psychopathology than ours. In their study, approximately one-quarter of children/adolescents with PDD were reported by their parents to have significant mood difficulties and one-quarter to have significant symptoms of attentional and behavioral dysregulation, with fewer having significant symptoms associated with ODD (15 %) or conduct disorder (16 %). A clinician-administered interview used in both patients and parents, as in this study, detected higher rates of OCD, attention deficit disorder, and irritability in adolescents. The K-SADS-PL seems to be more sensitive in detecting psychiatric symptoms than self-administered questionnaires. The differences found between self-reported questionnaires and a clinician-administered instrument supports the difficulties that ASD without mental retardation have in acknowledging their own emotional experiences. Thus, in line with the previously mentioned studies, our results highlight the need for routine psychiatric evaluation in children and adolescents with ASD, in order to enable early and appropriate intervention. The absence of valid diagnostic instruments for the ASD population may also lead to under-recognition of serious conditions with critical repercussions on patient quality of life.

Limitations

The sample size of this study may have prevented us from establishing more differences. In fact, for most K-SADS-PL

items, we found a higher number of ASD patients than controls with threshold and subthreshold levels, many of them not reaching statistical significance (likely a type II error). The results of this study cannot be extrapolated to all child and adolescent ASD without mental retardation patients. Eighty percent of our sample was recruited in an outpatient psychiatric clinic, and therefore comorbid psychopathology is probably inflated with respect to a general population of ASD adolescents (entirely recruited at a Family Association). However, the profile of comorbid symptoms is fully valid, as are the high rates of symptoms.

Despite the fact that subtle differences in IQ were found between ASD patients and controls, they did not influence the results of the analyses.

The psychopathological assessment did not include all possible disorders, as we did not include symptoms of substance abuse or mania. Nevertheless, the sample size was large enough to differentiate between the two groups with respect to many of the assessed variables.

The validity of the questions posed in the K-SADS-PL for psychiatric symptoms in ASD should be tested. Given the difficulties with self-awareness and the oddities in the expression of feelings that ASD patients have, it is possible that specific questionnaires should be developed for assessing psychopathology in ASD patients.

Finally, most patients were male, which coincides with the epidemiological data on ASD in the general population (approximately 9 males for each female), but does not allow us to extrapolate the collected data to female children and adolescents with ASD, given the small size of our sample of girls.

Conclusion

In conclusion, we present a profile of subclinical disturbances in children and adolescents with ASD suggesting failures in multiple psychopathologic domains, stemming from the presence of subthreshold symptoms. This happens at a fundamental time of life, late childhood and adolescence, when development in different areas determines future condition in adulthood.

Our findings suggest the need not only to be alert to the presence of a categorical disorder (as recommended by previous studies) but also to be aware of all disturbances that could signal the disorders. The identification of subthreshold symptoms in a population that is already vulnerable due to social, communicational, and cognitive difficulties warrants assessment of the impairment associated with those symptoms and their amenability to specific treatment.

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