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## Mood symptoms in children and adolescents with autism spectrum disorders



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### ABSTRACT

Asperger Syndrome (AS) and High Functioning Autism (HFA) are psychiatric conditions belonging to the Autistic Spectrum Disorders (ASDs), characterized by social dysfunction and focused interest, in the absence of mental retardation. Previous reports suggest that AS/HFA may be associated with important psychiatric comorbidities. Among the psychiatric internalizing disorders, depression and anxiety are probably the most common disorders. The aim of this study is to evaluate the prevalence of mood disorders and identifying peculiar clinical features in subjects suffering from AS and HFA. 30 male patients with AS/HFA, 30 male patients affected by Major Depression (MD) and 35 male Typically Developing (TD) comparison were assessed with the CDI and the CDRS-R. Participants' parents were invited to complete the CBCL and the P-YMRS. Moreover, the CGAS was rated by the clinicians. The evaluation of depressive symptoms showed that AS/HFA group reported higher depressive symptoms, as showed by CDI total, CBCL internalizing and CDRS-R total, compared to the TD group. No significant difference of depressive symptoms was found between the AS/HFA and the MD group, with the exception of CDRS-R total score. Moreover, linear regression analysis in the AS/HFA group between CGAS and depressive symptoms revealed that a higher level of depressive symptoms increased the risk of poorer global functioning. These results suggest that the depressive symptoms in AS/HFA patients may be associated with poorer global functioning, with a consequent impairment in their psychological profile and social adjustment, and should alert clinicians to the importance of assessing mood disorders in order to choose the appropriate treatment.

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## 1. Introduction

Asperger Syndrome (AS) and High Functioning Autism (HFA) are two conditions that often overlap and are included in the category of the Autistic Spectrum Disorders (ASDs). However, recent studies on the classification of ASDs assume a difference between these two conditions. In fact, HFA is diagnosed when an individual meets the criteria for autism in the presence of normal intelligence quotient, whereas AS is defined in terms of the individual meeting the same criteria for autism but with no history of language delay (Baron-Cohen, Richler, Bisarya, Gurunathan, & Wheelwright, 2003; Spek, Scholte, & Van Berckelaer-Onnes, 2011).

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Previous studies suggest that patients with AS show a different Intelligence Quotient (IQ) profile, characterized by a higher mean total and verbal IQ, compared to HFA (Ghaziuddin & Mountain-Kimchi, 2004). Nevertheless, individuals suffering from AS or HFA seem to show similar characteristics of low levels of conversational behaviour and problems in prosody characterized by poor nonverbal communication, an excessive use of formal language style and pedantic speech (Ghaziuddin, 2008; Klin, Pauls, Schultz, & Volkmar, 2005; Paul, Miles Orlovski, Chuba Marcinko, & Volkman, 2009; Wing, 1981). Moreover, it is possible that the main differences between them may decrease with age producing a similar behavioural and cognitive pattern during adulthood (Howlin, 2003).

Furthermore, as a clinical distinction between these conditions is difficult and the debate about the clinical course is still open, the DSM-5 suggests a new classification (American Psychiatric Association, 2013). This incorporates previously separate diagnoses into a continuum of ASDs based on the severity of symptoms (American Psychiatric Association, 2013; Ghaziuddin, 2010).

Behavioural evidence to date suggests that the management of children and adolescents with AS/HFA is a challenge and that behavioural symptoms are often linked to psychiatric disorders in comorbidity (Green, Gilchrist, Burton, & Cox, 2000; Hedley & Young, 2006; Howlin, 1997; Kuusikko et al., 2008; Mazzone, Ruta, & Reale, 2012; Meyer, Mundy, Van Hecke, & Durocher, 2006; Mukaddes & Fateh, 2010; Munesue et al., 2008; Newman & Ghaziuddin, 2008; Pine, Guyer, Goldwin, Towbin, & Leibenluft, 2008; Simonoff et al., 2008; Tani et al., 2006; Volker et al., 2010; Ruta, Mugno, D'Arrigo, Vitiello, and Mazzone (2010). Previous reports have shown the presence of different types of psychiatric disorders in persons with AS/HFA and important associations have been found with both internalizing, such as depression, bipolar disorder, anxiety disorder, obsessive compulsive disorders, and externalizing disorders including attention deficit and hyperactivity disorder, disruptive behaviour and conduct disorder (Green et al., 2000; Hedley & Young, 2006; Howlin, 1997; Kuusikko et al., 2008; Mazzone et al., 2012; Meyer et al., 2006; Mukaddes & Fateh, 2010; Munesue et al., 2008; Newman & Ghaziuddin, 2008; Pine et al., 2008; Simonoff et al., 2008; Tani et al., 2006; Volker et al., 2010; Ruta, Mugno, D'Arrigo, Vitiello, and Mazzone 2010). In a recent study, evaluating depressive symptoms in 35 adolescents with AS, Whitehouse, Durkin, Jacquet, and Ziatas (2009) showed that around two-thirds of the patients scored 15 or above in the self-report questionnaire CES-DC (Centre for Epidemiological Studies Depression Scale-Children's Version) indicating significant depressive symptoms (Weissman, Orvaschel, & Padian, 1980; Whitehouse et al., 2009). Indeed, literature data show that, while depression can occur across the entire spectrum of autism, patients who are higher functioning seem to be particularly affected (Kim, Szatmari, Bryson, Streiner, & Wilson, 2000; Weissman et al., 1980; Whitehouse et al., 2009).

Several studies have investigated the relationship between IQ, autism symptoms and depression in ASDs. However, the results are still controversial (Barnhill, 2001; Bellini, 2004; Burnette et al., 2005; Cederlund, Hagberg, & Gillberg, 2010; Ghaziuddin, Weidmer-Mikhail, & Ghaziuddin, 1998; Kim et al., 2000; Sterling, Dawson, Estes, & Greenson, 2008; Strang et al., 2012; Sukhodolsky et al., 2008; Weisbrot, Gadow, DeVincent, & Pomeroy, 2005; Vickerstaff, Heriot, Wong, Lopes, & Dossetor, 2007). For instance, Mazurek and Kanne reported, in a sample of ASD patients, an increased risk for depression related to higher IQ and fewer autism symptoms, whereas Simonoff et al. (2012), in a longitudinal study on 79 patients with ASDs, showed that intellectual ability did not predict severe mood dysregulation and problems in these patients (Mazurek & Kanne, 2010; Simonoff et al., 2012).

Although the association with depression is one of the most common comorbidities found in these patients, some persons with AS also show mood swing that may be correlated with bipolar disorders. For example, Munesue et al. (2008) have shown that in 44 consecutive outpatients with HFA, 36.4% were diagnosed with mood disorders. Of these, bipolar disorder accounted for 75% of cases (Munesue et al., 2008).

Despite the fact that comorbidity with mood disorders has been widely studied, several issues remain unsolved in order to understand the manifestation of symptoms in these patients. In fact, in the clinical practice, it remains difficult to identify psychiatric symptoms because typical autistic problems, such as the lack of emotional empathy and the deficits in theory of mind, can mask the psychiatric disorders in comorbidity (Klin et al., 2005; Mazzone et al., 2012). Moreover, to date, there are no scales specifically designed to assess mood disorders in people with AS/HFA and previous studies on comorbidities in ASDs have used various psychometric instruments that have been standardized on the general population, therefore probably not appropriate for this clinical population. Finally, to our knowledge, no previous study has investigated the clinical phenotype of depressive symptoms between ASDs and patients with depressive disorders in order to understand if depressive symptoms in persons with ASDs could have a different clinical expression.

Thus, the objective of this study was to evaluate the prevalence of mood disorders in a sample of patients suffering from Asperger Syndrome and High Functioning Autism with the aim of identifying peculiar clinical features in depressive symptoms, compared to a group of depressive patients and a group of healthy comparison. Moreover, to test the validity of the instruments used to assess the presence of depressive symptoms in our sample of ASDs, we used different tools completed by multiple sources (i.e. children, parents and clinicians).

## 2. Materials and methods

### 2.1. Sample characteristics

Thirty male patients suffering from Asperger Syndrome ( $n = 20$ ) and High Functioning Autism ( $n = 10$ ) (AS/HFA) (age range 7–16 years; mean age  $\pm$  SD:  $11.06 \pm 2.59$ ), 30 male patients affected by Major Depression (MD) (age range 7–17 years;

mean age  $\pm$  SD:  $12.76 \pm 2.8$ ) and 35 male Typically Developing comparison (TD) (age range 7–16 years; mean age  $\pm$  SD:  $11.45 \pm 2.3$ ) were enrolled in this study. All the patients referred to the Child and Adolescent Neuropsychiatry Unit of the Children's Hospital Bambino Gesù of Rome (Italy). Participants were included in the AS/HFA group if they have been diagnosed within the spectrum of autistic conditions according to the DSM-IV-TR criteria by an experienced clinician, confirmed using the Autism Diagnostic Observation Schedule (ADOS-G) (American Psychiatric Association, 2000; Lord, Rutter, DiLavore, & Risi, 2000). Specifically, 4 patients completed the Module 2 (mean total score  $\pm$  SD:  $9 \pm 2.3$ ) and 26 patients completed the Module 3 (mean total score  $\pm$  SD:  $10 \pm 2.6$ ) of ADOS-G, respectively. Moreover, to be enrolled in the AS/HFA group they had to present a mean Full-Scale Intelligence Quotient (FSIQ)  $\geq 85$  evaluated by Wechsler Intelligence Scale for Children-III edition (WISC-III) (mean FSIQ  $\pm$  SD:  $117.72 \pm 17.10$ ) (Orsini & Picone, 1995; Wechsler, Golombok, & Rust, 1992).

Participants were included in the MD group if they have been diagnosed by an experienced clinician according to DSM-IV-TR depression criteria. Furthermore, major depression diagnoses were confirmed using the K-SADS-PL completed by all parents and patients with a trained clinician (Kaufman et al., 1997). An inter-rater reliability analysis using the Kappa statistic was performed to determine consistency among DSM-IV-TR criteria and ADOS-G diagnosis for AS/HFA children, and among DSM-IV-TR criteria and K-SADS-PL diagnosis for depressed patients, returning both an almost perfect agreement (MD group: Kappa = 0.913,  $p < .001$ ; AS/HFA group: Kappa = 0.814,  $p < .001$ ). Participants of the MD group were also evaluated throughout WISC-III (mean FSIQ  $\pm$  SD:  $100.89 \pm 16.66$ ) (Orsini & Picone, 1995; Wechsler et al., 1992) in order to exclude patients with an intellectual disability.

Participants included in the TD group were selected to match the AS/HFA and MD groups in terms of age. Moreover, these subjects were all reported by parents to have had typical development, never having received any clinical diagnoses or special education services.

In order to exclude the presence of autistic traits in the MD and in the TD groups, all the parents completed the Autism-Spectrum Quotient-Italian Version questionnaire (AQ) (version Child, 4–11 years, and Adolescent, 12–18 years). All the children and adolescents included in the MD and in the TD groups resulted out of the AQ cut-off ( $>76$  for the Child version and  $>30$  for the Adolescent version) (MD, mean AQ child version  $\pm$  SD:  $47.3 \pm 28.23$ ; mean AQ adolescent version  $\pm$  SD:  $24.5 \pm 2.12$ ; TD, mean AQ child version  $\pm$  SD:  $39.1 \pm 13.15$ ; mean AQ adolescent version  $\pm$  SD:  $15.3 \pm 2.61$ ) (Auyeung, Baron-Cohen, Wheelwright, & Allison, 2008; Baron-Cohen, Hoekstra, Knickmeyer, & Wheelwright, 2006; Ruta, Mazzone, Mazzone, Wheelwright, & Baron-Cohen, 2012).

Additionally, all the study participants completed the Multidimensional Anxiety Scale for Children (MASC) to eventually identify the presence of anxiety symptoms (March, 1997). Only three patients showed a pathological level ( $>75$ ) of anxiety symptoms (2 AS/HFA and 1 MD patients).

The participants parents who accepted to take part in the research signed a consent form and children and adolescents assented to participation.

## 2.2. Assessment of mood disorders

All participants and their parents completed a battery of psychological tools for a comprehensive evaluation of mood disorders with an experienced and trained clinician.

The Italian version of Children's Depression Inventory (CDI) was used to rate depression symptoms (Frigerio, Pesenti, Molteni, Snider, & Battaglia, 2001; Kovacs, 1982, 1988). The CDI is a self-rating scale broadly used to assess depressive symptomatology in children and adolescents aged 7–17 years, with an excellent reliability of 0.87, as measured by Cronbach's  $\alpha$ . This scale consists of 27 items scored on a three-point scale indicating increasing severity of symptoms. According to the Italian validation criteria, 19-point cut-off indicates the ideal threshold for a child at risk of depression (Frigerio et al., 2001; Kovacs, 1982, 1988).

Depression symptoms were also investigated using the Children's Depression Rating Scale-Revised (CDRS-R) (Poznanski & Mokros, 1996). The CDRS-R is a clinician administered scale for rating the severity of depressive symptoms. The measure contains 17 items assessing somatic, cognitive, affective, and psychomotor symptoms, and draws on the respondent's responses and the behavioural observations of the interviewer. It is administered separately to the child and, if necessary, to an adult informant. The items rated cover schoolwork, social withdrawal, capacity to have fun, appetite, sleep, irritability, physical complaints, guilt, self-esteem, depressed feelings, suicidal ideation, morbid thoughts, weeping, and non-verbal items such as tempo of speech, depressed affect, and hypoactivity. A rating of 5 or higher indicates definite abnormal symptoms and a total of  $\geq 40$  is a risk indicator of depression. Good psychometric properties have been reported from the age group between 6 and 12 years (Cronbach's  $\alpha = 0.85$ ) (Poznanski & Mokros, 1996). Indeed, several recent studies have established the psychometric properties of the scale in the adolescent and adult age groups reporting an excellent internal consistency of Cronbach's  $\alpha$  ranging between 0.79 and 0.92 (Gibbons, Brown, Hur, Davis, & Mann, 2012; Mayes, Bernstein, Haley, Kennard, & Emslie, 2010; Tzilos, Zlotnick, Raker, Kuo, & Phipps, 2012).

The Parent-Young Mania Rating Scale (P-YMRS) was used to assess the presence and the severity of manic symptoms (Gracious, Youngstrom, Findling, & Calabrese, 2002; Young, Biggs, Ziegler, & Meyer, 1978).

The P-YMRS is a parent-report rating scale for children and adolescents between the ages of 5 and 17. It consists of eleven multiple-choice questions scored from 0 to 8 that parents are asked about the present state of their children. Items assess the following areas: elevated mood, increased motor activity/energy, sexual interest, sleep, irritability, speech (rate and amount), language (thought disorder), thought content, disruptive-aggressive behaviour, appearance, and insight. The

child's total score is determined by adding up the highest number circled on each question. Scores range from 0 to 60 and higher scores indicate greater symptom severity (Gracious et al., 2002). To our knowledge there are no studies that examined the psychometric properties of P-YMRS among children and adolescents with ASDs. In our study population, we used the cut-off scores of 17 for the probable mania group, and 27 for the mania group, on the P-YMRS total, which were defined as efficient and specific for the presence of manic symptoms in typically developing children and adolescents (Youngstrom, Gracious, Danielson, Findling, & Calabrese, 2003).

### 2.3. Evaluation of behavioural problems and global functioning

The Italian version of the Child Behaviour Checklist (CBCL) was used to rate children and adolescents' behavioural and emotional problems (Achenbach & Eofbrock, 1983). The CBCL is a 113-item questionnaire completed by parents on their perception of their child's behaviour. It provides scores for three broad-band scales: internalizing symptoms, externalizing symptoms and total behavioural problems. Sub-items of these three broad-band scales include eight syndrome scales. Raw scores for each clinical factor were transformed into T-scores based on published norms: T-scores > 63 were considered indicative of clinical impairment for the three broad-band scales, whereas T-scores  $\geq 70$  were considered indicative of clinical impairment for syndrome scales (Achenbach & Eofbrock, 1983). The psychometric properties of the CBCL show good validity and reliability (Frigerio et al., 2004, 2009).

In order to eventually identify the presence of anxiety symptoms, all the children and adolescents included in the study completed the Multidimensional Anxiety Scale for Children (MASC) (March, 1997). The MASC is a 39-item four point Likert-style self-report scale which is comprised of four subscales measuring physical symptoms, social anxiety, harm avoidance and separation anxiety. Raw scores were converted into standard T-scores, and a T-score >75 indicated the presence of anxiety symptoms. The MASC has been shown to have good internal consistency ( $\alpha = 0.60$  to  $\alpha = 0.85$ ) and high test-retest reliability ( $r = 0.79$  to  $r = 0.93$ ) (Frigerio et al., 2009; Mazzone, Vitiello, Incorpora, & Mazzone, 2006; Mazzone et al., 2007).

Moreover, in order to assess the presence of autistic traits in the MD and TD groups the parents of these children and adolescents completed the Autism-Spectrum Quotient-Italian Version questionnaire (AQ) (Auyeung et al., 2008; Baron-Cohen et al., 2006; Ruta et al., 2012). The AQ is a parent self-administered questionnaire used in both clinical and non-clinical samples that quantifies the number of autistic traits an individual possesses across five domains: social skill, attention switching, attention to detail, communication and imagination. It consists of two versions divided by age: a version for children from 4 to 11 years and a version for adolescents from 12 to 18 years. The AQ showed good test-retest reliability and high internal consistency.

Finally, all the children were evaluated by an experienced clinician on their global functioning using the Children's Global Assessment Scale (CGAS) (Shaffer et al., 1983). The CGAS is a numeric scale ranging from 1 (serious impairment) to 100 (superior functioning) that provides a global measure of level of functioning based on psychological, social and school/academic mental health of the subjects. In making their rating, the clinician use the glossary to determine the meaning of the points on the scale.

### 2.4. Data analysis

Data analysis were performed using the Statistical Package for Social Sciences (SPSS 16.0 for Windows). Inter-rater reliability analysis using the Kappa statistic were performed to determine consistency among DSM-IV-TR criteria and K-SADS-PL diagnosis, as well as among DSM-IV-TR criteria and ADOS-G diagnosis. Chi-square analysis were used for dichotomous variables and one-way ANOVA with Bonferroni post hoc comparisons were applied to continuous variables. Prevalence rates of mood symptoms were calculated on the total number of children assessed and on each of the three groups. Individual z-scores were considered as a measure of dispersion. Moreover, Pearson's  $r$  correlations and linear regression models were performed to the data in order to evaluate the association between clinical symptoms, behavioural and emotional problems, cognitive variables, global functioning and age. An alpha level of 0.05 was set for statistical significance.

## 3. Results

### 3.1. Participants' mood, behavioural problems and global functioning differences

Evaluating depressive symptoms by CDI self-report questionnaire, variance analysis indicated a significant difference in CDI total score ( $p < .001$ ) among the three groups. Particularly, the TD group showed lower mean scores in the CDI total score (mean  $\pm$  SD:  $7.29 \pm 3.883$ ) as compared to the AS/HFA group (mean  $\pm$  SD:  $12.33 \pm 7.373$ ) and the MD group (mean  $\pm$  SD:  $13.93 \pm 6.486$ ). Similarly, there was a significant difference on CDRS-R total score ( $p < .001$ ) among the three groups. Specifically, the TD group showed lower mean scores in the CDRS-R total score (mean  $\pm$  SD:  $36.64 \pm 4.845$ ) as compared to the AS/HFA group (mean  $\pm$  SD:  $50.36 \pm 8.445$ ) and the MD group (mean  $\pm$  SD:  $61.89 \pm 9.763$ ). Moreover, MD patients scored significantly higher in CDRS-R total score as compared to the AS/HFA group (mean  $\pm$  SD:  $61.89 \pm 9.763$  vs  $50.36 \pm 8.445$ ,  $p = .001$ ).

Differences on manic symptoms evaluated by P-YMRS questionnaire among the three groups revealed a significant difference in P-YMRS total score ( $p = .026$ ). The TD group showed lower mean scores on P-YMRS total score (mean  $\pm$  SD:  $6.61 \pm 5.696$ ) as compared to the MD group (mean  $\pm$  SD:  $9.013 \pm 2.186$ ). However, the TD group analyzed in contrast to the AS/HFA patients failed to reach statistical significance (mean  $\pm$  SD:  $10.14 \pm 6.964$ ).

Rating child behavioural and emotional problems a significant difference among the three groups was detected on CBCL total subscale ( $p < .001$ ) as well as internalizing ( $p < .001$ ) and externalizing ( $p < .001$ ) CBCL subscales. In more detail, the parents of AS/HFA and MD patients referred a larger degree of impairment on CBCL total (AS/HFA, mean  $\pm$  SD: 61.76  $\pm$  10.605; MD, mean  $\pm$  SD: 66.40  $\pm$  10.611) and along the CBCL internalizing (AS/HFA, mean  $\pm$  SD: 64.34  $\pm$  9.908; MD, mean  $\pm$  SD: 68.52  $\pm$  10.389) and CBCL externalizing (AS/HFA, mean  $\pm$  SD: 56.31  $\pm$  8.792; MD, mean  $\pm$  SD: 61.84  $\pm$  11.611) subscales compared to parents of TD subjects (CBCL total, mean  $\pm$  SD: 46.66  $\pm$  8.174; CBCL internalizing, mean  $\pm$  SD: 49.06  $\pm$  10.613; CBCL externalizing, mean  $\pm$  SD: 46.60  $\pm$  8.589).

Moreover, evaluation of anxiety symptoms showed a significant difference among the three groups on the MASC total score ( $p = .022$ ). Specifically, TD group reported lower mean score on MASC total score (mean  $\pm$  SD: 48.94  $\pm$  8.663) as compared to the AS/HFA group (mean  $\pm$  SD: 56.37  $\pm$  11.898), although failed to reach statistical significance in contrast to MD patients (mean  $\pm$  SD: 52.73  $\pm$  11.166).

Finally, clinical global functioning evaluation reported a significant difference among the three groups as shown by CGAS scores ( $p < .001$ ). In particular, clinicians detected a lower global functioning in AS/HFA (mean  $\pm$  SD: 64.17  $\pm$  10.339) and MD (mean  $\pm$  SD: 55.67  $\pm$  12.046) patients compared to TD subjects (mean  $\pm$  SD: 88.89  $\pm$  2.246). Furthermore, MD patients scored significantly lower in CGAS scores as compared to the AS/HFA group ( $p = .018$ ).

Multiple comparisons of the clinical characteristics in the three groups are provided in Table 1.

### 3.2. Prevalence and measure of variability of mood symptoms

The prevalence rates of mood symptoms were calculated using assessment tools cut-off basing on the established norms. Accordingly on the total number of children assessed, the presence of CBCL internalizing symptoms was reported in 18.9% ( $n = 18$ ) of the AS/HFA group, in 18.9% ( $n = 18$ ) of the MD group and in 3.1% ( $n = 3$ ) of the TD group. CDI total symptoms were detected in 8.4% ( $n = 8$ ) of the AS/HFA group, in 6.3% ( $n = 6$ ) of the MD group, in 0% ( $n = 0$ ) of the TD group, and CDRS-R total symptoms in 26.3% ( $n = 25$ ) of the AS/HFA group, in 31.5% ( $n = 30$ ) of the MD group and in 8.4% ( $n = 8$ ) of the TD group. Moreover, the presence of P-YMRS total symptoms was observed in 8.4% ( $n = 8$ ) of the AS/HFA group, in 5.2% ( $n = 5$ ) of the MD group and in 2.1% ( $n = 2$ ) of the TD group.

On the other hand, the presence of mood symptoms in the AS/HFA group was: 60% for CBCL internalizing subscale, 26.6% for CDI total score, 83.3% for CDRS-R total score and 26.6% for P-YMRS total score. Prevalence of mood symptoms in the MD group was: 60% for CBCL internalizing subscale, 20% for CDI total score, 100% for CDRS-R total score and 16.6% for P-YMRS total score. Finally, the presence of mood symptoms in the TD group was: 8.5% for CBCL internalizing subscale, 0% for CDI total score, 22.8% for CDRS-R total score and 5.7% for P-YMRS total score. As a measure of dispersion, the score of each participant was transformed in z-score basing on the mean score and the standard deviation of the three groups on each measure (CBCL internalizing subscale, CDI total score, CDRS-R total score and P-YMRS total score) (Fig. 1). The proportion of participants who showed a score above the mean ( $>1$  SD) on the CBCL internalizing subscale was 20% of the AS/HFA, 21.05% of the MD and 6.31% of the TD, whereas 7.36% of the TD resulted below the mean ( $<1$  SD). On the other hand, the proportion of participants who had a score below or above the mean on CDI total score was 20% of the AS/HFA, 21.05% of the MD and 8.42% of the TD. Relating to the CDRS-R total score, the proportion of participants who showed a score more than 1 SD from

**Table 1**  
Multiple comparisons of the clinical characteristics of the three groups (mean  $\pm$  SD).

	AS/HFA <sup>a</sup> group (N = 30)	MD <sup>b</sup> group (N = 30)	TD <sup>c</sup> group (N = 35)	ANOVA		Pairwise contrasts  * $p < .05$ ; ** $p < .01$ ; *** $p < .001$
				F	$p^d$	
CDI total <sup>e</sup>	12.33 $\pm$ 7.373	13.93 $\pm$ 6.486	7.29 $\pm$ 3.883	9.971	<.001	AS/HFA > *TD; MD > ***TD; AS/HFA = MD
CDRS-R total <sup>f</sup>	50.36 $\pm$ 8.445	61.89 $\pm$ 9.763	36.64 $\pm$ 4.845	38.405	<.001	AS/HFA > ***TD; MD > ***TD; MD > **AS/HFA
P-YMRS total <sup>g</sup>	10.14 $\pm$ 6.964	9.013 $\pm$ 2.186	6.61 $\pm$ 5.696	3.840	<.05	AS/HFA = TD; MD > *TD; AS/HFA = MD
CBCL total <sup>h</sup>	61.76 $\pm$ 10.605	66.40 $\pm$ 10.611	46.66 $\pm$ 8.174	34.982	<.001	AS/HFA > ***TD; MD > ***TD; AS/HFA = MD
CBCL int <sup>i</sup>	64.34 $\pm$ 9.908	68.52 $\pm$ 10.389	49.06 $\pm$ 10.613	30.632	<.001	AS/HFA > ***TD; MD > ***TD; AS/HFA = MD
CBCL ext <sup>i</sup>	56.31 $\pm$ 8.792	61.84 $\pm$ 11.611	46.60 $\pm$ 8.589	19.618	<.001	AS/HFA > ***TD; MD > ***TD; AS/HFA = MD
MASC total <sup>m</sup>	56.37 $\pm$ 11.898	52.73 $\pm$ 11.166	48.94 $\pm$ 8.663	3.999	<.05	AS/HFA > *TD; MD = TD; AS/HFA = MD
CGAS <sup>n</sup>	64.17 $\pm$ 10.339	55.67 $\pm$ 12.046	88.89 $\pm$ 2.246	60.290	<.001	AS/HFA > ***TD; MD > ***TD; MD > *AS/HFA

<sup>a</sup> Asperger and High Functioning Autism group.

<sup>b</sup> Major Depression group.

<sup>c</sup> Typically Developing group.

<sup>d</sup> Bonferroni correction was applied by multiplying the  $p$  by the number of comparisons.

<sup>e</sup> Children Depression Inventory total score.

<sup>f</sup> Children Depression Rating Scale-Revised total score.

<sup>g</sup> Parent-Young Mania Rating Scale total score.

<sup>h</sup> Child Behavior Checklist total score (T-Score).

<sup>i</sup> Child Behavior Checklist internalizing score (T-Score).

<sup>l</sup> Child Behavior Checklist externalizing score (T-Score).

<sup>m</sup> Multidimensional Anxiety Scale for Children total score.

<sup>n</sup> Children Global Assessment Scale.

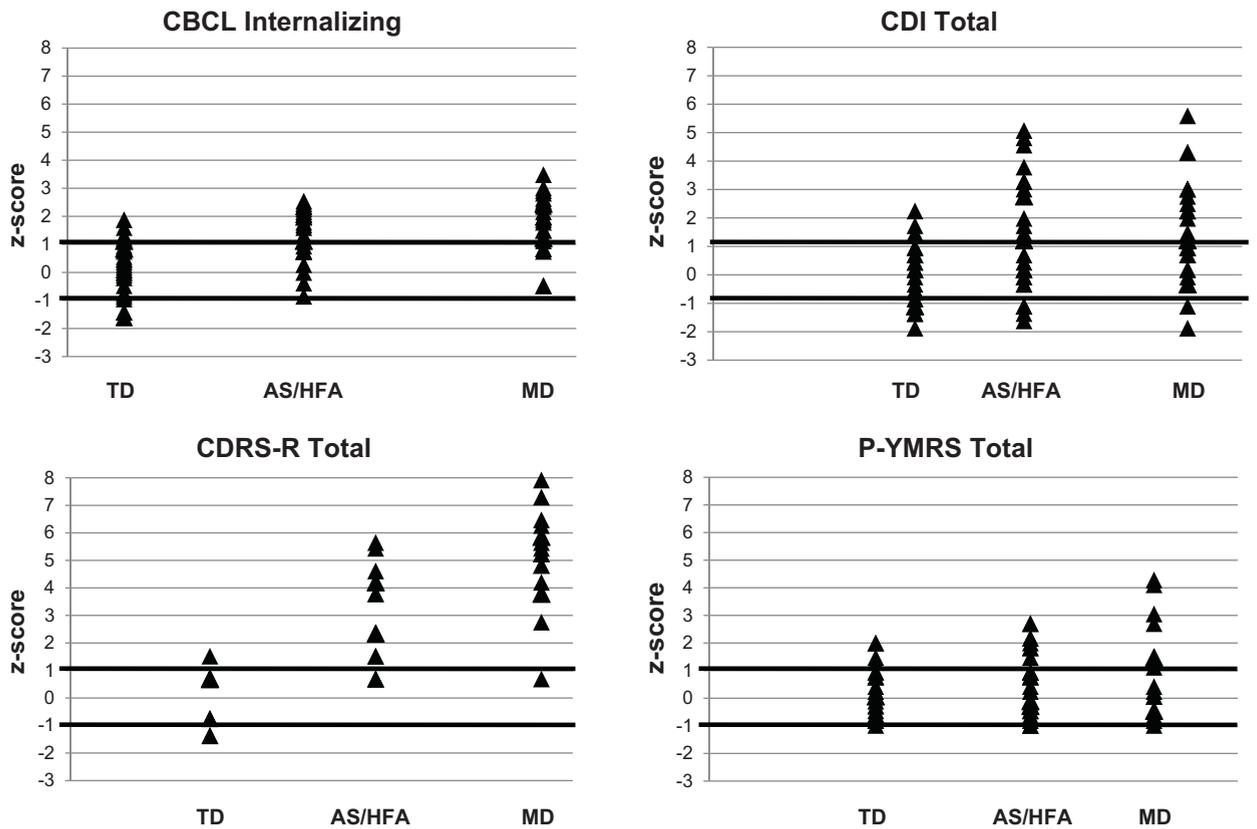


Fig. 1. Distribution of the scores of each participant of the three groups on mood symptoms measures.

the mean was 23.15% of the AS/HFA and 29.47% of the MD compared to 8.42% of the TD. Moreover, only the 6.31% of the TD participants reported a score below 1 SD from the mean on the CDRS-R total score. Finally, on the P-YMRS total score the 9.47% of the AS/HFA and the MD patients showed a score above the mean (>1 SD) compared to 5.26% of the TD group.

3.3. Symptoms severity and age

Analysis using linear regression models were performed to determine, in the AS/HFA group, the relationship between age and symptom severity (Fig. 2). Age was found to be significantly and positively associated with the subscale internalizing of

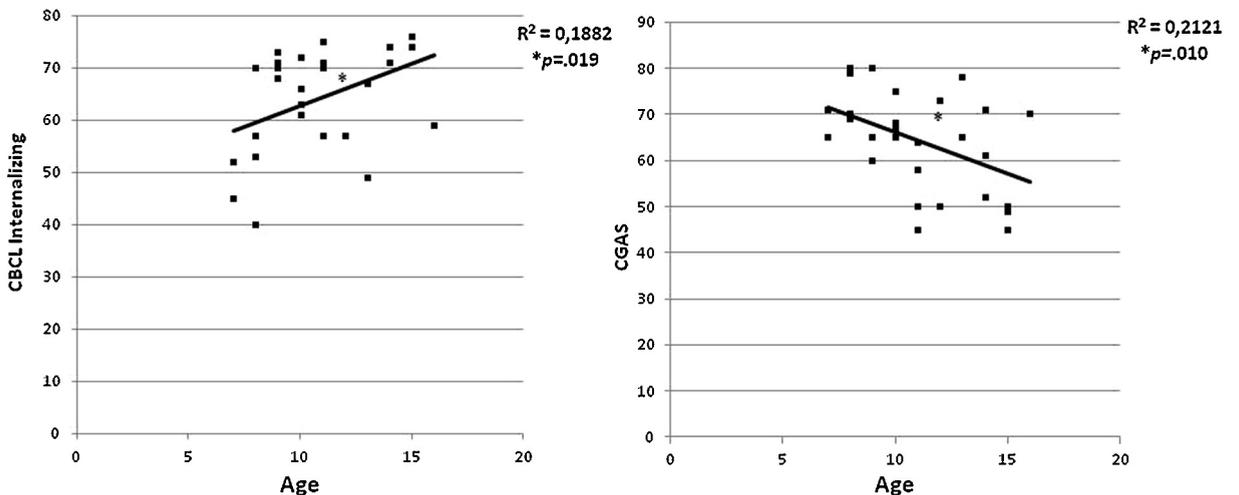


Fig. 2. Symptoms severity across age in AS/HFA group.

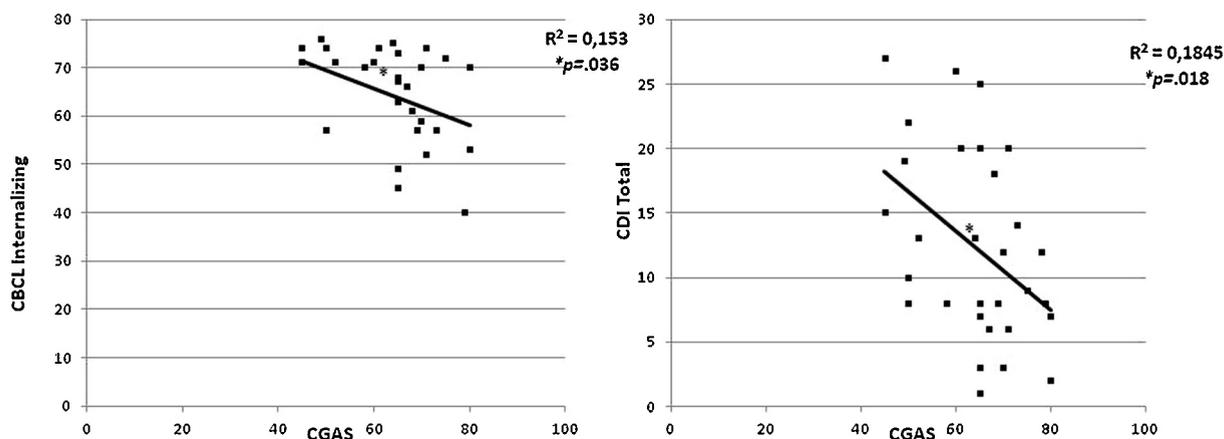


Fig. 3. Relationship between severity of depressive symptoms and global functioning in AS/HFA group.

the CBCL ( $R^2 = 0.188$ ,  $p = .019$ ), and negatively associated with CGAS ( $R^2 = 0.212$ ,  $p = .010$ ). There was no significant association between age and other assessment tools utilized to rate mood symptoms or with the IQ.

#### 3.4. Relation between depressive symptoms, behavioural problems and global functioning

Analysis using linear regression models were performed to determine the relationship between behavioural problems, severity of depressive symptoms and global functioning in the AS/HFA group. Particularly, there was a significant positive association between the CDI total score and the CBCL total subscale ( $R^2 = 0.300$ ,  $p = .002$ ), the CBCL internalizing subscale ( $R^2 = 0.287$ ,  $p = .003$ ), and the MASC total score ( $R^2 = 0.536$ ,  $p = .002$ ), and between CBCL externalizing subscale and P-YMRS total score ( $R^2 = 0.382$ ,  $p < .001$ ).

Moreover, analysis on the relationship between severity of depressive symptoms and global functioning revealed that CGAS was significantly and negatively associated with CBCL internalizing subscale ( $R^2 = 0.153$ ,  $p = .036$ ), and with CDI total score ( $R^2 = 0.1845$ ,  $p = .018$ ) and CDRS-R total score ( $R^2 = 0.303$ ,  $p = .041$ ), meaning that the presence of more depressive symptoms increased the risk of poorer global functioning in patients suffering from AS/HFA (Fig. 3). There was no significant association between IQ and mood symptoms, behavioural problems, or global functioning.

## 4. Discussion

The management of psychiatric comorbidities in patients with AS/HFA is a challenge for clinicians and families. Recognizing psychiatric disorders is often difficult in these patients because psychopathologic symptoms may be masked by those typical of AS/HFA (Mazzone et al., 2012). Previous reports have investigated the relationship between AS/HFA and psychiatric comorbidities showing that depressive symptoms are often associated with autistic symptoms (Barnhill, 2001; Kim et al., 2000; Mazzone et al., 2012; Meyer et al., 2006; Volker et al., 2010; Weissman et al., 1980; Whitehouse et al., 2009). In our study the self-ratings and the other informants' ratings accounted significantly more depressive symptoms in patients with AS/HFA than in controls. In more detail, our results showed that AS/HFA patients reported higher scores than TD subjects in different clusters of scales or questionnaires investigating depressive symptoms (i.e. CDI, CDRS-R and CBCL) by a multi-setting assessment. Specifically, AS/HFA patients reported a prevalence of depressive symptoms ranging from 8.4% to 26.3% of our total sample, depending on the tool used to evaluate the symptoms. These findings are consistent with the results of other reports detailing the incidence and prevalence of depression in AS and HFA patients (Ghaziuddin et al., 1998; Kim et al., 2000; Larsen & Mouridsen, 1997; Tantam, 1991).

Moreover, in order to shed light on the peculiar clinical phenomenology of depressive symptoms in persons with autism we seek to understand if a clinical overlapping was detected in MD patients. Of the scales used in our study, only one (CDRS-R total score) showed a significant statistical difference between AS/HFA and MD patients. Furthermore, the proportion of AS/HFA and MD patients who reported a score above the mean on the tools used to detect depressive symptoms was similar between the two groups. Therefore, the interpretation of this result highlights the pattern of mood profiles in autistic persons which reveal a trend of low mood symptoms, exceeding those in the general population.

Recent studies on the relationship between depressive symptoms and IQ in ASD patients have shown contrasting results (Barnhill, 2001; Bellini, 2004; Burnette et al., 2005; Cederlund et al., 2010; Ghaziuddin et al., 1998; Kim et al., 2000; Mazurek & Kanne, 2010; Simonoff et al., 2012; Strang et al., 2012; Sterling et al., 2008; Sukhodolsky et al., 2008; Weisbrot et al., 2005; Vickerstaff et al., 2007). Confirming previous studies reporting that intellectual abilities were not related to greater depressive symptoms (Simonoff et al., 2012; Cederlund et al., 2010), in our population the severity of depressive symptoms was not phenomenologically related to IQ.

We detected a negative association between the presence of depressive symptoms and the global functioning in AS/HFA patients, so that an increase of depressive comorbid symptoms in these patients may be associated with poorer global functioning, with a consequent impairment in their psychological profile and social adjustment (Mattila et al., 2010; Mugno, Ruta, D'Arrigo, & Mazzone, 2007). Furthermore, a positive association between age and CBCL internalizing subscale and a negative relationship with the CGAS scores were also found, suggesting that depressive symptoms and global functioning change along with age (Fig. 2).

In our evaluation we also observed a significant difference of externalizing symptoms, as showed by CBCL externalizing subscale, in patients with AS/HFA compared to normal control subjects. As before, no statistically significant difference was found between AS/HFA and MD patients. In line with other studies that reported externalizing symptoms in patients with depression during childhood, we could also look at our observation as a manifestation of mood dysregulation or depressive symptoms (Ehrenreich-May et al., 2010). Furthermore, other reports detected that an exacerbation of maladaptive behaviours with self-injury, hyperactivity and aggression could be associated with depression in ASDs (Clark, Feehan, Tinlin, & Vostanis, 1999; Cooke & Thompson, 1998). Another study reported an increase of oppositional behaviours correlated with depression (Kim et al., 2000). These findings support the idea that symptoms of depression could occur in AS/HFA and that these symptoms could have a different cluster of presentation.

Besides these significant results, the present study has to be understood in the context of ASDs. Because of this issue, the interpretation could be a challenge for several reasons. The first important limitation regards the core symptoms of ASDs that often mask the symptoms in comorbidity. Another limitation is related to the fact that our study is cross-sectional: to understand the developmental changes and to clarify the clinical phenotypic manifestation across the lifespan we need longitudinal studies (Mazzone & Curatolo, 2010). The sample was clinically referred and not intended to be representative of children with ASDs in the general population. Finally, as we pointed out in our previous paper (Mazzone et al., 2012) in the clinical practice, diagnostic tools, such as clinical interviews, self-report questionnaires and checklists, have been designed and standardized to investigate different clusters of psychopathological symptoms referring to the general population and they may not be appropriate for AS/HFA. However, to reduce the discrepancy in the results due to this limitation we used a multi-setting assessment. To point out is that our assessment tools were widely used in previous studies, but not all together in the same study.

## 5. Conclusion

Further research should better understand the clinical phenomenology in AS/HFA and the characteristics of mood disorders in these patients in order to clarify the natural developing patterns.

The recognition of psychiatric symptoms in comorbidity is also a crucial point for the treatment strategies of these patients. Finally, the identification and attribution of overlapping symptoms, either to the comorbid disorder or to the AS/HFA itself, may contribute to the choice of the more appropriate behavioural or pharmacologic therapy.

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## Conflict of interest

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