

Which panic-agoraphobic symptoms could be associated with the presence of autistic traits among patients with panic disorder?

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Abstract:

Objective: Panic Disorder (PD) is a psychopathological condition characterized by short-lived anxiety attacks in association with several physical symptoms followed by the fear of other attacks' possible occurrence or their consequences and avoidance behaviours. Recent literature highlighted a significant correlation between autism spectrum disorder (ASD) and anxiety disorder. To date the specific association between PD and autistic traits remains to be clarified. This study aimed to investigate the presence of an autism spectrum in patients with PD, specifically focusing on the presence of possible factors associated with these conditions.

Methods: 112 subjects were recruited: 55 subjects with a clinical diagnosis of PD and 57 healthy controls (HCs). All participants were evaluated with the Panic Agoraphobic Spectrum – Short Version (PAS-SV) and the Adult Autism Subthreshold Spectrum (AdAS Spectrum) questionnaire.

Results: Results outlined a significant correlation between agoraphobic-panic symptoms and autism spectrum, with significantly positive correlations of all AdAS Spectrum domains scores as well as its total score with all PAS-SV domains as well as with its total score. Moreover, atypical panic symptoms and anxious expectation and maladaptive behaviors were factors associated with a possible underlying presence of higher AT in PD subjects.

Conclusions: Our findings support the association between panic-agoraphobic dimension and ASD. Indeed, increased reactions to stressful life events due to autistic altered sensory reactivity may increase fears response such as anxious manifestations and maladaptive behaviours.

Keywords: autism spectrum disorder, autistic traits, panic disorder, agoraphobic disorder, panic-agoraphobic symptoms.

1. Introduction

Panic Disorder (PD) is a psychopathological condition included in the section “Anxiety Disorders” of the Diagnostic and Statistical Manual of Mental Disorders, 5th edition text revised (DSM-5 TR)¹. The clinical picture is characterized by short-lived anxiety attacks reaching their peak intensity in a few minutes in association with several physical symptoms¹. Moreover, panic attacks are frequently followed by the fear of other attacks’ possible occurrence or their consequences and avoidance behaviours, consisting in several maladaptive strategies to avoid the onset of a new crisis¹. To date, PD occurs together with Agoraphobic Disorder (AP) with a lifetime prevalence ranging between 0.5% to 1.8%^{2,3}. Indeed, PD often shares comorbidity with other anxiety disorders, major depression, and bipolar disorder¹.

A significant correlation between autism spectrum disorder (ASD) and anxiety disorders has been recently highlighted^{4,5}. Noteworthy, anxiety disorders range around 40% in young ASD patients⁵, while in adults they reach 84%⁴. Prevalence of anxiety disorders in autistic subjects is at least five times higher than in the general population⁶. For this reason, mood and anxious symptoms may overlap with ASD, making the diagnostic process more complex⁷. Recent research identified alexithymia, emotion regulation deficits, unknown intolerance, and sensory processing alterations as some of the most significant factors contributing to the development of anxious symptoms, and more specifically panic-agoraphobic symptoms, in autism^{8,9}.

According to the dimensional approach of “Spectrum Model”¹⁰⁻¹³, symptoms related to mental disorders are conceptualized as a continuum from the general to the clinical population, highlighting the importance of investigating not only full-fledged clinical pictures but also those symptoms and traits presenting as isolated, atypical or subthreshold features, which do not reach the diagnostic criteria but may nevertheless exert an impact on quality of life and/or complicate other comorbid conditions¹⁰⁻¹³.

In this framework, an increasing body of studies is highlighting the role of subthreshold autism symptoms in several psychiatric disorders¹⁴. The presence of a subthreshold autism spectrum was firstly investigated among first degree relatives of ASD probands, who often reported personal characteristics, behavioral and cognitive traits qualitatively similar to ASD symptoms, although not sufficient in number and/or intensity for reaching the clinical diagnosis¹⁵. Subsequently, autism spectrum symptoms were progressively conceptualized as a dimension continuously distributed in different population, with complete neurotypicality and full-fledged ASD at the extreme ends¹⁴.

Moreover, autistic traits seem particularly represented in specific populations, such as psychiatric patients affected by other mental conditions, for which autistic traits seem to constitute a vulnerability factor and contemporarily playing a detrimental role in the course of the disorder, including implying a higher suicidality risk.¹⁶⁻¹⁹

Despite several studies examined the existing relationship between anxiety disorder and ASD, and another study of our group highlighted greater panic-agoraphobic symptoms among patients with ASD²⁰ to date the specific association between PD and autistic traits remains to be clarified. In this perspective, this study aimed to investigate the presence of an autism spectrum in patients with PD, specifically focusing on the presence of possible factors associated with these conditions.

2. Materials and methods

2.1 Study sample and procedures

For this study, a total sample of 112 subjects was recruited between September 2022 and March 2023 at the Psychiatric clinic of the University of Pisa: 55 subjects with a clinical diagnosis of PD and 57 healthy controls (HCs). Subjects with intellectual disability, poor collaboration skills, an age under 18, language or intellectual impairment that would make it difficult to complete the exams, and continuous psychotic symptoms were excluded from the recruitment procedures. The study was conducted in accordance with the Declaration of Helsinki and the local Ethical Committee approved

the study protocol. All participants provided a written informed consent following a thorough explanation of the study and a chance for questions. All participants were evaluated with the Panic Agoraphobic Spectrum – Short Version (PAS-SV) and the Adult Autism Subthreshold Spectrum (AdAS Spectrum) questionnaire.

2.2 Measures

2.2.1 The PAS-SV

The PAS-SV is a self-report questionnaire composed of 78 dichotomous items, organized in 4 domains: panic symptoms, atypical panic symptoms, anxious expectation and maladaptive behavior, agoraphobia. The purpose of the questionnaire was to provide a valuable instrument for clinical practice and the study of panic-agoraphobic tendencies and panic attacks, both in its full-blown and milder subthreshold forms. During the validation study, the questionnaire showed good psychometric properties²¹.

2.2.2 The AdAS Spectrum

The AdAS Spectrum questionnaire is a 160-item self-report measure used to assess a wide variety of autism-related symptoms in individuals without cognitive or language impairments. The questionnaire is organized in 7 domains: *childhood and adolescence, verbal and nonverbal communication, empathy, inflexibility and adherence to routine, restricted interests and rumination, and hyper- and hyporeactivity to sensory input*. The questionnaire demonstrated strong internal consistency, outstanding test-retest reliability, and convergent validity with other dimensional measures of the autism spectrum were seen in the validation research²². The questionnaire also has two validated cut-off scores: 70 for identifying subjects with full-blown ASD, and 43 for determining the presence of significant autistic trait²³.

2.3 Statistical analysis

Chi-square and t-Student tests were used to compare sociodemographic characteristics between the two diagnostic groups. A further Chi-square analysis was used to compare the prevalence of clinically relevant autistic traits (ATs) or symptoms of possible full-blown ASD, based on the threshold score of the AdAS Spectrum, between the two diagnostic groups.

Subsequently, t-Student tests were used to compare AdAS Spectrum total and domains scores between the two groups. Pearson's correlation coefficients were then used to investigate the presence of significant correlations between AdAS Spectrum's and PAS-SV domains scores.

Lastly, using AdAS Spectrum total score as dependent variable and PAS-SV domains scores as independent variables, a linear regression analysis was performed in order to investigate the presence of possible factors associated with higher AdAS Spectrum total score among PAS-SV domains. All statistical analyses were performed with SPSS version 26.0.

3. Results

The total sample was made of 112 subjects divided in two categories: 55 subjects belonged to the PD (F=36; M=19; mean age: 42.22 ± 12.41 years) group and 57 to the HCs group (F=31; M=26; mean age: 38.21 ± 13.14 years). The two groups did not significantly differ for age or gender (see **Table 1**). Chi-square analysis showed that the PA group had a significantly higher percentage of subjects that showed clinically relevant ATs and full-blown ASD, according to the AdAS Spectrum threshold scores, compared to HCs (see **Table 2**). Student t-test results highlighted how PD subjects scored significantly higher than HCs in all AdAS Spectrum domains as well as in its total score (see **Table 3**). According to Pearson correlation analysis, all AdAS Spectrum domains scores as well as its total were significantly positively correlated with all PAS-SV domains as well as with its total (see **Table 4**). All correlations ranged from moderate to strong, with the only exception of PAS-SV *Agoraphobia* domain and AdAS Spectrum *Empathy* domain, for which the correlation coefficient was weak. Higher correlation coefficient scores were reported between AdAS Spectrum total score and PAS-SV total

and domains scores. From the linear regression analysis conducted, for which AdAS Spectrum total score was used as dependent variable and PAS-SV domains scores as independent variables, PAS-SV *Atypical panic symptoms* and *Anxious expectation and maladaptive behaviors* domains emerged as significant factor associated with a higher AdAS Spectrum total score (see **Table 5**).

4. Discussion

This study highlighted a significant correlation between agoraphobic-panic symptoms and autism spectrum. According to our data, patients with PD reported higher scores at AdAS Spectrum questionnaire. Conversely, all AdAS spectrum domains scores, and its total, were positively correlated with all PAS-SV domains and with the PAS-SV total score.

Research reported dysfunctional strategies in cognitive emotion regulation as a risk factor for anxiety disorders²⁴. Autistic subjects, in turn, are more prone since childhood to negative expectations about the future, poorer beliefs about their abilities, and greater self-blame. These dysfunctional cognitive evaluations are associated with increased levels of anxiety²⁵⁻²⁶ and maladaptive behaviors²⁷⁻²⁹ related to panic disorder. Current literature revealed a strong association between ASD and anxiety disorders (AD), although underlying psychopathological mechanisms remain poorly understood³⁰⁻³³. To date, very few studies focused on the presence of autistic traits (AT) in subjects with PD without a formal diagnosis of ASD²⁰. Panic-agoraphobic symptoms are a transdiagnostic entity often associated with a wide range of atypical and subthreshold manifestations, not necessarily codified in the DSM criteria. Among these, maladaptive behaviours such as increased sensitivity to medication and reassurance, separation anxiety, are also present in several patients suffering from PD or AP¹¹. In this perspective, several studies widely demonstrated that ASD subjects may express anxiety throughout atypical patterns or maladaptive behaviours, including unusual phobias³⁴⁻³⁵. According to our findings, both the specific domains of PAS-SV “*atypical symptoms*” and “*anxious expectation/maladaptive behaviours*” showed the strongest associations with the “*Hyper/Hypo Reactivity to sensory inputs*”

of AdAS Spectrum questionnaire. Previous research highlighted a significant correlation between autistic atypical responses to sensory inputs, and the atypical anxious manifestations or maladaptive behaviours^{34,36-37}. In this framework, sensory processing difficulties may predict anxiety manifestations in ASD subjects³⁷⁻⁴⁴. Finally, a tangible connection between the altered perceptions processing and emotional problems was observed in young ASD patients using electrophysiological studies⁴⁵.

Our study also showed that PD subjects who scored higher at the *Hyper/hyporeactivity to sensory inputs* domain of AdAS spectrum also presented higher levels of “*Panic symptoms*” and “*Panic symptoms perception*” domains scores. Starting from a neuro-anatomic point of view, this relationship could be explained by the role of the altered reactivity to sensory stimuli⁴⁶ due to limbic and glutamatergic system alterations⁴⁶⁻⁴⁸. According to the “Intense World Theory”, autistic subjects present hyperactivation of the glutamatergic circuits, leading to hyper-perception, hyper-attention and hyper-memory, together with hyper-emotionality deriving from amygdala altered function⁴⁹⁻⁵⁰. Noteworthy, when present at extreme levels, the perception of external stimuli may become extremely intense, and the memory of stressful events will also be more persistent and vivid, making these subjects unable to manage the external world information⁴⁹⁻⁵¹. In this perspective, the re-experiencing of minor traumatic events, due to the intense autistic ruminative activity, leads to the development of post-traumatic stress trajectories²⁰. As a result, autistic subjects would manifest increased reactions to stressful life events^{31,49,52-55}. Therefore, minimal stressing stimuli could represent a significant trigger to determine exaggerated fears response such as anxious manifestations and maladaptive behaviours⁴⁹. Moreover, while the autistic-like atypical brain may increase the ability to perform certain tasks in which the autistic subject excels, on the other hand, it could favor the development of repetitive behaviors and adherence to routines in order to reduce the possibility of encountering adverse or unexpected events⁵⁶. These behaviors, to a certain extent, may recall the maladaptive behaviors that patients with PD put into practice, with the purpose of reducing the risk of adverse

events that could trigger a panic attack. Thus, our findings confirm previous literature. Indeed, linear regression analyses revealed that “*atypical panic symptoms*” and “*anxious expectation and maladaptive behaviors*” PAS-SV domains are factors associated with a higher AdAS Spectrum total score.

Noteworthy, *anxious expectation and maladaptive behavior* PAS-SV domain was also highly correlated with the AdAS “*Restricted Interests and Rumination*” domain. Recurrent thinking is related to panic attacks and fear of consequences^{52,57} and may predict PD or AP⁵⁸⁻⁵⁹. However, ruminative thinking recurs in several psychiatric conditions such as ASD⁶⁰⁻⁶¹, hampering the correct coping strategies through the re-experiencing of stressful life events^{57,62}. The restricted and repetitive behaviors/thinking would represent an attempt to adapt to stressful external stimuli, overrepresented and altered in the world of autistic subjects⁴⁹, thus increasing anxiety. Moreover, the scarce tolerance to uncertain situations, and the consequently need to maintain rigid patterns of thinking and behavior, would justify increased anxious manifestations in autistic subjects⁶³⁻⁶⁵. In line with this model, several domains of PAS-SV were positively related to “*Inflexibility and Adherence to routine*” domain. According to our findings, autistic impairments in Verbal (and non-verbal) communication could also contribute to the correlation between AT and several PAS-SV domains. Indeed, altered communication leads to a reduced verbalization of internal stressful thinking and feelings, with consequent anxious manifestations, including both typical and atypical anxious symptoms^{35,66-67}. Furthermore, it is known that the limited skills in social interactions, as well as the misunderstanding of social signals⁶⁸⁻⁶⁹ expose autistic subjects to social rejection, embarrassment, and bullying⁷⁰⁻⁷¹. These episodes may lead to the increase of anxiety, anxious expectations and avoidance of social events, with the occurrence of panic-agoraphobic symptoms.

This study should be considered in lights of some limitations. First of all, the small sample size may limit the generalizability of our results. Moreover, the use of self-reported instrument may expose to bias related to over- or under-estimation of symptoms by participants. In addition, the cross-sectional design of the study did not allow us to make inferences about possible temporal or causal relationships

between the investigated variables. Finally, our work has been conducted on a non-autistic population and results might be not generalizable to autistic subjects.

Globally, our study confirmed the existence of a statistically significant relationship autism and panic-agoraphobic spectra. PD subjects reported higher AT, with all AdAS Spectrum domains scores as well as its total significantly positively correlated with all PAS-SV scores. Results highlighted that *atypical panic symptoms* and *anxious expectations*, and *maladaptive behaviors* are factors associated with an underlying presence of higher AT in PD subjects. In this framework, autistic altered reactivity to sensory input may play a central role. Increased reactions to stressful life events may lead to increased fears response such as anxious manifestations and maladaptive behaviours ascribable to PD dimension.

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The authors declare no conflict of interest.

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All data generated or analyzed during this study are included in this published article.

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Patient consent statement:

All recruited subjects consented to participate in the study.

Author Contributions:

Conceptualization: B.C., L.D.O; Methodology: B.C., I.M.C., S.P., L.D.O.; Formal analysis: B.C., G.M.; Investigation: B.C., B.N., C.B., G.C., D.L., F.P., C.P.; Supervision: B.C., I.M.C., L.D.O.; Writing original draft: C.B., C.P., G.C.; Writing review and editing: B.N., B.C., A.F.

5. References

1. American Psychiatric Association. (2022). *Diagnostic and Statistical Manual for Mental disorders* 5th edition, text revised. American Psychiatric Publishing.
2. Greene AL, Eaton NR. Panic disorder and agoraphobia: A direct comparison of their multivariate comorbidity patterns. *J Affect Disord.* 2016 Jan 15;190:75-83. doi: 10.1016/j.jad.2015.09.060. Epub 2015 Oct 9. PMID: 26480214.
3. Wittmann A, Schlagenhauf F, Guhn A, Lueken U, Gachlsdorf C, Stoy M, Bermpohl F, Fydrich T, Pfleiderer B, Bruhn H, Gerlach AL, Kircher T, Straube B, Wittchen HU, Arolt V, Heinz A, Ströhle A. Anticipating agoraphobic situations: the neural correlates of panic disorder with agoraphobia. *Psychol Med.* 2014 Aug;44(11):2385-96. doi: 10.1017/S0033291713003085. Epub 2014 Jan 7. PMID: 24398049.
4. Postorino V., Kerns CM, Vivanti G., Bradshaw J., Siracusano M., Mazzone L. (2017). Anxiety disorders and obsessive-compulsive disorder in individuals with autism spectrum disorder. *Current Psychiatry Reports*
5. van Steensel FJA, Bogels SM, Perrin S. (2011). Anxiety disorders in children and adolescents with autism spectrum disorders: a meta-analysis.
6. Kerns CM, Kendall PC, Berry L, Souders MC, Franklin ME, Schultz RT, Miller J, Herrington J. Traditional and atypical presentations of anxiety in youth with autism spectrum disorder. *J Autism Dev Disord.* 2014 Nov;44(11):2851-61. doi: 10.1007/s10803-014-2141-7. PMID: 24902932; PMCID: PMC5441227.

7. Wittkopf S, Stroth S, Langmann A, Wolff N, Roessner V, Roepke S, Poustka L, Kamp-Becker I. Differentiation of autism spectrum disorder and mood or anxiety disorder. *Autism*. 2022 Jul
8. MacLennan K, Rossow T, Tavassoli T. The relationship between sensory reactivity, intolerance of uncertainty and anxiety subtypes in preschool-age autistic children. *Autism*. 2021 Nov;25(8):2305-2316. doi: 10.1177/13623613211016110. Epub 2021 May 24. PMID: 34030518.
9. Kossowsky J, Pfaltz MC, Schneider S, Taeymans J, Locher C, Gaab J. The separation anxiety hypothesis of panic disorder revisited: a meta-analysis. *Am J Psychiatry*. 2013 Jul;170(7):768-81. doi: 10.1176/appi.ajp.2012.12070893. PMID: 23680783.
10. Dell'Osso L, Nardi B, Bonelli C, Gravina D, Benedetti F, Del Prete L, Massimetti G, Amatori G, Carpita B, Cremone IM. Validation of the short version of the obsessive compulsive spectrum questionnaire. *Front Psychol*. 2023 Jun 27;14:1157636. doi: 10.3389/fpsyg.2023.1157636. PMID: 37441332; PMCID: PMC10333544.
11. Dell'Osso L, Amatori G, Cremone IM, Massimetti E, Nardi B, Gravina D, Benedetti F, Muscatello MRA, Pompili M, Politi P, Vita A, Maj M, Carpita B. Autistic and Catatonic Spectrum Symptoms in Patients with Borderline Personality Disorder. *Brain Sci*. 2023 Aug 7;13(8):1175. doi: 10.3390/brainsci13081175. PMID: 37626531; PMCID: PMC10452061.
12. Dell'Osso L, Cremone IM, Nardi B, Amatori G, Bonelli C, Gravina D, Benedetti F, Del Prete L, Massimetti G, Carpita B. Measuring the neglected anxiety disorder: validation of the social anxiety spectrum-short version (SHY-SV) questionnaire. *BMC Psychiatry*. 2023 Oct 2;23(1):708. doi: 10.1186/s12888-023-05137-5. PMID: 37784074; PMCID: PMC10544616.
13. Cassano GB, Dell'Osso L, Frank E, Miniati M, Fagiolini A, Shear K, Pini S, Maser J. The bipolar spectrum: a clinical reality in search of diagnostic criteria and an assessment methodology. *J Affect Disord*. 1999 Aug;54(3):319-28. doi: 10.1016/s0165-0327(98)00158-x. PMID: 10467978.

14. Dell'Osso L, Lorenzi P, Carpita B. Autistic Traits and Illness Trajectories. *Clin Pract Epidemiol Ment Health*. 2019 Aug 30;15:94-98. doi: 10.2174/1745017901915010094. PMID: 31819756; PMCID: PMC6882132.
15. Carpita B, Carmassi C, Calderoni S, Muti D, Muscarella A, Massimetti G, Cremone IM, Gesi C, Conti E, Muratori F, Dell'Osso L. The broad autism phenotype in real-life: clinical and functional correlates of autism spectrum symptoms and rumination among parents of patients with autism spectrum disorder - Corrigendum. *CNS Spectr*. 2021 Aug;26(4):435. doi: 10.1017/S109285292000139X. Epub 2020 Jun 4. Erratum for: *CNS Spectr*. 2020 Dec;25(6):765-773. doi: 10.1017/S1092852919001615. PMID: 32493519.
16. Dell'Osso L., Cremone I. M., Chiarantini I., Nardi B., Pronestì C., Amatori G., Massimetti E., Signorelli M.S., Rocchetti M., Castellini G., Aguglia E., Politi P., Ricca V., Pini S., Carpita B. Autistic traits are associated with the presence of post-traumatic stress symptoms and suicidality among subjects with Autism spectrum conditions and Anorexia nervosa. 2024, *Journal of Psychiatric Research*, DOI:10.1016/j.jpsychires.2024.12.006.
17. Carpita B, Amatori G, Cremone IM, Bonelli C, Nardi B, Massimetti G, Pini S, Dell'Osso L. Major Depressive Disorder with Catatonia: A Phenotype Related to Autistic Traits and High Suicidality. *J Clin Med*. 2024 Aug 14;13(16):4796. doi: 10.3390/jcm13164796. PMID: 39200938; PMCID: PMC11355098.
18. Cremone IM, Nardi B, Amatori G, Palego L, Baroni D, Casagrande D, Massimetti E, Betti L, Giannaccini G, Dell'Osso L, Carpita B. Unlocking the Secrets: Exploring the Biochemical Correlates of Suicidal Thoughts and Behaviors in Adults with Autism Spectrum Conditions. *Biomedicines*. 2023 May 31;11(6):1600. doi: 10.3390/biomedicines11061600. PMID: 37371695; PMCID: PMC10295407.
19. Dell'Osso L, Nardi B, Bonelli C, Gravina D, Benedetti F, Amatori G, Battaglini S, Massimetti G, Luciano M, Berardelli I, Brondino N, De Gregorio M, Deste G, Nola M, Reitano A, Muscatello MRA, Pompili M, Politi P, Vita A, Carmassi C, Cremone IM, Carpita B, Maj M.

- Investigating suicidality across the autistic-catatonic continuum in a clinical sample of subjects with major depressive disorder and borderline personality disorder. *Front Psychiatry*. 2023 May 18;14:1124241. doi: 10.3389/fpsyt.2023.1124241. PMID: 37275986; PMCID: PMC10234210.
20. Dell'Osso L, Amatori G, Bonelli C, Nardi B, Massimetti E, Cremone IM, Carpita B. Panic-agoraphobic symptoms in adults with ASD: the role of ruminative thinking and inflexibility. *CNS Spectr*. 2024 May 9:1-7. doi: 10.1017/S1092852924000282. Epub ahead of print. PMID: 38720482.
21. Dell'Osso L, Amatori G, Nardi B, Bonelli C, Gravina D, Benedetti F, Massimetti E, Cremone IM, Carpita B. Validation of the Short Version of the Panic Agoraphobic Spectrum (PAS-SV) Questionnaire. *Clin Neuropsychiatry*. 2023 Apr;20(2):151-156. doi: 10.36131/cnfioritieditore20230207. PMID: 37234359; PMCID: PMC10206642.
22. Dell'Osso L, Gesi C, Massimetti E, Cremone IM, Barbuti M, Maccariello G, Moroni I, Barlati S, Castellini G, Luciano M, Bossini L, Rocchetti M, Signorelli M, Aguglia E, Fagiolini A, Politi P, Ricca V, Vita A, Carmassi C, Maj M. Adult Autism Subthreshold Spectrum (AdAS Spectrum): Validation of a questionnaire investigating subthreshold autism spectrum. *Compr Psychiatry*. 2017 Feb;73:61-83. doi: 10.1016/j.comppsy.2016.11.001.
23. Dell'Osso L, Carmassi C, Cremone IM, Muti D, Salerni A, Barberi FM, Massimetti E, Gesi C, Politi P, Aguglia E, Maj M, Carpita B. Defining the Optimal Threshold Scores for Adult Autism Subthreshold Spectrum (AdAS Spectrum) in Clinical and General Population. *Clin Pract Epidemiol Ment Health*. 2020 Dec 31;16:204-211. doi: 10.2174/1745017902016010204. PMID: 33719360; PMCID: PMC7931149.
24. Samson, A. C., Hardan, A. Y., Podell, R. W., Phillips, J. M., & Gross, J. J. (2015). Emotion regulation in children and adolescents with autism spectrum disorder. *Autism Research*, 8(1), 9-18.

25. Sharma, S., Woolfson, L. M., & Hunter, S. C. (2014). Maladaptive cognitive appraisals in children with high-functioning autism: Associations with fear, anxiety and theory of mind. *Autism*, 18(3), 244-254.
26. Gillott, A., Furniss, F., & Walter, A. (2001). Anxiety in high-functioning children with autism. *Autism*, 5(3), 277-286.
27. Xie, Shuqi, et al. "Adolescent anxiety disorders and the developing brain: comparing neuroimaging findings in adolescents and adults." *General Psychiatry* 34.4 (2021).
28. Jahromi, L. B., Meek, S. E., & Ober-Reynolds, S. (2012). Emotion regulation in the context of frustration in children with high functioning autism and their typical peers. *Journal of Child Psychology and Psychiatry*, 53(12), 1250-1258.
29. Rieffe, C., Oosterveld, P., Terwogt, M. M., Mootz, S., Van Leeuwen, E., & Stockmann, L. (2011). Emotion regulation and internalizing symptoms in children with autism spectrum disorders. *Autism*, 15(6), 655-670.
30. Lai, M. C., Lombardo, M. V., & Baron-Cohen, S. (2014). Autism. *Lancet* (London, England), 383(9920), 896–910. [https://doi.org/10.1016/S0140-6736\(13\)61539-1](https://doi.org/10.1016/S0140-6736(13)61539-1)
31. Ng-Cordell, E., Wardell, V., Stewardson, C., & Kerns, C. M. (2022). Anxiety and Trauma-Related Disorders in Children on the Autism Spectrum. *Current psychiatry reports*, 24(3), 171–180. <https://doi.org/10.1007/s11920-022-01331-6>
32. Chan, N., Fenning, R. M., & Neece, C. L. (2023). Prevalence and Phenomenology of Anxiety in Preschool-Aged Children with Autism Spectrum Disorder. *Research on child and adolescent psychopathology*, 51(1), 33–45. <https://doi.org/10.1007/s10802-022-00964-8>
33. Micai, M., Fatta, L. M., Gila, L., Caruso, A., Salvitti, T., Fulceri, F., Ciaramella, A., D'Amico, R., Del Giovane, C., Bertelli, M., Romano, G., Schünemann, H. J., & Scattoni, M. L. (2023). Prevalence of co-occurring conditions in children and adults with autism spectrum disorder: A systematic review and meta-analysis. *Neuroscience and biobehavioral reviews*, 155, 105436. <https://doi.org/10.1016/j.neubiorev.2023.105436>.

34. Kerns, C. M., Winder-Patel, B., Iosif, A. M., Nordahl, C. W., Heath, B., Solomon, M., & Amaral, D. G. (2021). Clinically Significant Anxiety in Children with Autism Spectrum Disorder and Varied Intellectual Functioning. *Journal of clinical child and adolescent psychology: the official journal for the Society of Clinical Child and Adolescent Psychology*, American Psychological Association, Division 53, 50(6), 780–795. <https://doi.org/10.1080/15374416.2019.1703712>
35. Ng-Cordell, E., Wardell, V., Stewardson, C., & Kerns, C. M. (2022). Anxiety and Trauma-Related Disorders in Children on the Autism Spectrum. *Current psychiatry reports*, 24(3), 171–180. <https://doi.org/10.1007/s11920-022-01331-6>
36. Mayes SD, Calhoun SL, Aggarwal R, Baker C, Mathapati S, Molitoris S, et al. Unusual fears in children with autism. *Research in Autism Spectrum Disorders*. 2013; 7:151–158. DOI: 10.1016/j.rasd.2012.08.002
37. Lau, B. Y., Leong, R., Uljarevic, M., Lerh, J. W., Rodgers, J., Hollocks, M. J., South, M., McConachie, H., Ozsivadjian, A., Van Hecke, A., Libove, R., Hardan, A., Leekam, S., Simonoff, E., & Magiati, I. (2020). Anxiety in young people with autism spectrum disorder: Common and autism-related anxiety experiences and their associations with individual characteristics. *Autism: the international journal of research and practice*, 24(5), 1111–1126. <https://doi.org/10.1177/1362361319886246>
38. Bang, P., Andemichael, D. K., Pieslinger, J. F., & Igelström, K. (2024). Sensory symptoms associated with autistic traits and anxiety levels in children aged 6-11 years. *Journal of neurodevelopmental disorders*, 16(1), 45. <https://doi.org/10.1186/s11689-024-09562-9>
39. McCormick, C., Hepburn, S., Young, G. S., and Rogers, S. J. (2016). Sensory symptoms in children with autism spectrum disorder, other developmental disorders and typical development: a longitudinal study. *Autism* 20, 572–579. doi: 10.1177/1362361315599755
40. Sparks, A., Gilbert Evans, S., Javadi, M., Lasalandra, B., Martens, E., Venkatesh, R., Vaccarino, I. T., & Vaccarino, A. L. (2024). Assessment of anxiety in children with

neurodevelopment disorders: Rasch analysis of the Spence Children's Anxiety Scale. *Frontiers in psychiatry*, 15, 1240357. <https://doi.org/10.3389/fpsyt.2024.1240357>

41. Robertson, A. E., and Simmons, D. R. (2013). The relationship between sensory sensitivity and autistic traits in the general population. *J. Autism Dev. Disord.* 43, 775–784. doi: 10.1007/s10803
42. Kamio, Y., Inada, N., Moriwaki, A., Kuroda, M., Koyama, T., Tsujii, H., et al. (2013). Quantitative autistic traits ascertained in a national survey of 22 529 Japanese schoolchildren. *Acta Psychiatr. Scand.* 128, 45–53. doi: 10.1111/acps.12034
43. Horder, J., Wilson, C. E., Mendez, M. A., and Murphy, D. G. (2014). Autistic traits and abnormal sensory experiences in adults. *J. Autism Dev. Disord.* 44, 1461–1469. doi: 10.1007/s10803-013-2012-7
44. Amos, G. A., Byrne, G., Chouinard, P. A., & Godber, T. (2019). Autism Traits, Sensory Over-Responsivity, Anxiety, and Stress: A Test of Explanatory Models. *Journal of autism and developmental disorders*, 49(1), 98–112. <https://doi.org/10.1007/s10803-018-3695-6>
45. Carter Leno, V., Chandler, S., White, P., Yorke, I., Charman, T., Pickles, A., & Simonoff, E. (2018). Alterations in electrophysiological indices of perceptual processing and discrimination are associated with co-occurring emotional and behavioural problems in adolescents with autism spectrum disorder. *Molecular autism*, 9, 50. <https://doi.org/10.1186/s13229-018-0236-2>
46. Tsuji, Y., Imaizumi, S., Sugawara, M., & Oiji, A. (2022). Internalizing problems and suffering due to sensory symptoms in children and adolescents with and without autism spectrum disorder. *Frontiers in psychology*, 13, 872185. <https://doi.org/10.3389/fpsyg.2022.872185>
47. Bellini S. The Development of Social Anxiety in Adolescents With Autism Spectrum Disorders. *Focus on Autism and Other Developmental Disabilities*. 2006;21(3):138-145.

48. Nimmo-Smith, V., Heuvelman, H., Dalman, C., Lundberg, M., Idring, S., Carpenter, P., Magnusson, C., & Rai, D. (2020). Anxiety Disorders in Adults with Autism Spectrum Disorder: A Population-Based Study. *Journal of autism and developmental disorders*, 50(1), 308–318. <https://doi.org/10.1007/s10803-019-04234-3>
49. Markram K, Markram H. The intense world theory - a unifying theory of the neurobiology of autism. *Front Hum Neurosci*. 2010 Dec 21;4:224. doi: 10.3389/fnhum.2010.00224. PMID: 21191475; PMCID: PMC3010743.
50. Markram H, Rinaldi T, Markram K. The intense world syndrome--an alternative hypothesis for autism. *Front Neurosci*. 2007 Oct 15;1(1):77-96. doi: 10.3389/neuro.01.1.1.006.2007. PMID: 18982120; PMCID: PMC2518049.
51. Haruvi-Lamdan N, Horesh D, Golan O. PTSD and autism spectrum disorder: Co-morbidity, gaps in research, and potential shared mechanisms. *Psychol Trauma*. 2018 May;10(3):290-299. doi: 10.1037/tra0000298. Epub 2017 Jul 20. PMID: 28726442.
52. Dell'Osso, L., Amatori, G., Bonelli, C., Nardi, B., Massimetti, E., Cremone, I. M., & Carpita, B. (2024). Autistic traits underlying social anxiety, obsessive-compulsive, and panic disorders. *CNS spectrums*, 1–34. Advance online publication. <https://doi.org/10.1017/S1092852924000154>
53. Rumball, F., Happé, F., & Grey, N. (2020). Experience of Trauma and PTSD Symptoms in Autistic Adults: Risk of PTSD Development Following DSM-5 and Non-DSM-5 Traumatic Life Events. *Autism research: official journal of the International Society for Autism Research*, 13(12), 2122–2132. <https://doi.org/10.1002/aur.2306>
54. Agebjörn, J., Gillberg, C., Eberhard, J., Billstedt, E., & Nyrenius, J. (2024). Association Between Autism and PTSD Among Adult Psychiatric Outpatients. *Journal of autism and developmental disorders*, 10.1007/s10803-024-06439-7. Advance online publication. <https://doi.org/10.1007/s10803-024-06439-7>

55. Demartini, B., Ingrosso, G., Serio, F., Nisticò, V., Broglia, G., Bertani, A., Faggioli, R., Gambini, O., Massimetti, G., Dell'Osso, L., & Carpita, B. (2024). Prevalence of autistic traits and their relationships with other psychopathological domains in young adults seeking psychiatric attention: a cluster analysis. *European psychiatry: the journal of the Association of European Psychiatrists*, 67(1), e71. <https://doi.org/10.1192/j.eurpsy.2024.1791>
56. Dell'Osso, L., Amatori, G., Giovannoni, F., Massimetti, E., Cremone, I. M., & Carpita, B. (2024). Rumination and altered reactivity to sensory input as vulnerability factors for developing post-traumatic stress symptoms among adults with autistic traits. *CNS spectrums*, 29(2), 119–125. <https://doi.org/10.1017/S1092852924000014>
57. Riley, K. E., Park, C. L., & Laurenceau, J. P. (2019). A Daily Diary Study of Rumination and Health Behaviors: Modeling Moderators and Mediators. *Annals of behavioral medicine : a publication of the Society of Behavioral Medicine*, 53(8), 743–755. <https://doi.org/10.1093/abm/kay081>
58. Drost, J., van der Does, W., van Hemert, A. M., Penninx, B. W., & Spinhoven, P. (2014). Repetitive negative thinking as a transdiagnostic factor in depression and anxiety: A conceptual replication. *Behaviour research and therapy*, 63, 177–183. <https://doi.org/10.1016/j.brat.2014.06.004>
59. Silveira, É. M., Júnior, Passos, I. C., Scott, J., Bristot, G., Scotton, E., Teixeira Mendes, L. S., Umpierre Knackfuss, A. C., Gerchmann, L., Fijtman, A., Trasel, A. R., Salum, G. A., & Kauer-Sant'Anna, M. (2020). Decoding rumination: A machine learning approach to a transdiagnostic sample of outpatients with anxiety, mood and psychotic disorders. *Journal of psychiatric research*, 121, 207–213. <https://doi.org/10.1016/j.jpsychires.2019.12.005>
60. McEvoy, P. M., Watson, H., Watkins, E. R., & Nathan, P. (2013). The relationship between worry, rumination, and comorbidity: evidence for repetitive negative thinking as a transdiagnostic construct. *Journal of affective disorders*, 151(1), 313–320. <https://doi.org/10.1016/j.jad.2013.06.014>

61. Watkins, E. R., & Roberts, H. (2020). Reflecting on rumination: Consequences, causes, mechanisms and treatment of rumination. *Behaviour research and therapy*, 127, 103573. <https://doi.org/10.1016/j.brat.2020.103573>
62. Luca M. (2019). Maladaptive Rumination as a Transdiagnostic Mediator of Vulnerability and Outcome in Psychopathology. *Journal of clinical medicine*, 8(3), 314. <https://doi.org/10.3390/jcm8030314>
63. Wells, A., (2009). *Metacognitive Therapy for Anxiety and Depression*. Guilford New York
64. Fergus, T. A., Valentiner, D. P., McGrath, P. B., Gier-Lonsway, S., & Jencius, S. (2013). The cognitive attentional syndrome: examining relations with mood and anxiety symptoms and distinctiveness from psychological inflexibility in a clinical sample. *Psychiatry research*, 210(1), 215–219. <https://doi.org/10.1016/j.psychres.2013.04.020>
65. Shi, H., & Hirai, M. (2024). Autistic traits linked to anxiety and dichotomous thinking: sensory sensitivity and intolerance of uncertainty as mediators in non-clinical population. *Scientific reports*, 14(1), 23334. <https://doi.org/10.1038/s41598-024-73628-w>
66. Oakley, B. F. M., Jones, E. J. H., Crawley, D., Charman, T., Buitelaar, J., Tillmann, J., Murphy, D. G., Loth, E., & EU-AIMS LEAP Group (2022). Alexithymia in autism: cross-sectional and longitudinal associations with social-communication difficulties, anxiety and depression symptoms. *Psychological medicine*, 52(8), 1458–1470. <https://doi.org/10.1017/S0033291720003244>
67. Hobson, H., Hogeveen, J., Brewer, R., Catmur, C., Gordon, B., Krueger, F., Chau, A., Bird, G., & Grafman, J. (2018). Language and alexithymia: Evidence for the role of the inferior frontal gyrus in acquired alexithymia. *Neuropsychologia*, 111, 229–240. <https://doi.org/10.1016/j.neuropsychologia.2017.12.037>
68. Rigby, S. N., Stoesz, B. M., & Jakobson, L. S. (2018). Empathy and face processing in adults with and without autism spectrum disorder. *Autism research: official journal of the International Society for Autism Research*, 11(6), 942–955. <https://doi.org/10.1002/aur.1948>

69. Pepper, K. L., Demetriou, E. A., Park, S. H., Boulton, K. A., Hickie, I. B., Thomas, E. E., & Guastella, A. J. (2019). Self-reported empathy in adults with autism, early psychosis, and social anxiety disorder. *Psychiatry research*, 281, 112604. <https://doi.org/10.1016/j.psychres.2019.112604>
70. Domes, G., Spenthof, I., Radtke, M., Isaksson, A., Normann, C., & Heinrichs, M. (2016). Autistic traits and empathy in chronic vs. episodic depression. *Journal of affective disorders*, 195, 144–147. <https://doi.org/10.1016/j.jad.2016.02.006>
71. Trundle, G., Jones, K. A., Ropar, D., & Egan, V. (2023). Prevalence of Victimization in Autistic Individuals: A Systematic Review and Meta-Analysis. *Trauma, violence & abuse*, 24(4), 2282–2296. <https://doi.org/10.1177/15248380221093689>