

## Original Research

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# Panic-agoraphobic symptoms in adults with ASD: the role of ruminative thinking and inflexibility

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**Abstract**

**Background.** Scientific literature has highlighted the link between autism spectrum disorder (ASD) and anxiety disorders, but few studies have delved into the relationship between ASD and panic-agoraphobic disorders. The aim of this study is to investigate the relationship between autism spectrum and panic-agoraphobic symptoms, examining whether and which autistic domains are predictive of the presence of specific panic-agoraphobic symptoms.

**Materials and methods.** Forty-five adult subjects with ASD and 50 healthy controls (HCs) were evaluated through the Structured Clinical Interview for DSM-5, Research Version and assessed with the Adult Autism Subthreshold Spectrum (AdAS Spectrum) and the Panic-Agoraphobic – Short Version (PAS-SV) questionnaires. Statistical analyses included Mann–Whitney *U* test, chi-square test, and a set of linear and logistic regression analyses.

**Results.** The PAS-SV total and domain scores were significantly higher in the ASD group than in the HC group. A higher AdAS total score appeared to be predictive of a higher PAS-SV total score. The AdAS domain *Restricted Interests and Rumination* would increase the risk of obtaining higher PAS-SV total and domain scores. Conversely, the AdAS Spectrum domain *Inflexibility and Adherence to Routine* would predict lower total PAS-SV score.

**Conclusion.** This study revealed a greater representation of panic-agoraphobic symptoms in adults with ASD, as well as an increased risk of showing such symptoms in the presence of significant autistic traits. Restricted interests and ruminative thinking emerged as predominant risk factors for panic-agoraphobic manifestations.

**Introduction**

Autism spectrum disorder (ASD) is a neurodevelopmental condition characterized by deficits in communication and social interaction, a pattern of repetitive behaviors or interests, and altered sensitivity to sensory stimuli.<sup>1</sup> The latest edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM) explicitly requires the clinician to specify whether the patient with ASD also presents with other mental or behavioral issues, allowing some “subthreshold” symptom information to be included in the diagnosis, considering their possible impact on the individual’s quality of life.<sup>2</sup> This choice is in continuity with a spectrum model applied to mental disorders, long supported in the scientific literature, and applied in several studies to the study on ASD.<sup>3</sup> Research on autism spectrum enabled to investigate the role of subthreshold autistic manifestations within the general population, where such manifestations would seem to be continuously distributed, and in specific populations in which they would be particularly represented, such as among individuals with other mental disorders.<sup>4</sup> As a matter of fact, ASD is distinguished by extremely high rates of comorbidity with other mental disorders, found in 70% of autistic patients.<sup>1</sup> In this regard, anxiety disorders (ADs) represent the most frequently co-occurring mental health concern in ASD, with prevalence rates at least 5 times higher than in the general population.<sup>5–7</sup> Among ADs, panic disorder (PD) and agoraphobia (AG) appear very frequently.<sup>8</sup> According to DSM-5, the diagnosis of PD is fulfilled by the presence of unexpected and recurrent panic attacks, at least one of which is followed by one or more of the following conditions that persist for at least 1 month: worry, fear, and behavioral change.<sup>1</sup> It is not uncommon for PD to be combined with AG, a diagnostic category defined by marked fear and anxiety in at least 2 agoraphobic situations, feared or avoided by the subject, invariably a source of fear or anxiety disproportionate to the actual danger.<sup>1</sup> A diagnosis of AG was observed in 80.9% of a PD sample, and most studies agree a presence of AG has negative effects on the severity, course, and response to treatment of PD.<sup>9</sup> Although some studies in the literature have noted the frequent comorbidity between ADs, such as PD and AG, and autism, few studies have yet evaluated the relationship between these disorders in adults and from a dimensional

perspective. Therefore, the aim of this study is to investigate the relationship between the autistic and panic-agoraphobic spectra in adult patients with ASD.

## Materials and methods

### Study sample and procedures

The total sample included 95 subjects divided into 2 diagnostic groups, assessed by trained clinicians according to the DSM-5 diagnostic criteria. Exclusion criteria were age under 18 years, language or intellectual difficulties that affected the ability to perform assessments, mental disability, poor ability to cooperate, and ongoing psychotic symptoms. More specifically, 2 groups were identified as follows: 45 adult subjects with a diagnosis of ASD without intellectual impairment of language development alteration and 50 healthy controls (HCs) with no current or past mental disorders and belonging to medical and paramedical staff. Patients with ASD were recruited among inpatients and outpatients followed at the Psychiatric Hospital of the University of Pisa. All subjects were between 18 and 60 years of age and signed a written informed consent. The Structured Clinical Interview for DSM-5, Research Version (SCID-5-RV)<sup>10</sup> was used to confirm the absence of mental disorders among HCs. The study was performed in conformity with the Declaration of Helsinki. The Ethics Committee of the Azienda Ospedaliero-Universitaria di Pisa approved all recruitment and evaluation procedures. Eligible subjects provided written informed consent after receiving a complete description of the study and being given the opportunity to ask questions. Subjects received no payment for their participation, according to Italian law.

### Measures

The assessment procedures consisted of the SCID-5-RV,<sup>10</sup> the Subthreshold Adult Autism Spectrum (AdAS Spectrum), and the Panic-Agoraphobic – Short Version (PAS-SV). The questionnaires were administered by psychiatrists trained and certified in the use of the instruments.

### The Adult Autism Subthreshold Spectrum (AdAS Spectrum)

The AdAS Spectrum is a questionnaire developed by Dell'Osso et al.<sup>3</sup> 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 nonclinical traits, typical and atypical manifestations, including some gender-specific features. The instrument is composed by dichotomous questions, grouped in seven domains: Childhood/Adolescence, Verbal Communication, Non-verbal Communication, Empathy, Inflexibility and Adherence to Routine, Restricted Interests and Rumination, and Hyper-Hypo Reactivity to Sensory Input. In the validation study,<sup>3</sup> the AdAS Spectrum questionnaire demonstrated an excellent reliability and a strong convergent validity with other scales employed in this field, such as the Autism-Spectrum Quotient Test<sup>11</sup> and the *e* Ritvo Autism and Asperger Diagnostic Scale 14-item version.<sup>12</sup>

### The Panic-Agoraphobic – Short Version (PAS-SV)

The PAS-SV<sup>13</sup> consists of 78 items, organized into 4 domains. The responses to the different items are coded dichotomously (yes/no), and the relative scores for the individual domains and appendices are derived by counting the number of positive responses. The Panic Symptoms domain (14 items) explores the presence of typical panic symptoms as reported in the DSM criteria for the presence of a panic

attack. The Atypical Panic Symptoms domain (14 items) explores the spectrum of atypical manifestations of panic, not covered in the DSM criteria but extensively described in the scientific literature. The Anxious Expectations and Maladaptive Behaviors domain (26 items) investigates the whole range of possible concerns and behaviors associated with the presence of panic, such as sensitivity to medication, sensitivity to reassurance, and separation anxiety. The AG domain (21 items) surveys the presence of AG and claustrophobia in a number of contexts, both covered and not covered by the DSM criteria for the diagnosis of AG.

### Statistical analyses

Analyses were conducted through the use of the Statistical Package for the Social Sciences (SPSS) version 26.0.<sup>14</sup>

Mann–Whitney *U* test and chi-square test were used for comparing sociodemographic variables between groups. The PAS-SV mean total and domains scores obtained by the 2 groups were compared through a Mann–Whitney *U* test. Finally, a set of linear regression analyses were performed to investigate the hypothetical predictive role of AdAS Spectrum total and domain scores on those obtained at the PAS-SV.

## Results

### Sample composition

No significant differences were reported among groups in terms of age ( $p = 0.91$ , chi-square = 0.012), and sex ( $p = 0.48$ ;  $F = 0.496$ ).

The ASD group ( $N = 45$ ) included subjects with a mean age of  $35.02 \pm 11.03$  years and consisted of 23 (51.1%) males and 22 (48.9%) females. The HCs ( $N = 50$ ) had a mean age of  $34.74 \pm 11.44$  years and consisted of 25 (50.0%) males and 25 (50.0%) females (Table 1). Regarding the level of education, the total sample consisted of 11 subjects (11.6%) with a second-level degree, 37 (39.0%) with a first-level degree, 38 (40.0%) with a high school diploma, 4 (4.2%) with a lower secondary school diploma, 4 (4.2%) with a primary school diploma, and 1 (1.0%) without a primary school diploma. Regarding employment status, 27 (28.4%) participants were students, 28 (29.5%) unemployed, 39 (41.05%) employed, and 1 (1.05%) retired.

### Comparisons between PAS-SV total and domain scores among groups

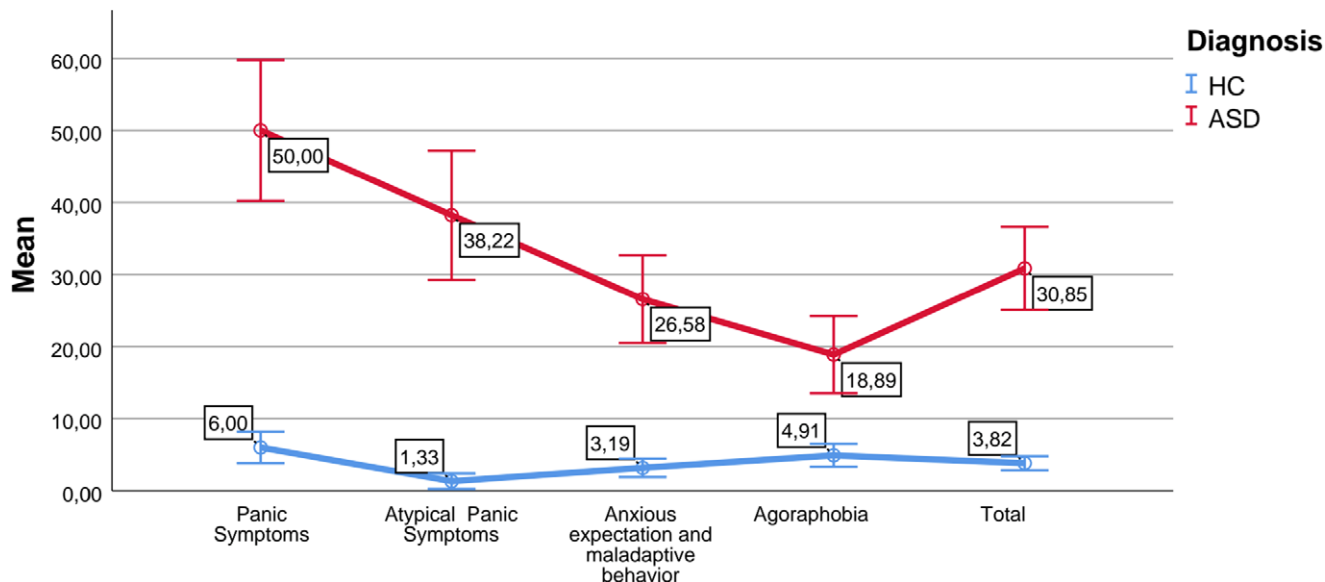
As showed by Mann–Whitney *U* test, the total PAS-SV total and domain scores were significantly higher in the ASD than in the HC group ( $p < 0.01$ ). Comparisons between PAS-SV total and domain scores among the 2 diagnostic groups are reported in Table 2 and graphically represented in Figure 1.

**Table 1.** Comparison of Sociodemographic Variables among ASD and HC Groups

	ASD ( $N = 45$ )	HC ( $N = 50$ )	<i>F</i>	<i>p</i>
	Mean $\pm$ SD	Mean $\pm$ SD		
Age	35.02 $\pm$ 11.03	34.74 $\pm$ 11.44	0.496	0.48
	<i>N</i> (%)	<i>N</i> (%)	Chi-square	<i>p</i>
Sex				
F	22 (48.9)	25 (50.0)	0.012	0.91
M	23 (51.1)	25 (50.0)		

**Table 2.** Comparison of PAS-SV Scores among ASD and HC Groups

PAS-SV	ASD (N = 45) mean ± SD Mean rank	HC (N = 50) mean ± SD Mean rank	p	Mann-Whitney U
Panic symptoms	7.00 ± 4.563 68.94	0.84 ± 1.076 29.15	<0.001	2,067.500
Atypical panic symptoms	5.73 ± 4.470 70.70	0.20 ± 0.571 27.57	<0.001	2,146.500
Anxious expectation and maladaptive behavior	7.18 ± 5.470 67.61	0.86 ± 1.212 30.35	<0.001	2,007.500
Agoraphobia	4.15 ± 3.913 62.08	1.08 ± 1.226 35.33	<0.001	1,758.500
Total	24.08 ± 14.943 70.34	2.980 ± 2.669 27.89	<0.001	2,130.500



**Figure 1.** Graphical representation of PAS-SV total and domain score comparisons among groups.

**Table 3.** Composition of the 2 Panic-Agoraphobic Severity (PAS) Groups: PAD and Non-PAD

PAS group		ASD (N = 45)	HC (N = 50)
Non-PAD	N	15	50
	% within PAS group	23.1%	76.9%
	% within diagnosis	33.3%	100%
PAD	N	30	0
	% within PAS group	100%	0%
	% within diagnosis	66.7%	0%

Pearson chi-square = 48.718.  
p < 0.01.

**Table 4.** Linear Regression Using AdAS Spectrum Total Score as Independent Variable and PAS-SV Total Score as the Dependent Variable

	B (SE)	p	Beta	t	95% CI
Total AdAS score	0.245 (0.26)	<0.01	0.697	9.366	9.366

Adjusted R<sup>2</sup> = 0.480.

Furthermore, the whole sample was divided into 2 groups: PAD (presence of PD and AG) and non-PAD (absence of PD and AG) through the use of a cutoff score of 16, able to discriminate between subjects with and without a clinically significant PAD, as shown by a recent study.<sup>15</sup>

The PAD group was composed by 30 individuals (31.6% of the sample) and consisted of 30 patients with ASD (100%) and no HCs (0%).

The non-PAD group numbered 65 subjects (68.4% of the sample) and was composed by 15 patients with ASD subjects (23.1%) and 50 HC (76.9%) (Table 3).

So, ASD subjects were found to be placed predominantly in the PAD group (66.7%) and for a small portion (33.3%) in the non-PAD group. In contrast, HCs were found to be 100% within the non-PAD group (Table 3).

**Regression analysis between AdAS Spectrum and PAS-SV total and domain scores**

A first linear regression analysis (Table 4) using AdAS Spectrum total score as the independent variable and PAS-SV total score as

**Table 5.** Logistic Regression Using AdAS Spectrum Domain Scores as Independent Variables and PAS-SV Total Score as the Dependent Variable

Total score	<i>B</i> (SE)	<i>P</i>	Beta	<i>t</i>
Restricted Interests and Rumination	1.024 (0.314)	0.002	0.456	3.259
Inflexibility and Adherence to Routine	−0.485 (0.161)	0.003	−0.388	−3.006

Adjusted  $R^2 = 0.568$ .**Table 6.** Logistic Regression Using AdAS Spectrum Domain Scores as Independent Variable and PAS-SV Domain Scores as the Dependent Variable

	<i>B</i>	<i>p</i>	<i>t</i>	Beta
Panic symptoms				
Inflexibility and Adherence to Routine	−0.108	0.021	−2.344	−0.287
Adjusted $R^2 = 0.611$				
Atypical panic symptoms				
Inflexibility and Adherence to Routine	−0.226	<0.01	−5.692	0.644
Restricted Interests and Rumination	0.303	0.001	3.930	0.483
Hyper–Hypo Reactivity to Sensory Input	194	0.044	2.043	0.238
Adjusted $R^2 = 0.422$				
Anxious expectations and maladaptive behaviors				
Inflexibility and Adherence to Routine	0.419	0.001	3.435	0.556
Restricted Interests and Rumination	0.575	0.045	2.038	0.466
Hyper–Hypo Reactivity to Sensory Input	−0.350	0.022	−2.336	−0.359
Adjusted $R^2 = 0.420$				
Agoraphobia				
Restricted Interests and Rumination	0.298	<0.01	3.782	0.613
Verbal Communication	0.670	<0.01	4.635	1.161
Childhood/Adolescence	−0.422	<0.01	−3.383	−0.873
Hyper–Hypo Reactivity to Sensory Input	−0.200	0.042	−2.062	−0.317

Adjusted  $R^2 = 0.420$ .

the dependent variable showed that a high PAS-SV total score would be predicted by a high AdAS Spectrum total score.

A second linear regression analysis (Table 5) was also performed using AdAS domain scores as independent variables and PAS-SV total score as the dependent variable, showing that a high score at Restricted Interests and Rumination and Inflexibility and Adherence to Routine AdAS Spectrum scores would be predictive, respectively, of a higher ( $B = 1.024$ ;  $p = 0.002$ ) and lower ( $B = -0.485$ ,  $p = 0.003$ ) PAS-SV total score.

A third set of linear regression analyses (Table 6) was conducted using AdAS Spectrum domain scores as independent variables and PAS-SV domain scores as the dependent variables, showing that higher score at the Inflexibility and Adherence to Routine AdAS Spectrum domain would predict lower scores at the Panic Symptoms PAS-SV domain ( $B = -0.108$ ;  $p = 0.021$ ). Higher score at the Inflexibility and Adherence to Routine AdAS Spectrum domain would predict lower scores at the Atypical Panic Symptoms PAS-SV domain ( $B = -0.226$ ,  $p < 0.01$ ), while higher scores at the Restricted Interests and Rumination (0.303;  $p < 0.01$ ;  $t = 3,930$ ) and Hyper–Hypo Reactivity to Sensory Input ( $B = 0.194$ ;  $p = 0.044$ ). AdAS Spectrum domains would be predictive of higher scores at the same PAS-SV domain. Higher score at the Restricted Interests and Rumination and Empathy AdAS Spectrum domains would be predictive of higher scores ( $B = 0.419$ ,  $p < 0.01$ ,  $t = 3,435$ ;  $B = 0.575$ ,  $p = 0.045$ ) at

the Anxious Expectations and Maladaptive Behaviors PAS-SV domain, while higher score at the Hyper–Hypo Reactivity to Sensory Input would be predictive of the lower scores ( $B = -0.350$ ,  $p = 0.022$ ). Higher score at the Restricted Interests and Rumination and Verbal Communication AdAS Spectrum domains would be predictive of higher ( $B = 0.298$ ,  $p < 0.01$ ;  $B = 0.670$ ,  $p < 0.01$ ) scores at the Agoraphobia PAS-SV domain, while Childhood/Adolescence and Hyper–Hypo Reactivity to Sensory Input would be predictive of lower ( $B = -0.422$ ,  $p = 0.001$ ;  $B = -0.200$ ,  $p = 0.042$ ) scores at the same PAS-SV domain.

## Discussion

The results of the study showed a significantly higher representation of panic-agoraphobic symptoms within the population with ASD compared to HCs, confirmed by the observation of a prevalence of ASD subjects within the group with panic-agoraphobic symptoms delineating a full-blown disorder. As mentioned in the Introduction, this initial finding appears to be in line with previous studies in the literature regarding the relationship between ADs and ASD; however, few studies have focused specifically on PD and AG in autism, especially in the adult population, from a dimensional perspective and with reference to the recent DSM-5 and



DSM-5-TR criteria. In fact, to the best of our knowledge, only one study in the literature seems to have investigated the presence of panic and AG symptoms in adults with ASD,<sup>16</sup> finding, in a sample of 34 autistic patients, significantly higher scores in the anxiety subscales of panic and AG than in HCs. Furthermore, Nimmo-Smith and colleagues<sup>6</sup> found a higher adjusted risks of PD in adults with ASD without intellectual disability (ID) had higher adjusted risks of PD than those without ID. It is important to note that PD was not considered as an exclusion criterion for the ASD group in our study. While individuals in the HC group were by definition free of a diagnosis of PD according to DSM-5 criteria, the same criteria were not applied to the ASD group. This may have influenced the composition of the ASD group and could potentially impact the interpretation of our findings.

Proceeding with the analysis of the results, the presence of significant autistic traits would increase the risk of presenting high panic-agoraphobic symptoms. At the basis of this finding, there could be numerous explanations. Behavioral alterations and difficulties in social interactions, as well as a misunderstanding of social signals, may predispose the individual to experiences of rejection and embarrassment.<sup>17</sup> Environmental stimuli could also be associated with an intrinsic biological vulnerability for anxiety symptoms, mediated, for example, by dysfunctions in the limbic system with a reduced arousal threshold at the amygdala level and behavioral inhibition.<sup>6,17</sup> Additionally, the atypical sensory processing typical of the disorder, present in 69–93% of ASD patients, including sensory hyper-responsiveness, could represent an additional predisposing factor to anxiety. In fact, effective sensory processing is essential for stress and danger management,<sup>18,19</sup> as well as for proper emotional regulation.<sup>20</sup> Some studies have identified a significant relationship between sensory processing difficulties and elevated anxiety symptoms in both autistic<sup>21</sup> and non-autistic individuals.<sup>7,22–24</sup> Furthermore, when controlling for autism traits, a recent study found that sensory hyper-reactivity is significantly related to separation anxiety,<sup>25</sup> which is a particularly interesting result considering that a childhood diagnosis of separation AD significantly increases the risk of adult-onset PD.<sup>26</sup>

The use of autism and panic-agoraphobia spectrum questionnaires has allowed us to analyze individual symptom domains belonging to both conditions, providing a more detailed picture of their relationship. Firstly, within the autism spectrum, the Restricted Interests and Rumination domain appears to increase the risk of obtaining a high PAS-SV total score. This result is broadly in line with literature data, which consistently demonstrate the association between restricted and repetitive behaviors (RRBs) and elevated anxiety symptoms in individuals with ASD.<sup>27</sup> Strong associations between studies have suggested that RRBs and anxiety symptoms are correlated, and the former precede the onset of the latter.<sup>27,28</sup> While RRBs may temporarily reduce anxiety symptoms, their perpetuation and amplification over time may distract from the implementation of adaptive coping mechanisms, thereby fueling feelings of anxiety. Therefore, their significant presence should raise concerns about the possible risk of developing ADs in the future, such as PD and AG, according to the results of our study.<sup>28</sup> Regarding the ruminative thinking, it has been proposed as a transdiagnostic construct associated with a wide range of anxiety, mood, personality, and post-traumatic stress disorders.<sup>29–31</sup> A recent study on a sample of 200 subjects with psychiatric diagnoses, including PD and AG, differentiated into 2 groups based on levels of mental rumination, demonstrated a specific association between the latter and the specific diagnosis of PD.<sup>31</sup>

On the contrary, the present study has highlighted how high inflexibility and adherence to routine may reduce the risk of experiencing panic-agoraphobic symptoms. This result could be explained by considering that individuals with ASD typically exhibit “intolerance of uncertainty,” characterized by the belief that uncertainty is negative and leads to poorer functioning in uncertain situations.<sup>33</sup> According to Pellicano and Burr (2012), difficulties in effectively dealing with uncertainty at the computational or neural level may give rise to psychological beliefs that uncertainty is negative and should be avoided. In order to reduce the sensation of uncertainty, individuals with autism may engage in increased mental rumination and hyper-vigilance to sensory stimuli, 2 factors that, in turn, contribute to elevated anxiety symptoms.<sup>34</sup> A rigid routine and inflexibility in habits, on the other hand, might enhance familiarity with frequented environments and reduce the likelihood of encountering unknown conditions, which are sources of uncertainty. This, in turn, makes the activation of mental rumination and hyper-vigilance to environmental stimuli less necessary, thereby providing protection against the development of panic-agoraphobic symptoms mediated by these factors. However, it is important to note that while this may serve as a strategy to avoid uncertainty, it may not necessarily be a functional coping strategy and may lean more towards avoidance. The findings discussed could also justify the observed protective role of inflexibility and adherence to routine in the presentation of typical and atypical panic symptoms, as further observed in the results of this study. According to our results, the risk of presenting atypical panic symptoms would instead be increased by the AdAS domains of altered sensitivity to sensory stimuli and mental rumination. Regarding the latter, we refer back to the concept discussed above of rumination as a transdiagnostic dimension and a factor in psychopathological maintenance. To offer possible explanations for the role of altered reactivity to sensory stimuli in increasing the risk of atypical panic symptoms, it is first necessary to reflect on the meaning of an “atypical” presentation of panic in individuals with ASD. Kerns and Kendall<sup>7</sup> proposed in their review that anxiety symptoms in individuals with ASD would be influenced in their manifestation by various factors, including verbal abilities and IQ, and could appear in both the expected form according to the DSM and in different ways. In a recent study, it was observed that in individuals with ASD, hypersensitivity positively predicted traditional anxiety symptoms but not atypical symptoms. In individuals with ASD and significant autistic traits, sensory sensitivity would be associated with a tendency to internalize experienced problems,<sup>35</sup> further increased by the typical camouflaging strategies employed by some autistic patients to compensate for the intrinsic difficulties of the disorder.<sup>36</sup> Anxiety symptoms in this subtype of ASD patients, characterized by high sensory alterations and a tendency to internalize, may therefore preferentially manifest in different or “atypical” ways than those traditionally understood in the DSM.

The panic-agoraphobic domain related to anxious expectation and maladaptive behaviors, representing the specification of Criterion B for PD,<sup>1</sup> is positively predicted by elevated levels of mental rumination and compromised empathy. It is not difficult to understand how rumination about the occurrence of panic attacks can strongly contribute to the development of anxious expectations and avoidance behaviors or other maladaptive behavioral strategies related to panic, thereby structuring a PD. The abstract and internal nature of rumination may indeed prevent the individual from responding adaptively to environmental changes or benefiting from corrective learning that allows the disconfirmation of negative

beliefs,<sup>37</sup> prompting avoidance. On the other hand, considering the importance of empathy in social interaction processes, it is understandable how atypical empathic responses can significantly contribute to the social difficulties of individuals with ASD, such as difficulties in understanding social dynamics, as well as related intense distress, contributing to anxious expectations and avoidance of social situations. Furthermore, reduced empathic abilities have been associated with lower emotional regulation skills and a greater tendency to act in socially and morally undesirable ways,<sup>38</sup> leading to the development of ADs through the genesis of uncontrollable and overwhelming emotional reactions.<sup>39</sup> Anxious expectations and maladaptive behaviors are, however, reduced in the presence of elevated levels of altered sensory sensitivity. Referring back to the possible explanation for the relationship between high sensory symptoms and increased atypical panic symptoms, it could be hypothesized that a greater tendency toward internalization and the development of camouflaging compensation strategies may reduce anxious expectations and replace the typical maladaptive behaviors reported in the DSM. The same reasoning, focused mainly on increased mimetic and compensatory abilities, could justify the observed protective role of altered sensory sensitivity in reducing agoraphobic behaviors, which are less represented even in the presence of high levels of autistic spectrum symptoms in childhood and adolescence, a factor that could certainly increase the likelihood of the individual building camouflaging strategies over time.

High levels of impairment in verbal communication, together with restricted interests and rumination, are predictive of pronounced agoraphobic behaviors. AG is notably characterized by the fear of not being able to independently find exits or receive help to leave a place from other people present.<sup>40</sup> In this regard, we believe that awareness of one's difficulties in verbal communication and thus not being able to make others understand the need for assistance may amplify the fear of being trapped in agoraphobic situations and increase the likelihood that such behaviors are perpetuated over time.

Some limitations in the present study should be taken into account: the relatively small sample size, the self-report nature of the questionnaires, which may have led to either overestimation or underestimation of the symptoms by the patients, and lastly, the cross-sectional design of the study, which restricts the exploration of temporal and causal relationships among the variables under investigation.

## Conclusion

In the perspective of characterizing ASD to enhance understanding of the complexity of this highly diverse neurodevelopmental syndrome and thereby improve diagnostic and treatment capabilities, the present study provides information on the presentation of the entire spectrum of panic-agoraphobic symptoms in ASD. It analyzes the interactions between these symptoms and specific autistic symptom domains. According to the observations, in conclusion, individuals with ASD are characterized by significantly higher levels of panic-agoraphobic symptoms compared to HCs, in most cases to the extent of outlining full-blown PD and AG disorders. The presence of significant autistic traits would also increase the risk of presenting symptoms within the panic-agoraphobic spectrum, with the domain most strongly associated being that related to restricted interests and rumination. Elevated levels of sameness, on the other hand, would protect against the development of such

manifestations, specifically typical and atypical panic symptoms. From the analysis of the interaction between individual autistic domains and panic-agoraphobic symptoms, it strongly emerges that inflexibility and rumination remained respectively negatively and positively predictive factors for the panic-agoraphobic spectrum as a whole. Other interactions between specific autistic and panic-agoraphobic symptom domains, discussed in the study, provide new insights into the relationship between autism and panic-agoraphobia, warranting, in our opinion, further in-depth researches.

**Author contribution.** Investigation: B.N., B.C., C.B., I.M.C., G.A.; Conceptualization: B.C., L.D., G.A.; Supervision: B.C., I.M.C., L.D.; Writing – review & editing: B.C., L.D.; Formal analysis: E.M.; Software: E.M.; Methodology: G.A.; Writing – original draft: G.A.

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