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Mood symptoms and suicidality across the autism spectrum

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ABSTRACT

Background: Autism spectrum is a psychopathological dimension which encompasses a wide range of clinical presentations: from subthreshold forms and autistic traits (AT), that can be found in the general population, to full-blown autism spectrum disorder (ASD). Many studies reported high rates of comorbidity between both ASD and AT and mood disorders, as well as a high prevalence of suicidal ideation among patients with ASD/AT. The aim of this study was to investigate the presence of mood symptoms and suicidal ideation and behaviors in patients with full-blown ASD and in subjects with AT, as well in a healthy control (HC) group, with a specific focus on which of the autistic features may be predictive of suicidal ideation and behaviors.

Methods: We recruited 262 adult subjects: 34 with ASD without intellectual impairment or language disability (ASD group), 68 fulfilling only one symptom criterion for ASD according to DSM-5 but who do not meet criteria for a full-blown diagnosis of ASD (AT group), and 160 HC. All subjects were assessed with the Structured Clinical Interview for DSM-5 (SCID-5); in addition, they were asked to fill two questionnaires: The Mood Spectrum, Self-report (MOODS-SR) and the Adult Autism Subthreshold Spectrum (AdAS Spectrum).

Results: ASD subjects reported significantly higher AdAS Spectrum and MOODS-SR total scores, as well as higher MOODS-SR depressive component total scores, when compared with AT and HC subjects. AT subjects scored significantly higher than the HC group. No significant differences were reported between ASD and AT subjects for the suicidality score according to MOODS-SR, despite both groups scored significantly higher than the HC group. The strongest predictor of suicidality score were MOODS-SR depressive component score and AdAS Spectrum *Restricted interests and rumination* domain score.

Conclusions: Our results highlight a correlation between autism and mood spectrum, as well as between suicidality and both ASD and AT. Subthreshold forms of ASD should be accurately investigated due to their relationship with suicidal thoughts and behaviors.

1. Introduction

Autism spectrum disorder (ASD) is a condition characterized by an impairment of verbal and non-verbal communication and a pattern of narrow interests and repetitive and stereotyped behaviors [1]. Although the etiology of ASD remains unclear, it is a highly heritable condition, with a strong genetic influence as well as a putative role of intrauterine environment [2,3]. For several decades, due to the early onset of the disorder, both clinical and research attention has mainly focused on investigating ASD in childhood, while in recent years an increasing number of studies is stressing how some subjects with mild forms of ASD might come to clinical attention only in adulthood, often at the same time when they develop other mental disorders such as mood, anxiety or trauma-related disorders [4–10]. Such a knowledge propelled new interest towards ASD symptoms in adults, as well as towards subthreshold forms of ASD. In particular, the relevance of subthreshold autism spectrum lies in the fact that, according to a wide number of studies, not only full-blown ASD, but also milder presentations or even subthreshold autistic traits (AT) might actually interfere with overall functioning, representing a significant risk factor for developing other psychiatric disorders, as well as suicidal ideation [6,11,12]. Although subthreshold ASD manifestations have been originally investigated among first degree relatives of ASD patients, where they are known with the label of broad autism phenotype, it has been shown that AT may be found also among clinical samples of patients with other mental disorders [7,12–15]. AT are also largely distributed among high-risk groups from general population, such as university students [16–22], who also display a high prevalence of social anxiety, a condition

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frequently associated to ASD, in particular among females, to substance use disorders and to mood disorders (MD) [23–31].

In the last two decades, some literature has especially focused on the relationship between ASD and MD, with an increasing number of studies highlighting common neurobiological and genetic underpinnings as well as high levels of comorbidity between these two conditions [32–34]. Among the latters, Hofvander et al. [35] pointed out a significant prevalence of MD among patients with a diagnosis of ASD (52% among subjects with Asperger's disorder and 60% among subjects with Autistic disorder), while Takara & Kondo [6] reported a high prevalence of ASD (16%) among first-visit adult patients requesting help for depressive symptoms. These data are corroborated by an increasing number of studies highlighting also a significant relationship between MD and AT [36–41]. The first study investigating AT and MD in adults was conducted by Matsuo et al. [40]. These authors reported that subjects with a diagnosis of major depressive disorder (MDD), bipolar disorder (BD) or schizophrenia showed higher AT compared to general population. More recently, Abu-Akel et al. [42] reported a prevalence of 47.2% of AT in a sample of 797 patients with bipolar I disorder (BD I). Borue et al. [43] found also, in a sample of youth with BD, that subjects with a comorbid ASD showed an earlier onset, a more frequent presence of mixed symptoms and further functional impairment. In this framework, authors also stressed the specific relationship between ASD and suicidal ideation/behaviors, focusing in particular on mild or high-functioning ASD presentations. Raja et al. [44] reported a higher prevalence of suicidal behaviors among patients with ASD attending psychiatric services for adults, while Kato et al. [4] reported a 7.3% rate of previously undiagnosed ASD among subjects with a history of suicidal attempts. Cassidy et al. [45] identified an increased rate of suicidal ideation in adults with Asperger's disorder, reporting also MD as a significant risk factor among adults with this condition. Another study [6] aimed also to examine whether ASD was a risk factor for suicide attempts among depressed adult patients: results from this sample reported a greater risk for suicide attempts, and for the employment of more lethal methods, among subject with ASD in comorbidity. In literature, a significant correlation between AT and suicidal thoughts and behaviors has also been reported, in both clinical and non clinical populations [6,11,12,14]. Pelton and Cassidy [11], in particular, highlighted also that burdensomeness and thwarted belonging seem to mediate the relationship between AT and suicidal behaviors among general population. In light of previous literature, the aim of this study was to evaluate mood spectrum symptoms and suicidal ideation and behaviors in a sample composed by a group of adult subjects with full-blown ASD and a group of adults with significant levels of AT and a healthy control (HC) group, with a specific focus on which of the autistic features may be predictive of suicidal ideation and behaviors. In line with previous studies which reported, as stated above, a relationship between ASD and AT respectively and MD, we hypothesize to find also a higher prevalence of the broad spectrum of mood symptoms in subjects with AT as well as in full-blown ASD patients, broadening the link between the dimensions of autism and mood spectrums. Moreover, although previous literature reports a higher prevalence of suicidal thoughts and behaviors not only among ASD patients, but also among subjects with high AT, no studies so far have explored whether differences in prevalence and severity of suicidal ideation and behaviors exist between these two groups. The specific interest in comparing ASD and AT subjects lies in the fact that, while previous literature recognized a transnosographic presence of the autism spectrum (both AT and ASD) in other clinical conditions, as well as the relevance of AT as a risk factor for developing psychiatric disorders [13], what is still unclear is whether an increase in autistic symptomatology, both under and over threshold, may be proportionally related to an increase also of comorbid symptomatology and of the severity of clinical correlates, such as suicidal ideation and behaviors. Our hypothesis is that subjects with AT and ASD will both show a higher prevalence of suicidal ideation and behaviors when compared with HC. In particular, we aim to clarify if AT do actually imply a risk factor for suicidality similar to full-blown ASD, hypothesizing that suicidal thoughts and behaviors will not differ between subjects with subthreshold autism and full-blown ASD.

2. Methods

2.1. Sample recruitment and assessment

We recruited a total of 262 subjects: 34 patients with ASD, 68 subjects with AT and 160 HC. The first group consisted of 34 adults with ASD with no intellectual or language impairment according to DSM-5 criteria, consecutively enrolled from a treatment program for autism (ASD group). The second group included 68 adult subjects that endorsed one out of two symptom criteria for ASD according to DSM-5, therefore not meeting criteria for a full-blown diagnosis of ASD (AT group). Subjects in this group were recruited among students attending three Italian universities of excellence ("Scuola Superiore di Catania" in Catania, "Collegio Universitario di Merito" in Pavia, "Scuola Superiore Sant'Anna" in Pisa). The third group was composed by 160 HC (subjects with no mental disorders according to SCID-5 and who do not fulfill any criteria for ASD, recruited on a voluntary basis). Subjects were enrolled and assessed between May 2015 and April 2016 at four university departments of psychiatry (Pisa, Napoli, Catania, Pavia).

All subjects who agreed to participate were administered the Structured Clinical Interview for DSM-5 (SCID-5) to evaluate the presence of mental disorders according to DSM-5 criteria [46]. In addition, participants were asked to fulfill the lifetime version of the Mood Spectrum Self Report (MOODS-SR) and the Adult Autism Subthreshold Spectrum (AdAS Spectrum). All participants received clear information about the study and had the opportunity to ask questions before they provided a written informed consent. The study was conducted in accordance with the declaration of Helsinki and the ethics committee of the Azienda Ospedaliero-Universitaria of Pisa approved all recruitment and assessment procedures.

2.2. Measures

2.2.1. The Mood Spectrum, self-report (MOODS-SR, lifetime version)

The MOODS-SR is an instrument composed by 161-items, developed with the aim to assess the broad spectrum of mood symptoms, including suicidal ideation and behaviors, across the lifetime. As a dimensional instrument, it allows to identify also mild and subthreshold manifestations, that may feature subclinical prodromal, residual or atypical clinical pictures. Items are grouped in seven domains, three assessing the

Table 1
Comparison of AdAS Spectrum and MOODS-SR total scores among groups.

	ASD group (N = 34) (Mean ± SD)	AT group (N = 68) (Mean ± SD)	HC (N = 160) (Mean ± SD)	F (2257)	p	Post hoc comparisons (p < 0.05)
AdAS Spectrum total	91.47 ± 22.45	55.823 ± 21.71	33.15 ± 20.09	118.28	<**0.001**	**ASD** > **AT** > **HC**
MOODS-SR total	116.63 ± 19.64	74.79 ± 26	53.31 ± 28.30	59.13	<**0.001**	**ASD** > **AT** > **HC**
MOODS-SR depressive	79.11 ± 14.11	42.32 ± 16.08	32.21 ± 16.96	79.91	<**0.001**	**ASD** > **AT** > **HC**
MOODS-SR manic	22.89 ± 7.83	23.25 ± 10.68	13.76 ± 11.25	15.48	<**0.001**	**ASD** > **HC** **AT** > **HC**

Table 2
Comparison of suicidality scores among groups.

	ASD group (N = 34) (Mean ± SD)	AT group (N = 68) (Mean ± SD)	HC (N = 160) (Mean ± SD)	F(2257)	p	Post hoc comparisons (p < 0.05)
Suicidality	1.147 ± 1.94	1.0 ± 1.486	0.312 ± 0.898	11.05	<**0.001**	**ASD** > **HC** **AT** > **HC**

manic/hypomanic pole and three assessing the depressive pole in the dimensions of cognition, energy and mood respectively, plus a further domain which explores the rhythmicity and vegetative functions. The questionnaire demonstrated a good internal consistency (the Kuder-Richardson's coefficient ranging from 0.79 to 0.92 among single domains) [47].

2.2.2. The Adult Autism Subthreshold Spectrum (AdAS Spectrum)

The AdAS Spectrum is a questionnaire developed by Dell'Osso et al. [48], and devised to assess not only full-blown ASD, but also the broader spectrum of subthreshold autism, in subjects with normal intelligence and without language impairment across the lifetime. It allows evaluating a wide area of clinical and non-clinical traits, typical and atypical manifestations, including some gender-specific features. The instrument is composed by 160 dichotomous questions, grouped in seven domains: *Childhood/adolescence, Verbal communication, Non-verbal communication, Empathy, Inflexibility and adherence to routine, Restricted interests and rumination, Hyper-hypo reactivity to sensory input*. In the validation study [48], the AdAS Spectrum questionnaire demonstrated an excellent reliability (Kuder-Richardson's coefficient of 0.964) and a strong convergent validity with other scales employed in this field, such as the AQ (Pearson's r correlation = 0.77) and the Ritvo Autism and Asperger Diagnostic Scale 14-item version (Pearson's r correlation = 0.83).

2.3. Statistical analyses

In keeping with previous studies [49], suicidal ideation and behaviors was evaluated by means of items from 102 to 107 of MOODS-SR, which explore the presence of suicidal ideation (102–104) or behaviors (106–107). The score obtained as a sum of positive answers to these items was labeled as "suicidality score". We performed five one way ANCOVA controlling for sex and age to compare among groups MOODS-SR total, manic component and depressive component scores, AdAS Spectrum total score and sucidality score. A chi-square test was utilized to compare the prevalence of positive answers to at least one suicidality item among groups. For gender comparison on suicidality score, we employed the non parametric Mann–Whitney *U* test. Chi-square test was utilized to evaluate gender differences with respect to the proportion of positive endorsement of at least one suicidality item. This analysis was repeated within each group. In order to evaluate the association between AdAS Spectrum total and domain scores and the MOODS-SR suicidality items, we performed a Spearman's correlation coefficient. Further, a multiple regression model with stepwise method was used to identify the best predictors of the suicidality score. Age, sex, AdAS Spectrum domain scores and MOODS-SR depressive and manic component scores were entered as independent variables. All analyses were performed using SPSS version 24 (IBM Corp., 2016).

3. Results

The overall sample was composed by 129 males and 133 females. A significant difference in gender distribution was found among groups, with AT subjects showing a greater percentage of males compared to HC (70.6% vs 39.4%, p < 0.001), while no significant differences were reported for the ASD group compared to HC (52.9% vs 39.4%, p < 0.145) and AT group respectively (52.9% vs 70.6%, p < 0.787). The mean age of the whole sample was 25.7 ± 8.9; AT subjects showed a significant lower mean age than ASD subjects (21.5 ± 3.1 vs 29.8 ± 12.1, p < 0.001) as well than HC group (21.5 ± 3.1 vs 26.5 ± 5, p < 0.001) without any significant difference between ASD and HC group. 57.35% of subjects in the AT group and 23.52% in the ASD group reported a comorbid mental disorder according to the SCID-5. Within AT group, 6 subjects (8.82%) reported a diagnosis of Bipolar Disorder, 2 (2.94%) of Panic Disorder, 23 (33.82%) were diagnosed with other anxiety disorders and 8 (11.76%) with a Feeding/eating Disorder. As for ASD group, 6 (17.75%) reported a diagnosis of other anxiety disorders and 2 (5.88%) of Feeding/eating Disorder. ASD subjects scored significantly higher than both AT and HC subjects in the AdAS Spectrum total score and in the MOODS-SR total and depressive component scores. ASD subjects scored higher than HC group also in MOODS-SR manic component score. AT subjects scored significantly higher than the HC group in AdAS Spectrum total score and in all MOODS-SR scores. Considering the covariates, sex and age were not significantly related to AdAS Spectrum total score (age: F(1,257) = 0.79, p = 0.375; sex: F(1,257) = 0.78, p = 0.377). Both the covariates were significantly related to MOODS-SR manic component score (age: F(1,257) = 9.52, p = 0.002; sex: F(1,257) = 4.49, p = 0.035), and MOODS-SR depressive component score (age: F(1,257) = 7.05, p = 0.008; sex: F(1,257) = 5.72, p = 0.018), while only the covariate age was significantly related to MOODS-SR total score (age: F(1,257) = 7.94, p = 0.005; sex: F(1,257) = 2.26, p = 0.134). After controlling for the effect of the covariates, there was still a significant effect of the diagnostic group on MOODS-SR manic component score (F(2,257) = 15.48; p < 0.001), MOOD-SR depressive component score (F(2,257) = 79.91; p < 0.001) and MOODS-SR total score (F(2,257) = 59.13; p < 0.001) (Table 1).

Moreover, we found significantly higher suicidality scores for both ASD and AT groups compared to HC, with no significant differences between ASD and AT subjects (Table 2). The covariates were not significantly related to suicidality score (age: F(1,257) = 0.01, p = 0.980; sex: F(1,257) = 0.42, p = 0.515). While comparing the rate of endorsement of at least one suicidality item among groups, ASD and AT subjects showed a significantly higher prevalence that HC (35.3% vs 42.6% vs 14.4%, χ^2 = 23.161, p = 0.001). No significant gender differences emerged within the three groups with regard to suicidality scores and for the rate of at least one positive response to suicidality items. Significant correlations were found between MOOD-SR suicidality score and

Table 3
Spearman's correlation between AdAS Spectrum domain scores and MOODS-SR suicidality score.

	AdAS Spectrum total	Childhood/adolescence	Verbal communication	Non-verbal communication	Empathy	Inflexibility/adherence to routine	Restricted interests/ruminations	Hyper/hypo-reactivity to sensory input
Suicidality	0.428*	0.390*	0.383*	0.380*	0.315*	0.356*	0.404*	0.366*

* p < 0.001.

Table 4
Multiple stepwise regression analysis.

	b(SE)	beta	t	p	C.I.$_{95\%}$	Correlation (zero order)	Correlation (part)	Collinearity statistic (tolerance)
Step 1								
K	−0.699 (0.152)		−4.61	<**0.001**	−0.99; −0.40			
MOODS-SR depressive component	0.035 (0.003)	0.542	10.03	<**0.001**	0.03; 0.04	0.542	0.542	
Step 2								
K	−0.723 (0.151)		−4.80	<**0.001**	−1.02; −0.43			
MOODS-SR depressive	0.027 (0.005)	0.419	5.64	<**0.001**	0.02; 0.04	0.542	0.302	0.519
AdAS-spectrum *Restricted interests/ruminations*	0.047 (0.020)	0.177	2.38	**0.018**	0.08; 0.09	0.468	0.127	0.519

$R^2 = 0.294$, corrected $R^2 = 0.291$ for step 1. $R^2 = 0.310$, corrected $R^2 = 0.304$ for step 2. Durbin-Watson = 1.995. F = 100.59 ($p < 0.001$) for step1; F = 54.102 ($p < 0.001$) for step 2. Excluded variables: gender, age, childhood/adolescence, verbal communication, non-verbal communication, empathy, inflexibility/adherence to routine, hyper/hypo-reactivity to sensor input. MOODS-SR manic component.

AdAS Spectrum total and domain scores, the highest coefficient emerging between MOOD-SR sucidality and AdAS Spectrum *Restricted interests and rumination* domain scores (See Table 3). The stepwise regression identified the "MOODS-SR depressive component score" and the AdAS Spectrum "*Restricted interests/Ruminations* domain" score as the best predictors of the suicidality score (see Table 4). All values of tolerance were >0.2, providing a good safeguard against collinearity.

4. Discussion

The aim of this study was to assess mood symptoms and suicidal ideation/behaviors among subjects with different levels of autism spectrum symptoms, with a special focus on evaluating whether some specific autistic dimensions may predict suicidal thoughts and behaviors. To the best of our knowledge, this is the first study addressing suicidal ideation/behaviors and its associated features in a sample composed by subjects with ASD and AT, compared to a group of healthy controls. We found no differences in suicidality scores between ASD and AT groups, while both showed a higher score than HC. This finding adds to previous literature pointing out the high rate of ASD among suicide attempters, as well as the high rates of suicidal thoughts and behaviors among patients with ASD across different age ranges [4,44,45,50–52]. Moreover, our results confirm some previous studies suggesting a relationship between suicidal thoughts and behaviors and AT as well [6,11,14], further highlighting the importance of detecting not only full-blown ASD, but also subthreshold psychopathological traits, due to the likelihood of AT of being associated with a broad range of psychiatric symptoms and conditions, from stress-related symptoms to suicidal ideation [4,5,13,53,54].

Parallel, the ASD group reported significantly higher MOODS-SR total score and MOODS-SR depressive component score than the AT group, and the AT group in turn scored significantly higher than the HC. On one hand, these results confirm previous studies highlighting a strong relationship between MD and both clinical and subthreshold ASD [32–34,38,40,42,55]; on the other hand, our data seem to point towards a further broadening of the link between the two psychopathological dimensions, which is not limited to full-blown ASD and MD manifestations, but also features the wider mood and autism subthreshold spectrums.

According to the SCID-5, the overall comorbidity with other mental conditions was higher among the AT group than in the ASD group (57.35% vs 23.52%). On one hand, this result may indicate that subthreshold autistic conditions, namely AT, are related to high levels of psychiatric comorbidity, which may even exceed the level of comorbidity of clinical ASD. On the other hand, the difference could be at least in part due to the difficulties of patients with more severe ASD to explain their feelings, resulting in greater diagnostic difficulties, especially in detecting symptoms of other disorders with overlapping features, such as social anxiety or depression [13,43,52,56].

Our study showed also a significant correlation between the AdAS Spectrum *Restricted interests and rumination* domain and suicidality scores. This finding adds to previous results from Pelton and Cassidy [46], who reported burdensomeness and thwarted belonging as mediating factors between AT and suicidality. Rumination is a pattern of repetitive thinking, usually associated to and exacerbating anxiety and depression, often affecting problem-solving and the processing of negative feelings and leading to social isolation [57–59]. Ruminative thinking has been described as one of the core symptoms of ASD [50], but it is frequently associated also with affective disorders, psychosis and to emotional dysregulation in borderline personality disorder [57,59–61], so that it might be better considered as a transnosographic dimension, coming across a number of mental disorders, and likely playing a role in the development of suicidal ideation and behaviors [4,22].

Our results should be considered in light of several limitations. First, the study design was cross-sectional, preventing us to infer causation from the associations found. Second, the sample recruited was relatively small and two self-report questionnaire were used to evaluate both mood and autism spectrum symptoms, enhancing the risk of under-/overrating of symptoms. Third, autism and mood spectrum symptoms may overlap to some extent, confounding one another. Moreover, our groups were not homogeneous for gender and age, and this may have affected our results; unfortunately, the limited sample size would not allowed us to perform a random extraction in order to obtain homogeneous groups. This is an exploratory study, and in this framework we chose to identify possible predictors of suicidality scores employing a stepwise regression, although this technique has been criticized in literature for being eventually exposed to bias. Globally, further studies are needed in wider samples, and with a longitudinal design, in order to confirm our findings.

In the context of these limitations, our study suggests that not only clinical ASD but also AT are associated with a broad variety of psychopathological dimensions, that include suicidal ideation and behaviors and the whole spectrum of mood manifestations, besides a number of comorbid mental disorders. Further, longitudinal studies are warranted in order to elucidate whether AT may have a causative relationship with the above clinical correlates [13,56].

Conflicts of interest

None

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