

# Autism Spectrum Disorder and Anorexia Nervosa. Is There a Link? An Italian Experience

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## Research

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# Abstract

**Background:** Potential overlaps exist between psychopathological features of Anorexia Nervosa (AN) and Autism Spectrum Disorder (ASD). The impact of malnutrition on autistic traits in patients with AN should be considered. This study aims to investigate possible associations between Eating Disorders (ED) psychopathology, ASD traits and BMI in a group of young patients with AN, using the EDI-3 (Eating Disorder Inventory-3) test and gold-standard measures for ASD.

**Methods:** Prospective study involving 23 inpatients admitted to an Italian Centre for paediatric ED. ASD traits and ED psychopathology were assessed administering ADOS-2 (Autism Diagnostic Observation Schedule-2), AQ (Autism Quotient) and EDI-3 tests. Both present and past autistic traits were investigated using different versions of AQ. Possible effect of BMI, Obsessive Compulsive Disorder (OCD) comorbidity and psychopharmacological treatments on results were evaluated with multiple linear regressions.

**Results:** An ASD diagnosis was possible in 22% of patients. EDI-3 Interpersonal Problems (IPC), Affective Problems (APC), and Global Psychological Maladjustment (GPMC) subscales showed correlations with different ASD measures on ADOS-2 and AQ. Scores for ASD and their correlations with EDI-3 subscales were independent of BMI, age, OCD and psychopharmacological treatments.

**Conclusions:** ASD traits presented high prevalence in a group of young inpatients with AN. These traits were significantly correlated to 3 specific EDI-3 subscales and independent of BMI. This is the first study to investigate the relationship between ASD traits as measured with gold-standard measures, EDI-3 scores, and BMI.

## Highlights

- In young patients with Anorexia Nervosa, scores on specific EDI-3 subscales assessing Eating Disorders psychopathology correlated with specific autistic traits, as measured by ADOS-2 and AQ.
- EDI-3 Interpersonal Problems (IPC), Affective Problems (APC), and Global Psychological Maladjustment (GPMC) displayed significant correlations with scores for autistic traits, mainly AQ Total, Social Skills, Attention Switching and Communication scores and ADOS-2 imagination score.
- The relationship between Eating Disorders psychopathology and autistic traits was independent of BMI, age, OCD comorbidity and psychopharmacological treatments.

## Main Text

### Introduction and aims

Eating Disorders (EDs) are pathologic conditions characterized by a persistent disturbance of eating or eating-related behaviour, resulting in altered consumption of food and significantly psychosocial functioning (APA, 2013). Anorexia nervosa (AN) is a severe ED, characterized by significantly low body

weight, intense fear of gaining weight, and undue influence of weight and shape on self-evaluation. AN has one of the highest prevalence among EDs: 1.4% for women and 0.2% for men (Galmiche et al., 2019). The incidence of AN requiring inpatient treatment in Italy for the age group 10–19 years is 22.8 per 100.000 women and 2.0 per 100.000 men (Gigantesco et al., 2010). The lifetime prevalence of psychiatric comorbidities is very high among individuals affected by AN, from 45–97% (Herpertz-Dahlmann, 2015). Among comorbid psychiatric conditions, Autism Spectrum Disorder (ASD) or autistic traits are frequently documented in patients with AN (Jagielska et al., 2018).

ASD is a pervasive neurodevelopmental disorder starting in infancy, defined by difficulties with reciprocal social interaction and repetitive, restricted behaviours and interests (APA, 2013). Ledford and Gast described prevalence rates of problematic feeding behaviours in ASD ranging from 46–89% (Ledford and Gast, 2006). Food selectivity represents the most predominant feeding problem, affecting approximately 70% of ASD patients. Feeding disorders as selective or scarce feeding may represent early warning signs of ASD and are frequently associated with delay or stagnation of development (Parmeggiani et al., 2019). Feeding difficulties should be investigated and considered together with the analysis of anthropometric parameters in children with ASD (Parmeggiani and Pruccoli, in press). In 2013, Huke and colleagues conducted the first systematic review and meta-analysis investigating the prevalence of ASD among patients with AN, reporting an average prevalence of 22.9% (Huke et al., 2013). More recent reviews have confirmed these findings (Westwood et al., 2017; Nickel et al., 2019). A second meta-analysis (Westwood et al., 2016) reported significantly greater autistic traits in AN patients than in healthy controls, although the latter did not meet the cut-off criteria for a diagnosis of ASD. The impact of BMI values on scores for ASD was not reported. All the reviews taken into consideration seem to indicate a higher prevalence of autistic traits and ASD in AN patients than in the general population.

Many common aspects between the neuropsychological profiles and the emotional and social functioning in AN and ASD make the potential link between the two disorders a subject of interest (Westwood and Tchanturia, 2017). Regarding empathy, fantasy and imagination, a review reports very similar profiles between patients with ED and subjects with ASD (Kerr-Gaffney et al., 2019). Theory of mind, the ability to infer the mental states of others, has been shown to present comparable impairment in ASD and AN (Leppanen et al., 2018). On the other hand, different researchers stated that malnutrition in patients with AN can determine mental rigidity, obsessive behaviours, and ritualism very similar to ASD symptoms and that these characteristics may then improve with normal nutrition (Mandy et al., 2015). Clinicians and researchers should investigate whether autistic traits in AN patients are an epiphenomenon of acute metabolic modifications or specific neurodevelopmental characteristics.

Psychopathological traits are more compromised when EDs overlap with ASD, especially regarding disturbances of thinking, cognitive inflexibility, ritualistic behaviour, mood disorders, phobic aspects, and social impairment. These aspects do not seem to be correlated with the severity of the malnutrition or the BMI (Tchanturia et al., 2019; Stewart et al., 2017). At present there are no protocols to treat patients with an ED associated with ASD or autistic traits: more studies are necessary to clarify this topic and be able to treat this group of patients with evidence-based guidelines (Kinnaird et al. 2019).

The aim of the present study was to investigate the relationship between ASD traits, ED psychopathology and BMI in a population of young inpatients with AN at an Italian Regional Centre for Feeding and Eating Disorders.

## Materials And Methods

Twenty-three inpatients were enrolled in the study. Inclusion criteria were: a primary diagnosis of AN according to DSM-5 criteria; an age between 11 and 17 years at the moment of hospitalisation; the presence of one or more symptoms suggestive for ASD such as: obsessive-compulsive traits, social withdrawal, scarce emotional reciprocity, shared attention deficit, narrow interests, ritualistic and stereotyped behaviour, verbal communication impairment. Patients unable to attend a thorough clinical evaluation including all selected standardised measures were excluded from the study. Diagnostic procedures for AN and autistic traits were carried out by clinical psychologists and child neuropsychiatrists belonging to the same Centre where the study was conducted.

A complete clinical evaluation of every patient investigated familial and personal history, mental status, anthropometric measures and medical complications of AN. Information was collected regarding the age of onset of AN and symptoms suggestive of ASD and the natural history of current ED and comorbid conditions.

The Eating Disorder Inventory-3 (EDI-3) (Garner, 2004) completed upon admittance to our Centre was collected: this self-assessment questionnaire is routinely employed in the diagnosis of EDs, as it focuses on the psychological domains which have been proven to be more compromised in ED patients. The result is expressed in the form of six Composite scores: Eating Disorder Risk (EDRC), Ineffectiveness (IC), Interpersonal Problems (IPC), Affective Problems (APC), Overcontrol (OC), Global Psychological Maladjustment (GPMC). These scores are the combination of twelve subscales: Drive for Thinness, Bulimia, Body Dissatisfaction, Low Self-Esteem, Personal Alienation, Interpersonal Insecurity, Interpersonal Alienation, Interoceptive Deficits, Emotional Dysregulation, Perfectionism, Asceticism, Maturity Fears.

Two certified psychologists (V.P. and M.A.) examined each patient for ASD with the Autism Diagnostic Observation Schedule-2 (ADOS-2, Module 4 for adolescents) (Lord et al., 2012). The ADOS-2 represents the gold-standard exam for the diagnosis of ASD (NICE, 2011). The Module 4 is used to assess adolescents and adults without language impairment. It expresses a score in the domains of language and communication, reciprocal social interaction, imagination, creativity, stereotyped behaviour, and restricted interests. The scores in the domains of language and communication, and reciprocal social interaction are then used to obtain a final score that can correspond to a diagnosis of "Autism", "Autistic Spectrum" or "Non-Spectrum".

On the same day, patients and/or parents were administered the Autism Spectrum Quotient (AQ) (Baron-Cohen et al., 2001; Ruta et al., 2012) under the supervision of a trained, research-reliable examiner. The test explores five different domains: social skills, attention shifting, attention to detail, communication,

and imagination. This study employed two different versions of the AQ for each patient: one was used to assess present symptoms and behaviour (AQ 12–15 years, which is a parent-report test or AQ 16+ years, which is a self-report test); the other was used to investigate ASD symptoms and behaviour in childhood (AQ 4–11 years, a parent-report test). This choice enables us to detect the possible presence of ASD features immediately after their typical onset age and before the appearance of an overlaying AN symptomatology.

## Statistical analysis

All statistical analyses were conducted using JASP, version 0.13.1 for Windows. Adopted alpha error rate was 0.05 (two-tailed), with conservative statistical power of 95%. Descriptive statistics for demographic and clinical variables were calculated for the whole sample, considering means and standard deviations. Descriptive analyses and comparisons for total scores and subscales of ADOS-2, AQ and EDI-3 were performed. Pearson's or Spearman's rho correlations were calculated for selected clinical variables (BMI, EDI-3 scores, AQ-scores, ADOS-2 scores). Shapiro-Wilk and Levene tests were used to assess normality of data distribution and homogeneity of variance. Multiple linear regressions controlling for age, BMI and OCD comorbidity were conducted to investigate significant correlations between EDI-3 scores and ASD measures.

### Ethical considerations

The study was approved by the local Ethical Committee (protocol code: ASD-AN-18). Written informed consent was obtained.

## Results

### Demographics

Twenty-three patients were enrolled in the study. Twenty were females (87%). The age range was 13 to 19 years (mean age 15.8 years  $\pm$  1.5). Mean BMI at evaluation was 16.8  $\pm$  2.1; mean BMI at admittance was 14.2  $\pm$  1.7. Sixteen patients (70%) were treated with psychiatric drugs. One patient (4%) presented a slight delay in language acquisition. Three patients (13%) had a family history of AN, while none had a family history of ASD. OCD was present in 16 patients (70%), depressive mood in 8 (35%), self-harming in 4 (17%), anxiety in 3 (13%), traits of Bipolar Disorder in 2 (9%).

## ADOS-2

The mean ADOS-2 total score was 4,1 ( $\pm$  5,0). The mean scores for the single subscales were: Communication: 1,3/8 ( $\pm$  1,7); Reciprocal social interaction: 2,2/14 ( $\pm$  3,2); Imagination/Creativity: 0,4/2 ( $\pm$  0,5); Stereotyped behaviour and restricted interests: 0,2/8 ( $\pm$  0,7). Three patients (13%) were classified in the "Autism" category, 2 as "Autistic Spectrum" and 18 as "Non-Spectrum". Five patients in total (22%)

scored therefore over-threshold in the ADOS-2. BMI was not significantly correlated to either ADOS-2 total score or any subscale.

## AQ

The Autism Spectrum Quotient (AQ) regarding the present symptoms was administered in both the 16+ years and in the 12–15 years versions, depending on the age of the patient. The mean total score in our sample was 21,9/50 ( $\pm 7,8$ ). The mean scores for the single subscales were: Social Skills 4/10 ( $\pm 2,9$ ); Attention Switching: 5,9/10 ( $\pm 1,9$ ); Attention to Detail: 5,6/10 ( $\pm 2,3$ ); Communication: 3,6/10 ( $\pm 2,1$ ); Imagination: 2,9/10 ( $\pm 1,8$ ). Out of 23, 2 patients (9%) scored clinically significant for ASD, 4 patients (17%) scored borderline clinically significant for ASD and 17 patients (74%) scored as non-clinically significant for ASD. BMI was not significantly correlated to either AQ-present total score or any subscale.

The AQ 4–11 years test was administered to the parents of the patients in order to collect data on the symptoms and behaviours that occurred in the patients' childhood. The mean total score in our sample was 54,8/150 (+/-22,4). The mean scores for the single subscales were: Social Skills: 11,7/30 (+/- 7,0); Attention Switching: 13,1/30 (+/- 5,8); Attention to Detail: 14,3/30 (+/- 4,8); Communication: 8,9/30 (+/- 5,9); Imagination: 8,9/30 (+/- 4,1). Out of 23, 6 patients (26%) scored clinically significant for ASD, 2 (9%) scored borderline clinically significant for ASD and 15 (65%) scored as non-clinically significant for ASD. BMI was not significantly correlated to either AQ-past total score or any subscale.

Comparing present and past versions of AQ, the mean scores of all patients at single items and subscales show no substantial modification from past to present. With the exception of "social skills" and "attention to detail" subscales, all past and present versions of subtests show strong significant correlations (Total:  $p < 0.001$ ; Attention switching:  $p = 0.009$ ; Communication:  $p = 0.004$ ; Imagination:  $p = 0.005$ ).

### ADOS-2 and AQ

Five patients out of 23 (22%) had a diagnosis of "Autism" or "Autism Spectrum" at the ADOS-2. Only one of these patients had corresponding high scores at both AQ questionnaires. Two patients scored above threshold at ADOS-2 and AQ past.

### ADOS-2, AQ and EDI-3

The analysis of correlations between EDI-3 scores and tests for ASD (ADOS-2 and AQ) revealed a series of statistically significant correlations. ADOS-2 total scores correlated with EDI-3 IC subscale. Significant correlations between ADOS-2 and EDI-3 subscales are shown in table 1. AQ-present total score and a series of AQ-present subscales (Social Skills, Attention Switching, Communication) were positively associated with 3 EDI-3 subscales (IPC, APC, GMPC). Correlations are shown in Table 2. AQ-past total scores showed no significant correlation with EDI-3 subscales. Significant correlations between EDI-3 subscales and ASD measures were assessed by conducting multiple linear regressions controlling for age, BMI, OCD comorbidity, treatment with/without antidepressants, and treatment with/without

antipsychotics. All the previously evidenced correlations remained statistically significant, with the exception of ADOS-2 Total score-EDI-3 IC correlation. Statistically significant correlations were: ADOS-2 imagination-EDRC:  $p = 0.024$ ; ADOS-2 imagination-IC:  $p = 0.031$ ; AQ total-IPC:  $p = 0.02$ ; AQ total-APC:  $p = 0.031$ ; AQ total-GMPC:  $p = 0.014$ ; AQ social skills-IC: 0.017; AQ social skills-IPC: 0.010; AQ social skills-APC: 0.010; AQ social skills-GMPC: 0.004; AQ attention switching-IPC: 0.015; AQ communication-APC: 0.049.

## Discussion

This is the first study comparing ASD traits, which were evaluated with gold-standard measures (ADOS-2 and AQ tests), to EDI-3 scores and BMI, in a sample of young patients hospitalized for AN. The investigation of ASD traits in childhood with the employment of the AQ “past version” represents a second new addition to the literature on the subject. Along with the quantitative measurement, multidimensional clinical evaluation of the patient was always taken into account since our Centre specializes in the diagnosis and treatment of both ASD and AN.

Five patients, of the 23 assessed (22%), obtained scores in the ADOS-2 compatible with a diagnosis of ASD. On the whole, 12 patients out of 23 (52%) scored above clinical thresholds for ASD in at least one test (ADOS-2, AQ childhood and adolescence). Notably, the patients, whom we analysed for this study, were considered on account of the presence of autistic features. The rationale for this choice was to explore and confirm possible criteria to select AN patients to be screened for ASD in clinical practice.

Our findings on the prevalence of ASD symptoms investigated with ADOS-2 in patients with EDs are consistent with most of the previous research. Particularly, a recent systematic review found a 26.5% prevalence of ASD in patients with ED (Nickel et al., 2019). A meta-analysis addressing the prevalence of ASD symptomatology among patients with AN found a wide spectrum of results, ranging from 4 to 52% (Westwood and Tchanturia, 2017).

Our finding of 26% patients scoring above thresholds for ASD in the AQ adolescence version is also consistent with previous research. Specifically, the mean score obtained in our population (21.9) confirms the results reported by a previous systematic review (Westwood et al., 2016). We documented strong correlations between the two versions of the AQ test, namely, total scores, as well as 4 out of 6 pairs of subscales, showed significantly correlated results between the childhood and adolescence version of the test. This could indicate that ASD traits pre-existed the onset of the ED. In this regard, ADOS-2 and AQ-adolescence total scores and subtests showed no direct correlation with patients' BMI. These findings suggest that autistic traits documented in adolescent patients with AN may not be due solely to the severity of their condition during clinical evaluation, which confirms and expands on existing evidence (Sedgewick et al., 2019).

Correlation measures between tests for ASD and indicators of EDs showed that scores obtained at specific EDI-3 subscales, particularly IPC, APC and GMPC, were significantly correlated with AQ and ADOS-2 scores: this could suggest an association between ED psychopathology as assessed with EDI-3

and ASD traits. Multiple linear regressions adjusted for age, BMI and OCD comorbidity confirmed these findings. These results corroborate and widen previous data (Dell’Osso et al., 2018) for they show correlations between subthreshold ASD symptoms and selected EDI-2 subscales. In particular, the authors found Interpersonal Distrust EDI-2 subtest to be significantly correlated with total scores obtained at the Adult Autism Subthreshold Spectrum and with the Non-verbal communication and Inflexibility and adherence to routine domains. However, the ADOS-2 schedule was not adopted in this study. More generally, these results corroborate several previous studies, showing difficulties in social interactions and low levels of social skills in patients with AN (Klump et al., 2000; Anckarsäter et al., 2011; Postorino et al., 2017).

The present study has a limited and non-homogeneous sample of patients with regard to gender, BMI, psychiatric drugs and interval of time passed from discharge to evaluation. The self-report and parent-report questionnaires employed in this study allowed us to include various perspectives in the evaluation of the patients; on clinical observation, however, some biased attitudes towards the tests were noted, both coming from patients and parents. Nonetheless, most patients and parents were observed to be objective and compliant, and the clinical perspective given by the ADOS-2 permitted a well-rounded investigation.

In conclusion our results, although consistent with previous studies, are unprecedented in literature and should be investigated in larger samples, given their likely importance for both clinical practice and research. They indicate the possibility that the EDI-3 – specifically its subscales IPC, APC, and GMPC – be employed as a preliminary measure to identify and examine patients with AN for ASD traits with gold-standard measures.

## List Of Abbreviations

ADOS-2: Autism Diagnostic Observation Schedule-2nd Edition; AN: Anorexia Nervosa; AQ: Autism Quotient; ASD: Autism Spectrum Disorder; BMI: Body Mass Index; DSM 5: Diagnostic and Statistical Manual of Mental Disorders, Fifth version; EDI-3: Eating Disorder Inventory-3; EDRC: Eating Concerns; IC: Ineffectiveness; IPC: Interpersonal Problems; APC: Affective Problems; OC: Overcontrol; GPMC: Global Psychological Maladjustment.

## Declarations

### Ethics approval and consent to participate

The study was approved by the Institutional Review Board of the University of Bologna and was performed in compliance with the Declaration of Helsinki and its later amendments. Parents gave informed consent to the processing of personal data at the time of the clinical evaluation.

### Availability of data and materials

The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

### **Consent for publication**

Not applicable.

### **Competing interests**

The authors declare that they have no competing interests.

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### **Authors' contributions**

AP reviewed literature data, wrote the manuscript, and revised the manuscript. AP, AS, LT, EM, VP, MA, PG and LS collected and analysed the data, and revised the manuscript. JP analysed and interpreted the patient data and wrote the manuscript. EF and DMC revised the manuscript. All authors read and approved the final manuscript.

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## Tables

### Table 1

EDI-3 domain scores compared with ADOS-2 domain scores (p-values).

	EDI-3 EDRC	EDI-3 IC	EDI-3 IPC	EDI-3 APC	EDI-3 OC	EDI-3 GPMC
ADOS-2 Total	0.164	<b><i>0.017</i></b>	0.084	0.296	0.420	0.173
ADOS-2 Communication	0.486	0.267	0.297	0.744	0.483	0.925
ADOS-2 Social Interaction	0.356	0.140	0.449	0.424	0.553	0.433
ADOS-2 Imagination and creativity	<b><i>0.026</i></b>	<b><i>0.007</i></b>	0.076	0.390	0.056	0.089
ADOS-2 Repetitive behaviours	0.616	0.873	0.334	0.121	0.400	0.192

Abbreviations: ADOS-2: Autism Diagnostic Observation Schedule-2nd Edition; EDI-3 = Eating Disorder Inventory-3; EDRC = Eating Concerns; IC = Ineffectiveness; IPC = Interpersonal Problems; APC = Affective Problems; OC = Overcontrol; GPMC = Global Psychological Maladjustment. Statistically significant correlations marked in bold, underlined and italics.

## Table 2

EDI-3 domain scores compared with AQ-adolescence domain scores (p-values).

	EDI-3	EDI-3	EDI-3	EDI-3	EDI-3	EDI-3
	EDRC	IC	IPC	APC	OC	GPMC
AQ-A Total	0.174	0.075	<b><u>0.019</u></b>	<b><u>0.043</u></b>	0.095	<b><u>0.023</u></b>
AQ-A Social Skills	0.339	<b><u>0.038</u></b>	<b><u>0.022</u></b>	<b><u>0.007</u></b>	<b><u>0.019</u></b>	<b><u>0.003</u></b>
AQ-A Attention Switching	0.332	0.059	<b><u>0.018</u></b>	0.267	0.319	0.105
AQ-A Attention to detail	0.106	0.351	0.413	0.379	0.292	0.300
AQ-A Communication	0.696	0.395	0.089	<b><u>0.038</u></b>	0.267	0.061
AQ-A Imagination	0.430	0.961	0.381	0.876	0.744	0.955

Abbreviations: AQ-A = Autism Quotient, Adolescence version; EDI-3 = Eating Disorder Inventory-3; EDRC = Eating Concerns; IC = Ineffectiveness; IPC = Interpersonal Problems; APC = Affective Problems; OC = Overcontrol; GPMC = Global Psychological Maladjustment. Statistically significant correlations marked in bold, underlined and italics.