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Autistic traits and perspective taking in youths with anorexia nervosa: an exploratory clinical and eye tracking study

Pamela Fantozzi¹, Lucia Billeci², Pietro Muratori¹, Sandra Maestro³, Filippo Muratori¹, Bhismadev Chakrabarti⁴ and Sara Calderoni^{1,5*}

Abstract

Background Despite their apparent dissimilarity, Anorexia Nervosa (AN) and Autism Spectrum Disorder (ASD) share many features, especially in terms of social and emotional difficulties. In recent years, empathic abilities in AN have been frequently assessed using self-report measures. Otherwise, the director task (DT) has been used to investigate the ability to take the visual perspective of another individual in a communicative context, using eye-tracking technology. The aim of the current study was to test the presence of autism-relevant features in AN, through: (i) comparing self-reported autistic traits and empathic abilities in a group of young inpatients with AN and age/gender matched healthy controls (HC); (ii) comparing performance on the director paradigm.

Methods The participants were females in the age-range between 11 and 18 years: 24 with AN and 23 HC. Autistic traits, empathic abilities, and severity of the eating disorder were respectively measured using: the Autism Quotient (AQ), the Interpersonal Reactivity Index (IRI), and the Eating Disorder Inventory-3 (EDI-3). Both groups performed a computerized task in which a director instructed them to move objects placed on a set of shelves using a mouse, while their eye gaze was tracked. A total of 36 shelf configurations, divided into three categories (with dimensional distractor – with spatial distractor – control), were created.

Results Subjects with AN showed higher autistic traits than HC. Eye-tracking data revealed that subjects with AN took longer to decide which object to select and where to move it, both in distractor-trials and in control-trials. In the AN group, we found a significant negative correlation between the total score of the AQ and the number of fixations to the irrelevant object in the dimensional control condition -in which the subjects were asked to focus on dimensional aspects of the object (large-small)-.

Conclusions Autistic traits were over-represented in a group of young inpatients with AN. Through the use of eye-tracking technology, this exploratory study documented some differences between AN inpatients and HC in their online processes during the perspective taking tasks, which could be considered a target of tailored intervention. A larger sample of patients is needed to confirm these preliminary findings.

*Correspondence:
Sara Calderoni
sara.calderoni@fsm.unipi.it

Full list of author information is available at the end of the article



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Plain English summary

Anorexia nervosa (AN) and Autism Spectrum Disorders share a number of common features, including social and emotional difficulties. In this framework, previous investigations have analyzed autistic traits and empathic abilities of AN patients with mixed results. In the current study, we assess in AN adolescents compared to healthy control peers: (i) autistic traits and empathic abilities using self-report measures; (ii) perspective-taking ability (a process related to cognitive empathy, i.e. the capacity to understand the emotional/mental experiences of others) using an eye-tracking metric from the 'director task'. Results indicated that autistic traits were over-represented in the group of adolescents with AN. The eye-tracking based measure of perspective-taking ability showed longer response latencies in AN subjects compared to the control sample, which may be an expression of the need for more time to "put themselves in the shoes of others". If confirmed, these findings suggest that tailored interventions focusing on perspective taking's abilities may be implemented in AN subjects.

Keywords Anorexia nervosa, Autism spectrum disorder, Perspective taking, Eye-tracking

Introduction

Anorexia Nervosa (AN) is a severe eating and feeding disorder with a typical adolescent onset, a marked female preponderance [1], and the highest lethality rate among psychiatric disorders [2]. AN is also associated with a high comorbidity [3], especially during the acute phase of the illness [4].

Relationship between anorexia nervosa and autism spectrum disorder

Among comorbid psychiatric conditions, Autism Spectrum Disorder (ASD) or autistic traits are frequently documented in patients with AN [3]. ASD is a neurodevelopmental disorder with a higher prevalence in males [5, 6], characterized by persistent deficits in social interaction and communication, as well as patterns of restricted and repetitive patterns of behaviors [7]. A systematic review by Huke and colleagues [8] identified that 22.9% of AN patients across multiple investigations also satisfied ASD criteria (range 8 to 37%). More recent reviews confirmed an overrepresentation of ASD symptoms in AN subjects [9–11]. Also, a meta-analysis including seven studies for a total of 328 AN patients and 1890 HC [12] reported significantly greater autistic traits in AN patients than in healthy controls, although the latter did not reach the cut-off criteria for a diagnosis of ASD. Growing research has attempted to elucidate the nature of the relationship between the two disorders, focusing on both shared underlying difficulties in executive functions [13], emotion recognition [14–16] and production [17, 18], and high levels of alexithymia [19, 20].

Empathy and theory of mind

Empathy is a complex multidimensional construct and a core component of social cognition. In recent years, the distinction between affective empathy (AE) and cognitive empathy (CE) has been receiving growing attention: the former is the capacity of sharing emotions with someone else, the latter is the capacity to understand

the mental state of someone else, without matching the other's affective state, and includes the ability of decoding and labeling emotions [21]. A recent systematic review and meta-analysis underlined similar empathy profiles between AN and ASD [22]. Theory of mind (ToM) is a core component of cognitive empathy and refers to the ability to infer information about other's emotions, intentions, knowledge, and beliefs from social interaction or given information [23]. Also, ToM involves cognitive as well affective aspects of mentalizing: cognitive ToM refers to our ability to make inferences regarding other people's beliefs, affective ToM refers to inferences one makes regarding others' emotions [24]. The meta-analytic review by Leppanen et al. [25] showed that autistic people and people with AN have similar theory of mind profiles, even if autistic people appeared to have more difficulties than those with AN, particularly in emotional ToM.

Director task

The director task (DT) has been used to investigate the ability to take the perspective of another individual into account in a communicative context [26–30]: the visual perspective taking. In these studies, all conducted on healthy subjects, the participant interacts with another agent (a "director") to act on a set of objects on a shelf. Crucially, some of the objects are blocked off from the director's point of view and are visible only to the participant. Thus, when the director talks about an object, the participant should ignore any object that is not visible to the director and instead select a referent from what is in the "common ground", that is, what is visible to both the participant and the director. This paradigm requires the participant to infer the speaker's referential intention (a mental state) based on beliefs that differ from his or her own due to the speaker's ignorance of the presence of an object that would be a potential referent for the instruction given. While the original DT used real shelves and objects as stimuli, the development of eye-tracking technology has made it possible to administer the paradigm

on a computer using an eye-tracker. The DT has been used on both adults [29–31] and evolutive age (children/adolescents) [28, 31, 32].

The current study aimed to compare autistic traits and empathic abilities in a group of young inpatients with AN and a typically developing group of healthy controls (HC) of comparable age, sex and IQ. Second, these two groups were compared on their visual perspective taking ability as measured using the DT.

We hypothesized that AN patients presented higher autistic traits and lower trait empathy than HC subjects. In the DT, we hypothesized that patients with AN made more errors, took longer to process the auditory instructions and presented a high number of fixations to the distractor than healthy controls. Exploratory analyses were conducted to evaluate possible correlations between specific eye-tracking measures and (a) autistic traits; (b) eating disorder severity across the whole sample.

Materials and methods

Participants

Twenty-four adolescent females with AN-restricting type (AN-R-nineteen) or AN-binge-eating/purging type (AN-B/P-five) were recruited at the inpatient eating disorder unit of the IRCCS Fondazione Stella Maris, a tertiary care university hospital in Pisa (Italy). Patients were selected from all consecutive participants admitted to the unit from July 2019 to June 2020 who satisfied the following criteria: diagnosis of AN-R or AN-B/P according to the Diagnostic and Statistical Manual of Mental Disorders-5th edition (DSM-5) criteria [33], female sex, age range between 11 and 18 years, and Raven's Standard Progressive Matrices (SPM) [34] $IQ \geq 85$. Exclusion criteria were: psychotic symptoms, current or history of substance abuse, medical conditions not correlated with the eating disorder, significant intrinsic instability requiring constant medical care supervision (such as severe bradycardia, dehydration, or electrolyte imbalance), and intellectual disability. Diagnostic procedures for AN and autistic traits were carried out by a multidisciplinary team that includes a child/adolescent neuropsychiatrist and a child/adolescent psychologist. The mean age was 15.37 years (range=13.33–18.25; $SD=1.52$). The mean body mass index (BMI) was 17.05 kg/m^2 (range=13.33–18.25; $SD=1.52$). The mean duration of illness was 23.91 months (range=4–60; $SD=19.29$). Twenty patients (83.33%) fulfilled the criteria for an Axis I mood and/or anxiety disorder (assessed through the Italian version of the Kiddie-Sads-Present and Lifetime Version [K-SADS-PL] [35]) and four of these twenty patients also met the criteria for an Axis II Borderline Personality Disorder (evaluated by the Structured Clinical Interview for DSM-IV Axis II Personality Disorders [SCID-II] [36]). Eleven patients (45.83%) received psychopharmacological

treatment with selective serotonin reuptake inhibitors and/or atypical antipsychotics and/or mood stabilizers, while the remaining thirteen subjects were medication-naïve.

The AN clinical sample was compared to a healthy control group (HC) composed of twenty-three healthy female adolescents of comparable age, IQ, and level of education. Subjects were recruited from a group of students of three different middle schools and one high-school of the metropolitan area of Pisa (Tuscany, Italy). For each participant in the control group, parents provided a history of normal development and no history of a clinical diagnosis or need for special education services. In this group, the height and weight were self-reported. Exclusion criteria were: a score of one of the three subscales related to the eating disorder of the Eating Disorder Inventory-3 (EDI-3) [37] ≥ 85 and Raven's Standard Progressive Matrices $IQ < 85$. The mean age was 15.37 years (range=11.08–18.42; $SD=2.21$). The mean body mass index was 20.14 Kg/m^2 (range=14.32–24.61; $SD=2.71$).

All AN patients and all HC, except two, were right hand dominant in agreement with what was evaluated with specific scale [38]. All participants had normal or corrected to normal vision (i.e., they were wearing their prescription contact lenses). All participants read and write the Italian language correctly.

Assessment instruments

Assessment of autistic traits

Autism-Spectrum Quotient (AQ): The AQ [39] is a 50-item self-report questionnaire, made up of ten questions organized in five subscales assessing five different areas: Social Skill (SS), Attention Switching (AS), Attention to Detail (AD), Communication (C), and Imagination (I). Participants are asked to indicate the grade of agreement with each statement in a 4-point Likert scale ranging from "strongly agree" to "strongly disagree". To measure the total AQ score, each item scores "1" if the respondent records the item/behavior either mildly or strongly. In all the other cases, the score is "0". Possible total scores range from 0 to 50. The Italian AQ [40] was judged reliably equivalent to the English version with Cronbach's-alpha for all subscales above 0.52.

Assessment of empathic abilities

Interpersonal Reactivity Index (IRI): the IRI [21, 41] is used to evaluate empathic abilities. The IRI is a 28-item self-reported questionnaire that allows a multi-dimensional assessment of empathy, which can be measured by two cognitive subscales (Perspective Taking [PT]; Fantasy [FS]) and two affective subscales (Empathic Concern [EC]; Personal Distress [PD]). Participants respond to each item using a 5-point Likert scale ranging from -2

“does not describe me well” to +2 “does describe me well”. Therefore, the scores of each subscale range between -14 and +14 points where higher scores indicate more empathic abilities. We administered the Italian version of the IRI [42], which has satisfactory and good internal consistency with Cronbach’s-alpha for all subscales above 0.63.

Assessment of eating disorder severity

Eating Disorder Inventory-3 (EDI-3): the EDI-3 [37] is used to evaluate the symptoms associated with FEDs. The EDI-3 is a 91-item self-report questionnaire, based on a 6-point Likert scale, divided into 12 subscales. The first three subscales (Drive for Thinness-DT, Bulimia-B, Body Dissatisfaction-BD) are strictly related to the eating disorder, while the remaining nine subscales (Low Self-Esteem-LSE, Personal Alienation-PA, Interpersonal Insecurity-II, Interpersonal Alienation-IA, Interoceptive Deficits-ID, Emotional Dysregulation-ED, Perfectionism-P, Asceticism-A, Maturity Fears-MF) assess psychological aspects especially associated with the development and the maintenance of FEDs. The questionnaire has high test/retest reliability and sound internal reliability. The Italian version of the EDI-3 [43] was judged reliably equivalent to the English version with Cronbach’s-alpha for all subscales between 0.72 and 0.95.

The Body Mass Index (BMI) is calculated by dividing body weight in kilograms by height in meters squared (kg/m^2).

The disorder duration is defined as the time interval between the onset of the first eating disorder symptoms and the administration of the tests.

Procedure

First, we assessed the prevalence of autistic traits and the empathic abilities among the AN group. For this, the AN group was respectively compared on the AQ scale and the IRI with the HC group. To compare the cognitive abilities and the eating disorder severity, the two groups respectively completed the Raven’s Standard Progressive Matrices and the EDI-3. All the instruments were filled

out by the AN group during the first days of the clinical assessment. The patients then performed the session of eye-tracking. The HC individuals filled out the questionnaires and performed the eye-tracking during the same session.

Eye-tracking paradigm

Stimuli

The task design and stimuli were based on previous studies that used the DT [32, 44, 45]. We adapted the DT so that it was suitable for our patients. Participants were presented with a visual scene of a 4×4 set of shelves containing six different inanimate objects and were asked to move one of the objects in each trial. To prevent the nature of the image could impact on the response in AN group, we did not use stimuli potentially related to the eating disorder, such as food or shape/weight. A photograph of the interlocutor (the “director”) facing the participants was visible from the shelves. Participants were asked to listen to the director’s instruction and to make the first click with the mouse, thanks to which the cursor appears in the center of the screen. They had to make the second and the third click respectively only when they had decided which object to select, and in which space to move it. Participants were told that they should take the director’s viewpoint into account when following the director’s instructions. They were told that objects in slots with an orange background were visible only to them, whereas the other objects could be seen from either side of the shelves. In distractor-trials, the instruction referred to one object (“target”) given the director’s point of view but would refer to another object (“distractor”) if one assumed participants’ perspective (Fig. 1a and b). As such, participants needed to take the director’s perspective into account in order to respond correctly. In control-trials, the distractor object was replaced by an irrelevant object and the instruction referred to an object that was visible to both participants and the director (Fig. 1c).

A total of 36 shelf configurations were created and presented with default randomization, divided in three

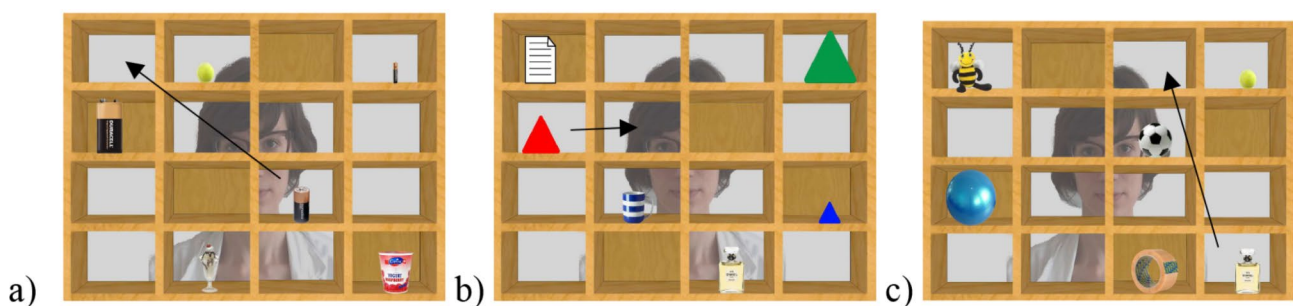


Fig. 1 Examples of trials: **a)** trial with dimensional distractor (“move the large battery next to the ball”), **b)** trial with spatial distractor (“move the triangle placed lower above the cup”), **c)** control-trial (“move the perfume next to the small ball”)

categories: 12 trials with dimensional distractor, 12 trials with spatial distractor, and 12 control-trials. All the images were controlled for color, brightness and contrast. The shelf configurations depicted six objects and included either three (distractor trials; Fig. 1a and b) or two (control trials; Fig. 1c) examples of the same objects that differ in size (large/small) or position (top/bottom). In distractor-trials, the distractor object (the top-most, bottom-most, smallest, or largest object) was in a slot with an orange background, whereas the target object (the second top-most, bottom-most, smallest or largest object visible to both the participant and the director) and the third object (e.g., the battery in the upper right corner shown in Fig. 1a, the green triangle shown in Fig. 1b) were in a clear slot. The rest of the objects were unique objects distributed among two clear slots and one with an orange background. If the selected object and the destination position were correct, the background of the slot turned green and the experiment continued. Conversely, if one of the two selections was incorrect, the background of the slot turned red and the subsequent trial was not displayed. If the subject selected the target and destination incorrectly two consecutive times, the instruction was repeated.

With the exception of the number of trials, the materials and design of the current study were very similar to a recent work by Thompson and colleagues [45]. Differently from the work by Symeonidou and colleagues [32], our study was characterized by: (i) a lower number of trials (36 shelf configurations vs. 48); (ii) a shorter overall duration of the experiment (20 min. vs. 45 min); (iii) the absence of no-director conditions (conditions without the director behind the shelf), which specifically investigated the executive functions [34]; (iv) the absence of inhibitory control tasks to measure participants' inhibitory control. In particular, compared to previous investigations [32, 45], we decided to use only 36 trials because preliminary tests revealed that our patients presented a decrease in attention with a higher number of shelf configurations.

Procedure

Participants were tested individually in one session lasting approximately 20 min.

As soon as the shelf configuration appeared on the screen, the instruction was read to the subject. Gaze behavior was recorded by the SMI RED 500 eye-tracking (SensoMotoric Instruments, Teltow, Germany). Data were acquired with a sampling rate of 120 Hz. The theoretical accuracy of the device was 1°. The eye-tracker recorded data from both eyes due to the reflection of near-infrared light on the cornea and pupil. It was positioned in front of the subject about 65 cm from the screen. The distance between the eye-tracker and

the screen and the tilt angle of the system were adjusted for each subject allowing a good recording of their eyes. The stimuli were implemented in the Matlab environment and were interfaced with the eye-tracker via dedicated Psychtoolbox libraries. The eye-tracking data were recorded using SMI's iViewX software. The experiment was preceded by a training phase that allowed the subject to become familiar with the task. This was followed by a 5-point calibration phase, using a small red circle that moved across the screen. A fixation cross appeared on the screen between trials.

The training phase comprised six trials (the first three showing the director's perspective, the second three the proband's perspective, which was maintained throughout the experiment; the latter three trials consisting in succession of a control trial, a dimensional distractor trial and a spatial distractor trial). At the end of the training phase, the proband was asked if he/she experienced any difficulties. In case the subject expressed doubts, the training was repeated. Trials from the training phase were not used for data analysis.

After the training, the stimuli were presented to the subjects as indicated in the previous section.

Eye-tracking data analysis

The following measures were obtained by analyzing eye-tracking-data:

- Accuracy: The percentage of errors with respect to the number of trials. Both the case where a wrong object was selected and the case where a wrong destination was selected were considered as error conditions. It was calculated separately for distractor trials and control trials.
- Temporal measures: Two temporal measures were considered: (i) the response latency and (ii) the trial duration. Response latency refers to the time distance between the appearance of the stimulus and the first click made by the subject. Trial duration refers to the total time between the appearance of the stimulus and the conclusion of the trial. These measures were calculated only for trials in which subjects made no errors (correct trials). Measures were calculated separately for distractor-trials and control-trials.
- Fixations: Number of fixations to the distractor (distractor condition) or to the irrelevant object (control condition).
- Target advantage score: The average probability of looking at the target object minus the average probability of looking at the distractor (distractor-trial) or at the irrelevant object (control-trial) [46, 47]. A gaze at the target is defined as a gaze at the object or box in which the object is contained;

Table 1 Comparison between AN group and HC group on demographic data

	AN (n=24)	HC (n=23)	Group comparison
	M (SD)	M (SD)	
Age (years)	15.37 (1.52)	15.37 (2.21)	$t_{(45)} < 0.001, p = 1.0$
IQ	111.66 (13.18)	112.95 (9.75)	$t_{(45)} = 0.38, p = 0.71$
BMI (Kg/m ²)	17.05 (1.74)	20.29 (2.74)	$t_{(45)} = 4.86, p < 0.001$

Abbreviations AN, patients with Anorexia Nervosa; HC, healthy controls; IQ, intelligence quotient; BMI, body mass index

Table 2 Comparison between AN group and HC group on: AQ scores, IRI scores, and EDI-3 scores

	AN (n=24)	HC (n=23)	Group comparison
	M (SD)	M (SD)	
AQ			
AQ total	20.68 (6.0)	14.25 (4.18)	$F_{(1,27)} = 15.10, p < 0.001$
Social Skill	4.05 (2.52)	1.35 (1.27)	$F_{(1,27)} = 17.88, p < 0.001$
Attention Switching	5.96 (1.50)	3.45 (1.54)	$F_{(1,27)} = 27.33, p < 0.001$
Attention to Detail	4.55 (2.00)	4.55 (2.26)	$F_{(1,27)} = 0.01, p = 0.93$
Communication	3.66 (2.26)	2.15 (1.31)	$F_{(1,27)} = 5.94, p = 0.02$
Imagination	2.5 (1.60)	2.75 (1.77)	$F_{(1,27)} = 0.27, p = 0.60$
IRI			
Cognitive Empathy	5.83 (7.76)	8.64 (6.54)	$F_{(1,27)} = 1.7, p = 0.20$
Affective Empathy	4.91 (6.47)	4.36 (5.60)	$F_{(1,27)} = 0.09, p = 0.77$
Perspective Taking	2.86 (5.04)	3.85 (4.23)	$F_{(1,27)} = 0.24, p = 0.63$
Fantasy	2.78 (5.03)	4.46 (3.80)	$F_{(1,27)} = 1.54, p = 0.22$
Emphatic Concern	4.41 (4.39)	6.35 (4.23)	$F_{(1,27)} = 1.63, p = 0.21$
Personal Distress	0.48 (5.13)	-2.14 (4.04)	$F_{(1,27)} = 3.50, p = 0.07$
EDI-3			
DT	17.5 (9.37)	6.5 (6.38)	$F_{(1,27)} = 18.87, p < 0.001$
B	6.5 (8.74)	3.7 (2.99)	$F_{(1,27)} = 2.15, p = 0.15$
BD	23.23 (11.66)	13.7 (8.16)	$F_{(1,27)} = 9.28, p = 0.004$
LSE	14.17 (6.27)	6.36 (5.03)	$F_{(1,27)} = 21.95, p < 0.001$
PA	12.48 (5.17)	5.14 (3.91)	$F_{(1,27)} = 30.02, p < 0.001$
II	13.70 (7.58)	5.05 (3.75)	$F_{(1,27)} = 22.68, p < 0.001$
IA	11.96 (5.74)	4.41 (3.20)	$F_{(1,27)} = 28.92, p < 0.001$
ID	15.74 (9.69)	4.68 (5.40)	$F_{(1,27)} = 22.20, p < 0.001$
ED	10.48 (8.37)	3.27 (3.52)	$F_{(1,27)} = 13.69, p = 0.001$
P	7.78 (5.29)	4.36 (3.24)	$F_{(1,27)} = 6.66, p = 0.013$
A	9.48 (6.68)	3.45 (2.69)	$F_{(1,27)} = 14.69, p < 0.001$
MF	13.13 (6.30)	11.46 (4.86)	$F_{(1,27)} = 1.06, p = 0.31$

Abbreviations AN, patients with Anorexia Nervosa; HC, healthy controls; AQ, Autism Quotient; EDI-3, Eating Disorder Inventory-3; DT, Drive for Thinness; B, Bulimia; BD, Body Dissatisfaction; LSE, Low Self-Esteem; PA, Personal Alienation; II, Interpersonal Insecurity; IA, Interpersonal Alienation; ID, Interoceptive Deficits; ED, Emotional Dysregulation; P, Perfectionism; A, Asceticism; MF, Maturity Fears

conversely, a gaze at the distractor (or at the irrelevant object in the control condition) is defined as a gaze at the object or box in which the object is contained. These measures were calculated only for correct trials and separately for dimensional and spatial trials.

Statistical analysis

All analyses were processed in SPSS 20.0 for Mac. A Student's *t*-test was used to compare anthropometric measures. A multivariate analysis of variance (ANOVA) with age as covariate was used to compare the AN group and the HC group in terms of behavioral measures. Regarding eye-tracking measures in the ANOVAs trial type (dimensional, spatial and control) was used as an intra-subject factor. In case of significant differences, post-hoc analysis was performed for the variables found to be significant.

Pearson correlations were used to study possible bivariate relationships. Correlations were further checked by applying the false discovery rate (FDR) test to control false positive cases.

Statistical significance was set up at $p < 0.05$.

Results

Clinical characteristics

Table 1 shows no significant differences between AN and HC in age ($t(54) > 0.0001, p = 1.000$) and IQ ($t(45) = 0.38, p = 0.710$). As expected, AN group, compared to HC group, had a statistically significant lower BMI ($t(45) = 4.86, p < 0.001$).

Scores obtained on the EDI-3 by the AN and HC groups are reported in Table 2. AN had a statistically significant higher score on two subscales related to the eating disorder (Drive for Thinness and Body Dissatisfaction), as well as on the psychopathological subscales Low Self-Esteem, Personal Alienation, Interpersonal Insecurity, Interpersonal Alienation, Interoceptive Deficits, Emotional Dysregulation, Perfectionism and Alienations. No significant differences were found on the Maturity Fear scale.

Self-report questionnaires

Scores obtained on the AQ by the AN and HC groups are reported in Table 2. AN had a statistically significant higher score on AQ total scale as well as on Social Skill, Attention Switching and Communication AQ subscales. No significant differences were found between AN and HC groups on Attention to Detail and Imagination AQ subscales.

Scores obtained on the IRI by the AN and HC groups are reported in Table 2.

Eye-tracking results

Accuracy

No significant differences were found in the percentage of errors respect to the number of trials committed by the clinical group compared to the control group, neither in distractor-trials nor in control-trials, both as regards the selection of the object and as regards the selection of the destination (interaction size x trial type x group: $F(1,41) = 1.98, p = 0.15$).

Temporal measures

We found a significant effect of the group on response latency (interaction trial type \times group: $F(1,42)=4.51, p=0.039$). Post-hoc analysis highlighted a significant difference for both the distractor condition ($F(1,42)=6.25, p=0.017$) and the control condition ($F(1,42)=5.96, p=0.019$). The clinical sample took longer to decide which object to select and where to move it both in distractor-trials (AN: 4.235" (SD=0.71) vs. HC: 4.087" (SD=0.64)) and in control-trials (AN: 4.578" (SD=0.68) vs. 4.188" (SD=0.62)) than the control sample. For both groups, latency was higher in control-trials than in distractor-trials. Figure 2.

No significant differences were found between the two groups, neither in distractor-trials nor in control-trials on trial duration (interaction type of trial \times group: $F(1,42)=1.84, p=0.18$).

There was a significant effect of the type of trials ($F(1,42)=4.91, p=0.032$): for both groups, the trial duration increased in control-trials compared to distractor-trials.

Fixations & target advantage score

No significant differences were found between the two groups in the number of fixations to the distractor, neither in the spatial condition nor in the dimensional condition, and in the number of fixations to the

irrelevant object (interaction size \times type of trial \times group: $F(1,44)=0.002, p=0.97$).

No significant differences were found between the two groups in the target advantage score, neither in control condition nor in distractor condition, both in spatial trials and in dimensional trials (interaction size \times type of trial \times group: $F(1,44)=0.06, p=0.81$). There was a significant interaction with age (interaction size \times age: $F(1,44)=4.58, p=0.038$). There was also a significant interaction with the type of trial (interaction size \times type of trial: $F(1,44)=4.34, p=0.043$): for both groups, the target advantage score was higher in the condition with spatial distractor (interaction size \times age: $F(1,44)=4.83, p=0.03$).

Correlations

In AN group, we evaluated possible correlations between the fixations and the target advantage score and (a) the subscales of the AQ, (b) the three eating subscales of the EDI-3 (Drive for Thinness, Bulimia and Body Dissatisfaction) across the whole sample (Table 3). The correlations were calculated separately for distractor-trials and control-trials. After applying the FDR correction, only the correlation between fixations in control trials for the dimensional condition remains significant. However, since this is an exploratory study, we decided to report the significances not surviving FDR correction also. None

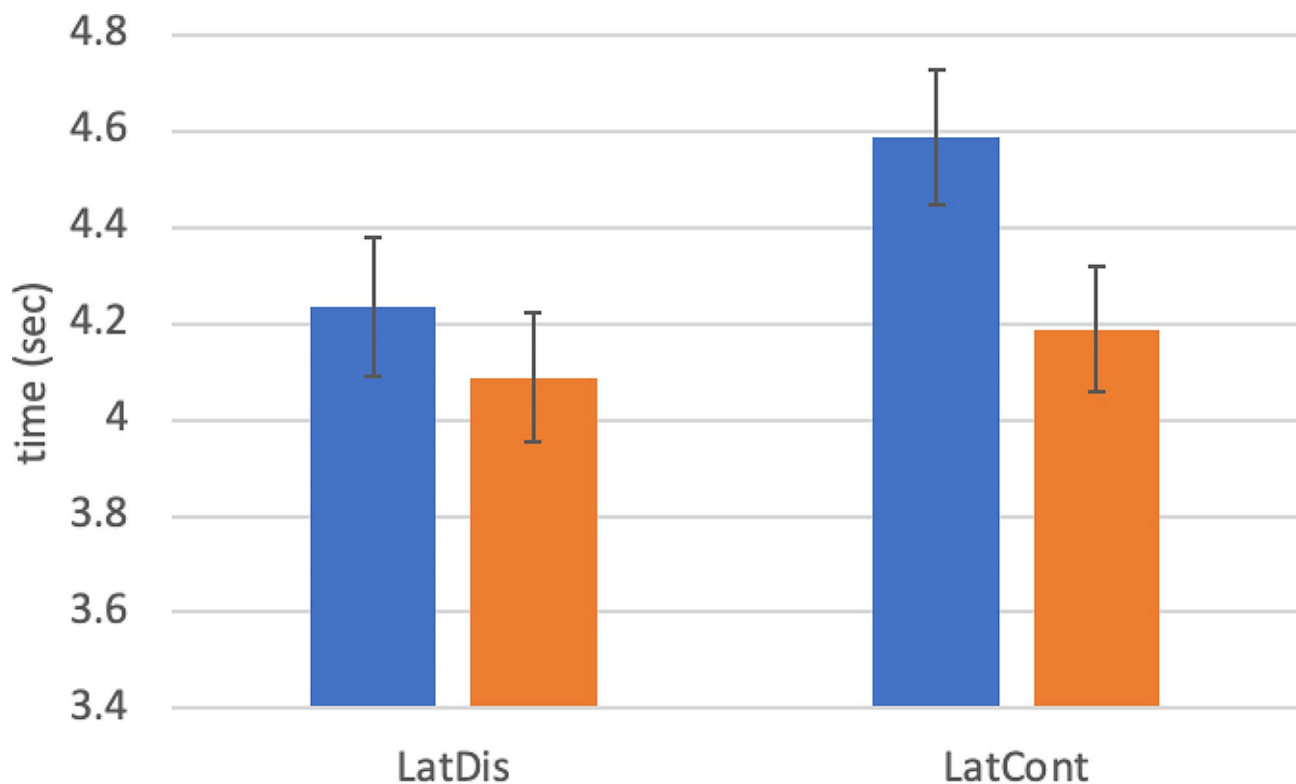


Fig. 2 Latency responses (means + standard errors) in distractor-trials (LatDis) and in control-trials (LatCont) for the clinical sample (AN) and for the control group (HC)

Table 3 Correlations between fixations and target advantage score and the subscales of the AQ and the eating subscales of the EDI-3, both in distractor-trials (Dis) (with spatial distractor-Sp and with dimensional distractor-Dim) and in control-trials (Cont)

	AQ	SS	AS	AD	C	I	DT	B	BD
Sp-DisFix	-0.105	-0.09	0.077	-0.187	-0.046	-0.043	0.018	0.053	-0.081
Sp-DisScore	-0.177	-0.26	0.04	-0.088	-0.14	-0.017	-0.255	0.325	-0.183
Dim-DisFix	-0.342	-0.312	-0.088	-0.269	-0.286	-0.038	0.082	0.328	0.016
Dim-DisScore	-0.38	-0.433*	0.102	-0.493*	-0.182	-0.038	-0.434*	-0.168	-0.259
Sp-ContFix	-0.286	-0.388	-0.112	-0.075	-0.239	0.01	0.058	0.17	-0.133
Sp-ContScore	0.2	-0.044	0.103	0.231	0.263	0.106	0.173	0.101	0.217
Dim-ContFix	-0.563**	-0.434*	0.054	-0.432*	-0.392	-0.505*	-0.119	0.066	-0.312
Dim-ContScore	0.171	-0.008	-0.064	0.195	0.145	0.302	0.131	-0.049	0.28

Abbreviations Sp: spatial criterion, Dim: dimensional criterion, DisFix: fixations in distractor-trials, ContFix: fixations in control-trials, DisScore: target advantage score in distractor-trials, ContScore: target advantage score in control-trials; AQ: AQ, total score of the Autism Quotient, SS, Social Skill, AS, Attention Switching, AD, Attention to Detail, C, Communication, I, Imagination; EDI-3: DT, Drive for Thinness, B, Bulimia, BD, Body Dissatisfaction; **:significant after FDR correction, * $p < 0.05$ (without FDR correction)

of the significant correlation found in the clinical sample was detected in the control sample.

Discussion

The primary goal of this study was to compare autism-relevant symptoms in a group of female adolescents with AN and a matched control group, using established questionnaire measures (AQ and IRI). As expected, subjects with AN showed significantly higher autistic traits than HC.

Furthermore, we evaluated the ability of perspective taking in both groups using the DT. We observed that subjects with AN took longer to decide which object to select and where to move it, both in distractor-trials and in control-trials. In AN group, we found a significant negative correlation between the number of fixations to the irrelevant object in the dimensional control condition and the total score of the AQ. In addition, performance on trials with dimensional distractor was negatively correlated with reduced social skills and a greater severity of the eating disorder.

Self-report questionnaires

As expected, the AN group had a statistically significant higher score on AQ total scale as well as on Social Skill, Attention Switching, and Communication subscales of the Autism-Spectrum Quotient [39]. Although the clinical sample also obtained a higher score on the Attention to Detail and Imagination subscales, the differences with HC were not statistically significant. These data are in line with a previous study conducted by our research group [48], in which a sample of 25 patients with AN-R was compared with a control group of 170 individuals. Even if only a few studies enrolled subjects under 18 years old [49–52], impairments of social skills and communication [53, 54] and of the abilities of attention switching [49] are frequently reported in AN.

A systematic review and meta-analysis assessing the use of AQ or abbreviated version (AQ-10) to examine

whether patients with AN had elevated levels of autistic traits, supported previous findings of higher prevalence of ASD in AN [12]. The Authors suggested that elevated levels of autistic traits in AN could indicate the presence of a neurodevelopmental disorder prior to the onset of the eating disorder. At the same time, other Authors suggested that anxiety and depressive symptoms, as measured with self-administered questionnaires, could have a major role in increasing autistic traits in AN-R [48], that could exacerbate factors that maintain the eating disorder [55].

Levels of empathy were measured using the Italian version of the Interpersonal Reactivity Index (IRI) [21, 41, 42]. No significant differences were found for either Cognitive and Affective Empathy scale or for the IRI subscales in the two groups.

Our results are in contrast with those reported in a recent review and meta-analysis [22]. The Authors examined the cognitive-affective empathy profile in adolescent and adult patients with eating disorders through the use of self-report measures. The meta-analysis of 8 studies showed that patients with AN had significantly lower cognitive empathy scores than HC, with a small effect size. However, the Authors suggested some caution in interpreting the results, due to the limitations of self-report empathy measures.

Eye-tracking results

To our knowledge, this is the first study in which an eye-tracking paradigm aimed at investigating perspective-taking skills is applied on a group of adolescents with Anorexia Nervosa. Previous studies using eye-tracking task in AN examined attention to food stimuli [56–59], to body stimuli [60–66], and to social or emotional stimuli [67–72], or assessed cognitive flexibility [73].

The two groups did not differ in percentage of errors, neither in distractor-trials nor in control-trials, both as regards the selection of the object and as regards the selection of the destination. Therefore, the two groups

appeared to perform similarly in the eye-tracking paradigm.

Even if some researchers argued that the (DT) assesses implicit mentalizing-as spontaneous or automatic representations of the mental state of others e.g., [44, 74]-, others [75] suggested that DT performance depends on explicit mentalizing-on instructed or deliberate representation of mental states-. In this latter case, the DT could fail in detecting possible impairment in implicit mentalizing, as documented in a previous study on adult males with Asperger syndrome [76]. Conversely, studies which demonstrated ToM deficit in subjects with AN investigated the implicit aspects of ToM [17, 77–79]. In this context, it was hypothesized that the DT is unreliable as a test of ToM use in communication, since optimal performance in DT is possible by using selective attention alone, and not necessary ToM [80].

Unlike the works by Dumontheil et al. [44] and Symeonidou et al. [32], we detected no significant age-related differences in participants' percentage of errors: these mixed results could be partly attributed to the narrow age-range of our sample compared to the two previous investigations in which subjects from childhood to adulthood were recruited.

We found a significant difference between the two groups in response latency (the time distance between the appearance of the stimulus and the first click made by the subject, i.e., the moment in which the decision-making process has been completed) both in distractor-trials and in control-trials: the clinical sample took significantly longer to decide which object to select and where to move it in both types of trials. We could speculate that the clinical sample showed an increased reaction time than HC.

There was no significant difference in duration (the total time between the appearance of the stimulus and the conclusion of the trial, i.e., the moment in which the subject provides the correct answer) between the two groups. Once subjects with AN made the first click, allowing the cursor to be displayed, they could be more accurate and faster in providing the correct answer than controls. This precision could be explained by the high levels of perfectionism that characterize AN patients, as demonstrated by the significantly higher score of the clinical group in the Perfectionism subscale of the EDI-3 [37]. The P subscale evaluates the extent to which a person places a premium on achieving a high goal and standard of personal achievement. Perfectionism represents a risk and maintenance factor for AN [81, 82] and is also configured as a predictor of worse prognosis and frequent dropouts in the treatment [83, 84]. Lloyd et al. [85] investigated the impact of perfectionism in a group of 82 subjects with AN (mean age 21.14 years) on two performance tasks, reporting that subjects with AN took longer

to complete the task and performed better than controls. Indeed, slow but accurate task switching performance in AN is also consistent with the results of a large synthesis of 23 studies and 165 experimental methods across the eating disorders literature which found a general “slow down” in choice reaction time task, especially when the task involved a decision component than when it did not [86].

The total duration of trials was slightly longer for both groups in control-trials than in distractor-trials. No differences were reported between the director trials with and without distractor. In our case, in distractor-trials, in which the choice was made between three objects, the subjects could approach the trials in a more efficient way than in control-trials, in which the choice took place between two objects. Another possible explanation is that, in the absence of the distractor, the subjects took longer to complete the decision-making process because, before providing the correct answer, they made sure that the distractor was actually not present.

It is widely accepted that fixations can indicate how we process information during spoken language comprehension [87, 88]. By measuring when participants fixate their gaze to an object, we can identify which object they are considering as a possible referent at a given point in time. There was no significant difference in the number of fixations to the distractor, neither in spatial condition, nor in dimensional one, and in the number of fixations to the irrelevant object, between the two groups. Furthermore, no significant difference was found in the target advantage score. We can therefore conclude that the two groups process the auditory information in the same way.

In both groups, the target advantage score with spatial distractor (the average probability of looking at the target object minus the average probability of looking at the distractor), improved with increasing chronological age of the subject. Our data are not comparable with those of Symeonidou et al. [32], since these Authors performed a temporal division of the pronounced sentence, evaluating the target advantage score in different moments of the verbal information processing by the subject. If we assume the target advantage score as a measure of ToM, however, our data appears in line with the hypothesis according to which the ToM undergoes a process of evolution during adolescence.

In AN group, we found no significant correlations for the number of fixations to the distractor in trials with dimensional distractors (Table 3).

We detected negative correlation between the target advantage score with dimensional distractor (the average probability of looking at the target object minus the average probability of looking at the dimensional distractor) and the Social Switching and Attention to Detail subscales of the AQ (Table 3), which respectively investigate

the interest in others and the social adjustment skills, and the tendency to extremely focus on details [39].

We also identified a negative correlation between the target advantage score with dimensional distractor and the Drive for Thinness subscale of the EDI-3, which investigates aspects of concern relating to the shape of one's body [37].

In dimensional control trials, a significant negative correlation between the number of fixations to the irrelevant object and the total score of the AQ was detected. We also found a negative correlation with the Social Switching, Attention to Detail, and Imagination subscales of the AQ, which disappeared after applying the FDR correlation.

In trials with spatial distractors and in spatial control trials, no significant correlations both for the number of fixations and for the target advantage score were identified (Table 3).

Although with due caution, it is interesting to note that the only correlations detected occur in dimensional distractor trials or in dimensional control trials. In both cases, subjects are asked to focus on the size of the objects (large vs. small). One key symptom of AN is a distortion of the perceptive component of the body image [7], in particular, AN patients tend to overestimate the size of their body [89]. In turn, disordered perception of their own body could lead to increased anxiety and social withdrawal related to their appearance [90]. The literature suggests that subjects with eating disorders who report more autistic features present more severe psychopathology and complex illness profiles, with more comorbid anxiety [91]. Therefore, we could speculate that, in the dimensional control trials, subjects with AN and higher autistic traits presented fewer fixations to the irrelevant object because they looked more at the two objects that differed in size.

Conclusions

This is the first exploratory study analyzing, at the same time, the clinical profile -on gold standard measures- and the ability of perspective taking -through the use of eye-tracking technology- in a group of young inpatients with AN.

Subjects with AN showed a high prevalence of autistic traits on the AQ. Unlike IRI, the eye-tracking technology detected some differences between AN and HC in their process during the perspective taking tasks. When performing the DT, the clinical sample presented longer response latencies than the control sample and no difference in overall trial duration. Longer reaction time in AN could be firstly dependent on task difficulty. In this regard, Ferraro et al. [86] sustain that the AN population tends to slow down as task difficulty increases compared to controls. A second hypothesis, not mutually exclusive

with the first, is that subjects with AN take more time to “put themselves in the shoes of others” than HC. In this line, task-based measures might capture the subtle differences that self-report instruments might miss.

As widely documented in literature, the presence of such ASD symptoms in AN has been associated with the need for more intensive treatments and poorer outcome [12, 92, 93]. In particular, regardless of psychotherapeutic and psychoeducational interventions, some studies report that a specific focus on perspective taking's abilities may be helpful by allowing patients with eating disorders to see themselves as separable from their illness [94, 95].

The results of this study need to be considered in light of a number of limitations and directions for future research. Firstly, it is important to emphasize the exploratory nature of this study, in which the limited number of patients and HC recruited prevents us from performing a more powerful statistical analysis of the data. Therefore, the findings of the study need to be confirmed with a larger sample to increase the level of evidence. Secondly, the current sample of patients lacks of homogeneity as far as AN subtypes and psychotropic medication. Regarding this latter aspect, although the clinical tolerance of second-generation antipsychotics and mood stabilizers in AN is globally good and the side effects are usually mild and transient [96, 97], we cannot exclude that these treatments may have played a role in the delay in latency times in the AN group. Finally, considering the bi-directional relationship between AN and ASD [9] (i.e. being autistic increases a person's risk of AN, and vice-versa having AN increases their chance of being autistic), a possible future investigation would explore how a group of ASD females -matched by age and QI with the current sample- perform the same DT, in order to evaluate distinct and shared findings with the AN group.

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Author contributions

Conceptualization, P.F., S.M., F.M., B.C. and S.C.; Methodology, L.B., F.M. and B.C.; Software, L.B. and P.M.; Validation, L.B., B.C. and S.C.; Formal analysis, L.B., P.M. and B.C.; Investigation, P.F. and L.B.; Resources, P.F., S.M., F.M. and S.C.; Data curation, P.F., L.B. and S.C.; Writing—original draft preparation, P.F., L.B., S.M. and F.M.; Writing—review and editing, B.C. and S.C.; Visualization, S.M., F.M. and S.C.; Supervision, F.M., B.C. and S.C.; Project administration, P.F., F.M. and S.C.; Funding acquisition, F.M. and S.C. All authors have read and agreed to the published version of the manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Regional Ethical Committee of Meyer Hospital (Florence, Italy), number 64/2019. Written informed consent from participants and a parent or guardian of the patients and from healthy individuals and their parents was obtained.

Competing interests

The authors declare no competing interests.

Author details

¹IRCCS Fondazione Stella Maris, Viale del Tirreno 331, Pisa I-56018, Italy
²Institute of Clinical Physiology, National Research Council of Italy (CNR), Pisa, Italy

³Residential Eating Disorder Treatment Center "Orti di Ada", Pisa, Italy

⁴Centre for Autism, School of Psychology & Clinical Language Sciences, University of Reading, Reading, UK

⁵Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy

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