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Original article

Autistic traits and rumination as vulnerability factors towards post-traumatic stress symptoms: shaping psychopathological trajectories

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SUMMARY

Recent studies on Autism spectrum disorder, while focusing on adult subjects, stressed the presence of full-threshold and subthreshold autistic symptoms in clinical populations, also providing valuable insights on how neurodevelopmental alterations may increase the risk towards the development of other psychiatric conditions. The present review takes into account the most recurring topics in this literature, such as the research on autistic traits and ruminative thinking, collecting evidences on the effects of these elements in clinical presentations. In particular, while autistic traits and ruminative thinking seem to act as vulnerability factors towards the development of post-traumatic symptoms after life events, they could be considered the starting point of different kinds of psychopathological trajectories depending from the specific neurobiological asset and its interactions with environment. In order to rethink the literature within a coherent theoretical framework, the Adult Autism Subthreshold Model is then discussed.

Key words: autism spectrum disorder, post-traumatic stress disorder, borderline personality disorder

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Autism spectrum: a constantly evolving picture

Autism Spectrum Disorder (ASD) is defined as a condition characterized by alterations in brain connectivity with cascading effects on several neuropsychological functions. This early-onset disorder features communication deficits, alterations in social cognition, repetitive, stereotyped behaviours. Intellectual impairment might also be present [1,2]. The pathogenesis of ASD remains largely unknown; however, given its high heritability [3], a strong genetic influence is expected, and several genetic mutations associated with ASD have been identified, many of which are involved in the synaptogenesis and synaptic functioning. These observations trace back to the first outlines of this syndrome by Kanner and Asperger, who both independently reported how first and second degree relatives of the observed children shared some psychopatological features with their offspring [2,4,5].

A growing body of studies also stresses how environmental conditions, in particular those linked with intrauterine life and/or increased level of oxidative stress, may play a pivotal role towards neurodevelopmental alterations [6,7]. From a neurobiological point of view, some literature stressed that ASD should be considered as a condition predisposing to a subsequent development of alterations within brain connectivity, particularly concerning social brain areas implicated in specific aspects of mentalization, social cognition, and emotional processes [8,9].

Since the first observations by Kanner and Asperger, increasing literature has also stressed the presence of a broad spectrum of milder symptoms (which would feature social difficulties, cognitive and behavioural traits) among parents and siblings of ASD subjects, leading to shape the concept of a "broad autism phenotype" (BAP) [10-12]. Moreover, the introduction of specific psychometric instruments such as the Autism Spectrum Quotient (AQ) [13] and Adult Autism Subthreshold Spectrum (AdAS Spectrum) [11,14] allow to properly investigating the presence of autistic traits (AT) in both clinical and general population. Results from these studies highlighted how AT seem to be continuously distributed in the general population, being more frequent amongst some high-risk groups [11,13,15-22]. AT are reported to be particularly represented also in clinical samples of patients with other psychiatric disorders [20,21,23-31]. In this framework, DSM-5 switched from the previous distinction between high functioning autism (namely, Asperger's Disorder) and autistic disorder, featuring the broader category of "Autism Spectrum Disorder" [1]. Also neuroimaging studies have shown a continuity between ASD and BAP [10], while genetic studies reported how different phenotypes (non-clinical samples, AT, BAP, full-blown ASD) share a genetic risk continuously distributed across the population, implying that clinical thresholds, classically intended, could be considered arbitrary, since the disorder exists as a quantitative extreme of a continuum [32]. In a broader perspective, it is noteworthy that, while a wide literature reported, as described above, the presence of AT in patients with other psychiatric disorders [20,21,23-31], genetic studies seem to confirm this data, highlighting common underpinnings between ASD and mood disorders [33], which would involve in particular pathways regulating circadian rhythms [33,34]. Furthermore, recent biochemical studies reported also an involvement of pro-inflammatory cytokines, neurotrophins, and dysregulations of the immune system in ASD as well as in post-traumatic stress disorder (PTSD) and mood disorders [35-39]. On the other hand, neuroimaging and neurocognitive studies reported shared traits between AT and Feeding and eating disorders (FED). These elements, which are currently object of increasing investigation in the scientific literature, may suggest that the autism spectrum continuum should eventually be extended to other disorders, that have been traditionally considered as part of distinguished categories [40].

The transnosographic role of AT and ruminative thinking

The ASD comorbidity has been quite consistently described as an overlap with Attention deficit hyperactivity disorder (ADHD), anxiety and mood disorders [41]. Further studies, however, have proved a wider range of interactions.

Expanding on Gillberg et al. (1996) [42] seminal notion of overlapping features between Anorexia nervosa (AN) inflexibility and behavioural rigidity and the characteristic insistence on sameness which lies amongst the core symptoms of ASD, several studies explored the overlap between ASD clinical features and FED, particularly AN [43]. AN patients exhibit behavioural rigidity with a focus on food and weight (that may fit into unusual restricted/repetitive interests and behaviours), deficits in emotional intelligence and in theory of mind tasks, social anhedonia, and attention to detail, all typical features of ASD [27,43]. Moreover, ASD individuals show a high prevalence of food problems: the habit to be selective about food as well as the aversion to certain textures, colors, smells and temperatures are often associated with underweight [11]. A recent study reported a higher rate of AT amongst FED patients when compared with healthy controls, especially in subjects with restrictive patterns, suggesting that a restrictive food behaviour may be considered as part of an ASD female phenotype: interestingly, this hypothesis may lead to a different interpretation of the striking gender differences in both ASD (diagnosed mainly amongst males) and AN (diagnosed mainly amongst females) [28]. Recently, increasing literature is stressing the presence of sex-specific presentations of the autism spectrum, which may result in an underestimation of these conditions among females [20,27,29,43]. In particular, females with ASD/AT often show an apparently higher adjustment to social interactions, often through the employment of camouflaging and of other copying strategies which features the imitation of others' behaviours [2,27,28]. As a consequence of the higher awareness of their own social difficulties, females seem to show a higher social anxiety [11,28,44,45] It is noteworthy that social anxiety is another disorder with a significantly higher prevalence amongst females, and which seem to share with ASD an impairment of the social brain [15,46-49]. Moreover, the pattern of restricted interests and repetitive behaviours is often centered on subjects quite different from those typically reported amongst males, such as spending time with animals, reading fictions or focusing on food and diet [11,20,44]. As reported above, this latter data is supported by the body of studies that is stressing how AN may be better considered as a female phenotype of ASD [2,20,29,43].

However, this is not the only interesting overlap between autism spectrum and other psychiatric conditions, from a transnosographic point of view. In particular, an increasing number of evidences has been reported on the relationship between trauma and stress-related symptoms and AT/ASD. While trauma and autism had been linked since classical psychodynamic theories [50], early

evidence-based research on the topic yielded conflicting results. Among the first studies, focusing on a child population, some reported either no [41] or low [51] correlation between neurodevelopmental disorders and trauma or stress related symptoms in ASD patients, while others highlighted a quite relevant prevalence of PTSD in ASD [52] or, conversely, found that suicidal thoughts and behaviours, associated with depression and PTSD, were quite high amongst young ASD patients [53].
The different methodological approach and the heterogeneous population considered probably accounts for these conflicting data. Moreover, it has been widely considered how full-blown ASD patients might be unable to properly report traumatic events and to have them positively screened with a psychometric instrument, since the condition itself prevents proper mentalization and expression of traumatic and/or stressful situations [54,55].
A significant association of rumination and trauma/stress-related symptoms with mood symptoms and suicidality was also highlighted [22]. This is quite a specific indication: it is widely known, from a behavioural and cognitive point of view, how negative beliefs in both anxiety-related disorders and mood disorders are maintained by a stream of negative, ruminative automatic thoughts. A cyclic model about maintenance mode for depression, dubbed "vicious flower" has been described in 2010 [56], while one involving ruminative thinking in the maintenance process of anxiety and panic related symptomatology is known since the early '90 [57].
Hence, rumination and trauma/stress-related symptoms may be the common mediators of AT, mood spectrum symptoms [12,21,22,25,26,58,59] and suicidal ideation interplay [12,21,22,24,60]. According to the cognitive model of PTSD, excessive rumination over traumatic or highly distressing experiences may lead to faulty processing and the development of post-traumatic stress symptoms [61]. In this sense the presence of a BAP, which includes among its features the presence of rumination, could have a crucial role in the development of PTSD following a traumatic event [54,61-66]. Conversely, PTSD is characterized by a decreased interest or participation in daily activities and a feeling of detachment from others, thus resembling autistic symptoms as suggested by high scores in questionnaires assessing AT [29].
Negative ruminative thinking is particularly interesting from a transnosographic point of view, as it appears to be strictly implied in many different psychiatric disorders, such as Obsessive-compulsive disorder, affective disorders, psychosis, Borderline personality disorder (BPD) and PTSD [67-69]. It has been described as one of the main symptoms of ASD [70], belonging to the domain of restrictive/repetitive activities. This repetitive thought pattern is associated with demoralization, anxiety and bad ideation [71], which negatively influences problem solving and worse feelings processing, eventually leading to social isolation [56]. Several authors believe that negative ruminative thinking can play a role in the development of depression [71,72] and suicidal ideation and behaviours [21,22,24]. Acting as intermediary, rumination seems to increase the risk of depressive episodes, their duration and their severity, in response to negative life events [73,74]. Subjects with ASD [24]/AT [25] showed high rates of adjustment disorders, which may also be related to increased suicidality [24,53]. Recent data showed also an association between AT and PTSD [21,58], with higher rates of PTSD in subjects with AT after traumatic events. Therefore, it is possible that ASD subjects represent a low resilience group more vulnerable to develop trauma/stress-related symptoms and disorders [21]. In this regard, individuals with high levels of AT may show altered coping strategies and reduced attitude to manage with stressful situations. It has also been suggested that the vulnerability of patients with AT towards the development of trauma/stress symptoms after being exposed to life events could play a further role in the development of mood disorders [22].
A strong relation between ASD/ATs and suicidal ideation/behaviours, both in clinical and non-clinical samples, was also observed [12,21,22]. A high prevalence of suicidality has been reported in patients with ASD of different age groups [22,24,25,53,75-78], and, conversely, a diagnosis of ASD was found in 7.3% of subjects with a suicide attempts history [24]. More recently, a significant association between AT and suicidality has also been found, both in general population and in psychiatric patients [21,25,29]. It has also been proposed that burdensomeness and thwarted belonging may mediate the relationship between ATs and suicidal behaviour in general population [79]. A recent study reported a similar presence of suicidality between ASD and subjects with AT, and both groups showed a higher score than healthy controls [21]. Even in depressed subjects the presence of comorbid ASD is related to an increase in suicidality levels [25,78]. In these patients ASD is also associated with methods of greater lethality for suicide attempts [25].

BPD: where all comes together

According to DSM-5 BPD is a condition with a significantly higher prevalence among females, which begins in early adulthood and shows as his core feature a pervasive pattern of instability of interpersonal relationships, self-image, and affects, along with marked impulsivity [1,27]. Typical symptoms may include also a marked fear of being abandoned, feelings of emptiness and inappropriate anger, self-harming or suicidal threats and behaviours, dissociative symptoms and/or paranoid ideation [1,80].

A consistent number of studies highlighted a possible role of negative ruminative thinking in BPD [80-83], which may be implied in maintaining and increasing BPD psychopathology, as previously evidenced also for depressive symptoms [31,72,73,84-86]. In particular, BPD patients show a higher tendency to maladaptive cognitive processes, including rumination [82]. Also amongst depressed patients, on which many studies about rumination were focused, some authors highlighted a specific relationship between BPD and rumination [80,87,88]. This data increased the interest in investigating the specific relationship between rumination and BPD psychopathology, while recent research highlighted that BPD patients seem to show a specific vulnerability to develop stress-related rumination, and in particular rumination after negative interpersonal events and interpersonal exclusion, with slower recovery from distress [89-91]. Other studies stressed also how aggressive behaviours in these patients seem to be linked to the presence of anger rumination [89,92]. These findings are of particular interest in light of previous literature that reported a significant role of ruminative thinking for the development of psychiatric disorders after being exposed to traumatic events [40,59]. It should be noted that many studies highlighted also the presence of traumatic experiences, frequently in childhood, in clinical histories of BPD patients, often hypothesizing for this condition a pathogenetic mechanism which would imply the interaction between genetic vulnerability and early life events [20,30,31,93-99]. In this framework, according to a dimensional approach, some authors raised the hypothesis that PTSD may occur not only after being exposed to highly traumatic events (like those listed in criterion A of DSM-5) but also as a consequence of prolonged and/or repeated milder stressful experiences (and in particular interpersonal victimization, such as being exposed to bullying episodes, sexual harassment, or other aggressive behaviours, including by caregivers) [100-103]. The exposure to this kind of events may lead to the development of a specific phenotype of PTSD, called "Complex PTSD" (cPTSD) [100-103]. It is noteworthy that this condition, which often takes a chronic course, is considered to be characterized by a higher presence of dissociative symptoms and negative alterations of emotions and cognitions, including emotional dysregulation, negative self-image, maladaptive and self-injuring behaviours [104-106]. Moreover, it has been pointed out that chronic cPTSD may result, in time, in a deep instability of emotions, self-perception and interpersonal relationships, with marked impulsivity and often associated with substance abuse and self-injuring [54,104]. Such a clinical picture is consistently similar to that of BPD, and some authors also stressed that these subjects may actually receive more frequently a diagnosis with BPD instead that get their trauma-related condition recognized, especially if they not report a history of major traumas [104,105,107]. These considerations led to increase the interest in exploring the relationship between BPD and trauma and stress-related conditions: recently, a study by Dell'Osso et al. [80] evaluated the association of BPD, rumination, PTSD and mood spectrum (another dimension which has been frequently associated with BPD in the literature) in a sample of BPD patients with or without mood disorders and in healthy controls. The study reported a significantly higher presence of rumination (as measured by the Ruminative Response Scale, RRS) and PTSD-criteria fulfillment in BPD patients than in controls. Although BPD patients with mood disorders showed a higher rate of rumination and PTSD than patients with only BPD, according to the regression analysis results, the effect of rumination and PTSD symptoms seemed to prevail on the effect of mood symptoms in predicting BPD, confirming the association between BPD, PTSD and rumination and possibly implying a significant role of PTSD and rumination in BPD psychopathology. In this framework, increasing literature is suggesting the presence of overlapping features between ASD and BPD [2,29,108]. Some authors pointed out that distinguishing ASD without intellectual disabilities from personality disorders in adults could be challenging due to similarities in the pervasive pattern of behaviours that strikingly affect social functioning [109], and in particular BPD and ASD seem to share a common core in the impaired understanding of and reacting to emotions and interpersonal challenges [110]. BPD subjects often show significant empathy and theory of mind alterations, as well as difficulties in recognizing and interpreting emotions [111-113], which may be at the basis, together with the emotional dysregulation, of the pattern of instability in social relationships [2,21,29,54]. On the other hand, subjects of the autism spectrum often report a higher vulnerability to traumatic experiences, even if of milder intensity [54], which may result in a higher frequency of trauma and stress-related disorders, in particular adjustment disorders and cPTSD [60]. Treatments targeting social brain mechanisms, such as psychotherapies targeting mentalization or theory of mind, as well as intranasal administration of oxytocin, have been conducted in both BPD and ASD patients [114-117]. Studies that investigated comorbidity rates between ASD and BPD, reported a 15% prevalence of ASD amongst subjects with BPD, stressing also a higher suicidality and lower global functioning in the comorbid group [118]. On the other hand, a 9 to 10.6% prevalence of BPD has been reported among subjects with ASD [23,103]. Concerning AT, a study reported that about a half of 38 patients with BPD showed the presence of significant AT as measured by the AQ [119]. Dudas et al. [110] found that BPD patients reported higher levels of AT than controls, while comorbid

patients showed the highest levels of AT as measured by the AQ. More recently, Dell'Osso et al. [29] reported, in a sample of 50 BPD patients and 69 controls, significantly higher levels of AT (as measured by both the AQ and the AdAS Spectrum) in the BPD group. Moreover, in the same sample AT showed a significant impact on suicidality and exposure to physical or sexual abuse during lifetime. A similar result was reported by another study conducted in a non-clinical population of college students, where authors highlighted a higher risk of suicidal ideation amongst subjects who show both AT and BPD traits [120].

In a broader framework, it is noteworthy that, while BPD is a diagnosis with a strikingly higher prevalence amongst females, ASD is, conversely, diagnosed mostly amongst males; and this might lead to considerations similar to those raised about AN [1,20,27,43,121].

These data, together with the evidence of overlapping features and frequent comorbidity between the two disorders, led to hypothesize that BPD may be considered a female presentation of the autism spectrum, which may occur in particular when the subject is exposed to traumatic or stressful events during lifetime [2]. While FED may represent another possible trajectory for female autism spectrum in addition to BPD, on the other hand, it should be noted how BPD and FED showed significant comorbidity rates [122], further supporting the autism spectrum model for these conditions.

How ASD related traits shapes illness trajectories

As discussed above, recent studies stress the continuous distribution of AT in the general and clinical populations: within this framework, crossing the full-threshold symptomatology seems to be a matter of quantity rather than quality. These findings might be interpreted in light of a new coherent, dimensional and quantitative psychopathological model, such as the Adult Autism Subthreshold Spectrum Model (AdAS Spectrum Model) [2], rather than within a rigid categorical approach. The AdAS Spectrum Model is a comprehensive psychopathological theory which places on the same continuum full-blown symptoms, mild and atypical manifestations, behavioural traits, and personality features associated with the ASD diagnostic category. These traits may act as risk factors for other mental disorders, being continuously distributed from normality to pathology and including also non-clinical aspects of neuroatypicality, such as originality, creativity, divergent thinking [2,123]. This model considers firstly, as widely reported, the continuous distribution of AT. From this point of view, the ASD clinical phenotypes appear as an extreme manifestation of a gradual quantity. Moreover, the AdAS Spectrum Model features, amongst the possible psychopathological trajectories in the same continuum of the autism spectrum, also other kinds of clinical expressions, such as Schizophrenia, mood disorders, FED or BPD [124,125], proposing a coherent explanation of the higher rates of AT amongst clinical samples. In a broader perspective, according to this model, AT may be considered as the psychopathological correlate of the presence of a neurodevelopmental alteration that lead to different trajectories depending form the timing and the entity of the alteration and from its interaction with environment and life events [125]. Their presence may result not only in the development of psychopathological trajectories, but also allow hyperadaptive manifestations of atypical behaviours related to geniality [54,126,127]. At the same time, however, they act as a source of greater vulnerability and as risk factor for mental disorders and suicidality [2,22,25,125].

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