

Social Cognition in Anorexia Nervosa: Evidence of Preserved Theory of Mind and Impaired Emotional Functioning

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Abstract

Background: The findings of the few studies that have to date investigated the way in which individuals with Anorexia Nervosa (AN) navigate their social environment are somewhat contradictory. We undertook this study to shed new light on the social-cognitive profile of patients with AN, analysing Theory of Mind and emotional functioning. Starting from previous evidence on the role of the amygdala in the neurobiology of AN and in the social cognition, we hypothesise preserved Theory of Mind and impaired emotional functioning in patients with AN.

Methodology: Thirty women diagnosed with AN and thirty-two women matched for education and age were involved in the study. Theory of Mind and emotional functioning were assessed with a set of validated experimental tasks. A measure of perceived social support was also used to test the correlations between this dimension and the social-cognitive profile of AN patients.

Principal Findings: The performance of patients with AN is significantly worse than that of healthy controls on tasks assessing emotional functioning, whereas patients' performance is comparable to that of healthy controls on the Theory of Mind task. Correlation analyses showed no relationship between scores on any of the social-cognition tasks and either age of onset or duration of illness. A correlation between social support and emotional functioning was found. This latter result seems to suggest a potential role of social support in the treatment and recovery of AN.

Conclusions: The pattern of results followed the experimental hypothesis. They may be useful to help us better understand the social-cognitive profile of patients with AN and to contribute to the development of effective interventions based on the ways in which patients with AN actually perceive their social environment.

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Introduction

Anorexia nervosa (AN) is a severe mental disorder characterised by refusal to maintain body weight at or above a minimally normal level for age and height, intense fear of gaining weight or becoming fat, and disturbance in the way in which one's body weight or shape is experienced [1]. Up to 80% of sufferers (predominantly females) engage in excessive exercise, in addition to self-starvation, to reduce their body weight [2–3]. The etiology of AN is not fully understood, but a crucial role is seemingly played by the complex interplay among biological, genetic, psychological, and socio-cultural factors [4]. AN has a prevalence of about 0.3% in young women [5] and has the highest mortality rate among psychiatric disorders [6]. Two forms of AN are described in the DSM-IV [1], the restrictive subtype (AN-R) and the binge-purge subtype (AN-BP). AN-R subtype refers to individuals who restrict food without regularly engaging in binge-eating or purging

behavior (i.e. self-induced vomiting or the misuse of laxatives, diuretics, or enemas) while the AN-BP subtype refers to individuals who regularly engage in binge-eating or purging behavior. The distinction between these two subtypes has been questioned by authors that have performed longitudinal study indicating that the migration from a diagnostic category to another is very common between AN subtypes [7–8].

In sharp contrast to other psychiatric [9–13] and neuropsychological disorders [14–18], in which social-cognitive competences have already been investigated extensively and for a long time, only recently have researchers and clinicians started to investigate the domain of social cognition in patients with AN. Social cognition is the ability to construct mental representations of the relations that exist between oneself and others and to flexibly use these representations to function effectively in one's social environment [19–20]. Social cognition is a sum of different processes and depends on the exchange of specific signals such as

facial expression, body movement, and eye gaze [21]. Examples of abilities referable to the domain of social cognition are both our capacity to represent other people's intentions and beliefs (i.e. Theory of Mind) [22–23], and the capacity to share the emotions and sensations of others (i.e. empathy) [24–25]. These distinct capacities display different ontogenetic trajectories reflecting the different developmental pathways of their underlying neural structures and represent the bases of any interpersonal relations [26–27].

The findings of the few studies that have to date investigated the way in which individuals with AN navigate their social environment are somewhat contradictory. With regard to Theory of Mind (ToM), Tchanturia et al. [28] assessed whether individuals with AN show a deficit in their ToM ability by administering to 20 female participants with AN two ToM tasks-a story-comprehension task previously employed to study children with autism [29] and a cartoon task previously employed to measure ToM in stroke patients [30]. Their findings show that the proportion of individuals who perform poorly on ToM tasks is higher among women with AN than among matched healthy controls, but also show that AN participants have impairments in both the ToM and control tasks. The authors thus suggest no evidence of any selective ToM impairment in AN sufferers. In a next study, Hambrook and Tchanturia [31] have explored Machiavellian competence in AN. Machiavellianism is the tendency to deceive and manipulate others for personal gain, and correlates with high manipulativeness, insincerity, and callousness [32]. This competence is closely connected to ToM ability, as it requires the comprehension of others' thoughts and intentions in order to predict how they will behave and how one can manipulate them. To study Machiavellianism in people with AN, Hambrook and Tchanturia [31] used the Mach-IV, a self-report questionnaire composed of 20 statement items. Their results indicated no significant differences between people with AN and healthy controls. In contrast with these findings, more recently, Russell et al. [33] found ToM impairments in the Reading the Mind in the Eyes task (RME, see below for a detailed description of this task) in a group of 22 patients with AN. This last result was not replicated by Oldershaw et al. [34], who did not find impaired performance in the RME task in people with AN, but did find impairments in two different versions of this task (the voice and films containing a social scene versions). Interestingly, in two studies by Harrison and her colleagues [35-36] people with AN performed poorer than healthy controls on the RME task, while in a further work [37] these authors found only a statistical trend (p = .091) toward a significant difference between AN patients of the restrictive subtype and healthy controls and no difference for the bingepurge subtype.

Conflicting results were also found by Hambrook et al. [38]. They predicted that AN patients would display an empathising/systemising psychometric profile similar to that found in people with autism spectrum disorders. To this end, three standardised self-report measures were administered: the Autism-Spectrum Quotient [39], the Systemizing Quotient [40] and the Empathy Quotient [41]. The results revealed that women with AN and healthy controls did not differ in scores on either the Empathy Quotient or the Systemizing Quotient, but at the same time, that AN patients did report significantly higher total Autism-Spectrum Quotient scores than did healthy controls. According to Hambrook et al. [38], this latter result suggests that AN patients experience difficulties similar to those found within the autism spectrum disorders.

With regard to emotional functioning, Guttman and Laporte [42], using the Interpersonal Reactivity Index [43], an

instrument for assessing four dimensions of empathy, did not find any difference between AN patients and healthy controls; however, empathy disorders were found in AN patients by Gillberg et al. [44] on the basis of structured clinical interviews. Interestingly, these two studies converge in ascribing to individuals with AN alexithymic disorders, the single rather well-established result in the AN literature concerning social cognition [45-47]. Furthermore, although different studies have found in people with AN difficulty recognising emotions from facial expression and vocal tone [48-50], recently Rozenstein et al. [51] have shown that patients with AN are as fast and as accurate in matching both facial identity and facial emotions as their unaffected sisters and unrelated healthy controls. In an attempt to systematize this literature, Zucker et al. [52] generated the hypothesis that individuals with AN fail to process facial regions as a result of elevated levels of anxiety around emotional experience that lead to prolonged avoidance of salient facial cues, promoting inaccurate interpretation. According to these authors, such chronic avoidance would lead to decreased experience in the processing of faces and increased dysfunction over time.

Faced with the discordant literature described above, we undertook this study to shed new light on the social-cognitive profile of patients with AN, analysing ToM and emotional functioning. To this end, we used a set of validated experimental tasks widely employed in the social-cognition literature: the Reading the Mind in the Eyes (RME) test, the Empathy Quotient (EQ), and the Twenty-Item Toronto Alexithymia Scale (TAS-20) (see below for a detailed description of these tasks). Furthermore, as a potential role of social support in the treatment and recovery of AN was proposed [53], we also used the Multidimensional Scale of Perceived Social Support (MSPSS) with the aim to explore this proposal and to check for possible correlations between the social-cognitive profile and the social support subjectively perceived by the patients with AN.

The experimental hypothesis of the present study is based on the neuroimaging and neuropsychological evidence that ToM and emotional functioning are associated with overlapping but distinct brain networks [54-56]. Common areas of activation are the prefrontal cortex, the superior temporal sulcus, and the temporo-parietal junctions. These areas form the basis for making inferences about mental states [57-59]. However, the appreciation of the emotional states requires the additional engagement of emotional networks, and particularly of the amygdala [55-56,60-61]. In fact, while the amygdala is not involved in mentalising (i.e. ToM) per se [62] and is not necessary for ToM expression [63-65], its role in processing basic and social emotions, related both to the self and to others, is well known [27,55,65-67]. Interestingly, an increasing number of neuroimaging studies [68-77], adopting different experimental paradigms, have shown structural and functional alterations of the amygdala in people with AN and have highlighted the crucial role of this brain structure in the neurobiology of AN. Thus, starting from the neuroimaging evidence according to which a) the amygdala plays a pivotal role both in the neurobiology of AN and in all facets of emotional processing, and b) the amygdala is not necessary for ToM, in the present work we hypothesise that the performance of patients with AN will be significantly worse than that of healthy controls on tasks assessing emotional functioning (i.e. the EQ and the TAS-20), whereas AN patients' performance will be comparable to that of healthy controls on the ToM task (i.e. the RME).

Methods

1. Ethics Statement

The study was approved by the Spedali Civili Hospital of Brescia's ethics committee and was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants, and written parental permission was requested and received for participants under 18.

2. Participants

Thirty women diagnosed with AN according to the DSM-IV [1] were recruited from the Regional Center of Eating Disorders at the Spedali Civili Hospital of Brescia, Italy. Sixteen participants fell into the restrictive subtype (AN-R), and 14 into the bingepurge subtype (AN-BP) at the time of the study. Consensus diagnoses were obtained from senior psychiatrists who assessed the patients in clinical interviews and by use of the Structured Clinical Interview for DSM-IV [78]. Exclusion criteria were comorbidities of the following types: mental retardation, cognitive disorders, psychosis, major depression, and personality disorders.

Thirty-two women were involved in the healthy control (HC) group. Exclusion criteria for the HC group were the presence or history of a neurological or psychiatric disorder, substance abuse, or dependence. Furthermore, a HC participant was included in the study only when she had both a Body Mass Index (BMI = Kg/m²) between 18.50 and 24.99 (i.e. within the normal range of weight according to the World Health Organization [79]), and a score below the cut-off of 30 on the Eating Attitudes Test [80], a standardised 40-item self-report scale measuring the risk of an eating disorders. All the participants were native Italian speakers.

3. Procedure

All participants were tested individually in a quiet room. Testing required one session lasting about 45–60 minutes. Tasks were administered to all participants in random order. BMI was calculated based on the weight and height of participants measured on the day of testing.

4. Materials

4.1 Reading the mind in the eves (RME) test. The RME is an advanced ToM test measuring an adult's mentalising ability [81]. In the test, the experimenter presents a set of 36 photographs of the eve region of various human faces. Participants are required to choose among four words that are printed on the page that the picture appears on, using the criterion of which word best describes the mental state of the person depicted in the photograph. Participants have unlimited time to decide, and a glossary is provided. In order to pass this test, participants have to put themselves into the mind of another person and recognize his or her complex mental state, an ability that emerges around the time of adolescence. In the gender-recognition control task, participants are asked to judge the gender of the person in each of the 36 photographs. For both experimental (mental state attribution) and control (gender attribution) conditions, the maximum score is 36.

The RME test is administrable in adults at least 16 years old. For this reason, we excluded participants below this age from both the AN and HC groups.

4.2 Empathy quotient (EQ). The EQ is a validated self-report questionnaire for the assessment of the capacity to empathize with other, i.e. to recognize another's affective state and to respond with an appropriate emotion to this [41]. The EQ contains 40 empathy items and 20 filler items included to distract the participant from a relentless focus on empathy. On each

empathy item a person can score 2, 1, or 0, so the EQ has a maximum score of 80 (higher scores represent greater empathy). The EQ is able to pick up considerable individual, gender, and group differences, in both general-population and clinical samples.

4.3 Twenty-Item toronto alexithymia scale (TAS-20). The TAS-20 is the most commonly used measure of alexithymia, i.e. a deficit in the cognitive processing and regulation of emotion, resulting in difficulties in describing and identifying feelings [82]. The TAS-20 [83] is a validated self-report scale comprised of 20 items. People being assessed are asked to rank their own answers on a five-point Likert scale, with 5 indicating the highest degree of agreement and 1 the highest degree of disagreement with the affirmation expressed in each item. The TAS-20 has a three-factor structure: difficulty in identifying feelings (Factor 1, items 1, 3, 6, 7, 9, 13, 14), difficulty communicating feelings to other people (Factor 2, items 2, 4, 11, 12, 17), and externally oriented thinking (Factor 3, items 5, 8, 10, 15, 16, 18, 19, 20).

The total alexithymia score is the sum of responses to all 20 items. The TAS-20 cut-off scores are as follows: \leq 51 no alexithymia, 52–60 borderline alexithymia, \geq 61 alexithymia. This scale has shown good internal consistency and test-retest reliability, as well as convergent, discriminant and concurrent validity [84], and it is currently one of the most utilised instruments in alexithymia and emotion research.

4.4 Multidimensional scale of perceived social support (MSPSS). The MSPSS [85] is a validated self-report measure of subjectively assessed social support. This questionnaire provides assessment of three sources of social support: family, friends, and significant others. The MSPSS consists of 12 items, each scored on a seven-point Likert-type scale, easy to understand (requiring just a fourth-grade reading level) and suitable for young populations. The maximum score is 84; higher scores indicate greater perceived support. The MSPSS has been shown to be relatively free of social-desirability bias [86].

4.5 Beck depression inventory, revised version (BDI-II). The presence of symptoms related to depression was evaluated by means of the BDI-II, a 21-item multiple-choice self-rated scale [87]. The total score was obtained considering all items, rated from 0 to 3. A total scores of 0–13 indicates minimal depression, 14–19 mild depression, 20–28 moderate depression, and, finally, scores higher than 29 are indicative of severe depression.

4.6 Eating attitude test (EAT). The EAT [80] is the most broadly used self-report questionnaire in the field of eating disorders. The 40 items composing the EAT are presented in a sixpoint forced-choice Likert-type scale ranging from 1 (never) to 6 (always). Of these response options, three are scored with 1, 2 or 3, and the rest with 0. Total EAT score ranges from 0 to 120, and the clinical cut-off point is usually considered to be 30.

5. Statistical Analyses

Data were analysed using the Statistical Package for the Social Sciences (SPSS), version 18.0. Graphical and statistical exploration of the data by means of box plots, histograms, Q-Q plots and normality tests indicated a normal distribution of all measures; hence, parametric tests such as the unpaired t-test and Pearson's correlation coefficients were used, as appropriate. All tests were two-tailed and were conducted at the 5% level of statistical significance.

Results

Preliminary analyses revealed no differences between the participants of the AN-BP subtype and those of the AN-R subtype in any of the demographic, clinical, or experimental variables considered, except for age (AN-BP = 22.43, AN-R = 17.38; unpaired t-test, df = 28, t = 2.473, p = .020), education (AN-BP = 14.43, AN-R = 12.13; df = 28, t = 2.384, p = .024) and duration of illness (AN-BP = 5.86, AN-R = 1.69; df = 28, t=2.320, p=.028). These results are in line with those indicating that the AN patients of the restricting type tend to have a shorter duration of illness and to be younger (and consequently with less years of education) than those of the binge-purge subtype, and suggesting that the AN-R subtype represents a phase in the course of AN rather than a distinct subtype [7-8]. For this reason, and since no significant differences were found in any experimental variables considered, we collapsed the two subtypes of AN into a single group for further analyses.

Descriptive and Clinical Data

Participants' demographic and clinical data can be seen in Table 1. The two groups were comparable on age, years of education and height. Self-evidently, there were statistically significant differences for the weight and BMI variables. BMI ranged from 12.27 to 17.79 in the AN group and from 18.56 to 24.61 in the HC group. The AN group was significantly more depressed than the HC group, as measured by the BDI-II. According to the cut-off scores of the BDI-II, 33% of the patients with AN (10/30) had minimal or mild depression and 67% (20/30) had moderate or severe depression, compared with 94% (30/32) with minimal or mild depression and 6% (2/32) with moderate or severe depression in the HC group (data not shown in table). All of the participants in the HC group were well below the cut-off of the EAT, with a minimum of zero and a maximum of 21.

Social-cognition Tasks and Social-support Questionnaire

In table 2 are reported the participants' scores to the ToM and emotional functioning tasks, and to the social-support question-naire. For the RME, the number of correct responses for both the experimental (mental-state attribution) and the control (gender attribution) tasks were considered. Statistical analyses revealed the absence of significant differences on both the experimental and control tasks. The groups demonstrated significantly different

results for both the EQ and TAS-20 tasks, with AN patients showing a lower degree of empathy and a higher degree of alexithymia. According to the cut-off scores of the TAS-20, 17% of the patients with AN (5/30) had borderline alexithymia and 47% (14/30) had high alexithymia, compared with 9% (3/32) with borderline alexithymia and no occurrence of high alexithymia in the HC group (data not shown in table). The group of patients with AN scored significantly higher than the HC group on all the three factors of the TAS-20. This result remains significant also after using the Bonferroni correction for multiple testing (.05/3). Finally, compared to the HC group, a lower level of perceived social support as assessed by the MSPSS was found in the AN group.

Correlation Analyses

The correlation analyses for the AN group are shown in Table 3. Given the exploratory nature of these analyses, there is no correction for multiple comparisons. No significant correlations were found between BMI, age of onset, or duration of illness and any of the clinical or experimental tasks. Equally, no correlations were found between the RME task and any of the other measures. A positive correlation was found between TAS-20 and BDI-II, whereas negative correlations was found between EQ and TAS-20 and between BDI-II and MSPSS. Interestingly, for what concerns the MSPSS, a positive correlation was found with EQ and a negative correlation with TAS-20, even when controlling for BMI, BDI-II, age of onset, and duration of illness (partial correlations, $r = .593 \ p = .001 \ \text{and} \ r = -463 \ p = .017, \text{ respectively}.$

Discussion

The main aim of the present study was to investigate social cognition in patients with AN. The pattern of results followed the experimental hypothesis: more precisely, the performance of patients with AN is significantly worse than that of healthy controls on tasks assessing the emotional functioning (i.e. EQ and TAS-20), whereas patients' performance is comparable to that of healthy controls on the ToM task (i.e. RME). Interestingly, correlation analyses showed no relationship between scores on any of the social-cognition tasks and either age of onset or duration of illness.

Our results are in line with previous studies showing emotional functioning deficits in people with AN [44-47] and unimpaired performance in the ToM domain [28,31]. On the contrary, we

Table 1. Demographic and clinical characteristics.

	AN group Mean (SD)	HC group Mean (SD)	t-test results
	(n = 30)	(n = 32)	(df = 60)
Age, years	19.73 (6.06)	20.47 (2.72)	t = −.623, p = .536
Years of education	13.20 (2.85)	14.13 (1.76)	t = -1.551, p = .126
Height (cm)	162.11 (5.03)	164.66 (5.95)	t = -1.814, $p = .075$
Weight (kg)	39.54 (4.57)	54.78 (4.72)	t = −12.916, p<.001
Body Mass Index (Kg/m²)	15.06 (1.74)	20.21 (1.45)	t = −12.668, p<.001
Age of onset	15.77 (3.74)	-	-
Duration of illness	3.63 (5.27)	-	-
EAT (maximum score = 120, cut-off = 30)	-	7.59 (4.98)	-
BDI-II (maximum score = 63)	26.40 (13.39)	8.94 (6.66)	t=6.563, p<.001

HC = Healthy controls, AN = Anorexia nervosa, SD = Standard deviation, df = Degrees of freedom, cm = centimeters, Kg = Kilograms, BMI = Body Mass Index, EAT = Eating Attitudes Test, BDI-II = Beck Depression Inventory-II. doi:10.1371/journal.pone.0044414:t001

Table 2. Participants' scores to the tasks assessing ToM and emotional functioning, and to the social-support questionnaire.

	AN group Mean (SD)	HC group Mean (SD)	<i>p</i> value	
	(n = 30)	(n = 32)	(df = 60)	
ToM and emotional functioning tasks				
RME experimental (maximum score = 36)	25.60 (3.93)	26.97 (3.33)	t = -1.484, p = .143	
RME control (maximum score = 36)	34.20 (1.79)	34.69 (1.45)	t = -1.183, p = .241	
EQ (maximum score = 80)	44.17 (11.47)	50.72 (8.35)	t = -2.584, $p = .012$	
TAS-20 Global score (maximum score = 100)	56.70 (12.94)	40.47 (7.77)	t=6.032, p<.001	
TAS-20, Factor 1 (max. score = 35)	21.30 (6.61)	14.00 (3.19)	t=5.954, p<.001	
TAS-20, Factor 2 (max. score = 25)	16.80 (4.57)	12.06 (3.35)	t=4.678, p<.001	
TAS-20, Factor 3 (max. score = 40)	18.60 (5.63)	14.41 (3.56)	t = 3.528, p = .001	
Social-support questionnaire				
MSPSS (maximum score = 84)	68.27 (12.48)	75.03 (5.63)	t = -2.780, p = .007	

HC = Healthy controls, AN = Anorexia nervosa, ToM = Theory of Mind, SD = Standard deviation, df = Degrees of freedom, RME = Reading the Mind in the Eyes, EQ = Empathy Quotient, TAS-20 = Twenty-item Toronto Alexithymia Scale, EAT = Eating Attitudes Test, MSPSS = Multidimensional Scale of Perceived Social Support. doi:10.1371/journal.pone.0044414.t002

found divergent results from those of Russell et al. [33]: these authors used the RME to test the ToM ability in a sample of 22 English female participants with AN and found that they performed more poorly than the HC group. Although slight cultural differences between their sample and the one investigated in the present study (composed of Italian females with AN) may have influenced responses to the RME at least to some degree, we believe that the difference between the results of these two studies is mainly due to methodological issues. First of all, in the study by Russell et al. [33] there was a statistically significant difference between the AN and HC groups on both mean age and years of education. It is now well known that mean age is a particularly important variable when assessing ToM ability with the RME, as different studies have recently found age-related effects on performance in this task [88-90] and a neuroimaging study has demonstrated age-related differences in the neural activation associated with the RME in adolescents [91]. Education is another relevant variable, as it seems reasonable to expect that average

length of educational experience might potentially impact understanding of the target word and the three foil words. Until now, it has never been clearly shown that scores obtained on this test do not strongly depend on the individual's general intelligence [92]; it has even been suggested that intelligence quotient may predict performance on the RME in AN patients [34]. For these reasons, we suggest that future research should pay particular attention to the participants' demographic variables, avoiding comparisons between the performance of samples that are not well matched for age or education. Furthermore, in the present study we assigned to the HC group only participants with a BMI between 18.50 and 24.99 (i.e. within the normal range of weight according to the World Health Organization) and a score below the cut-off of 30 on the EAT (i.e. without the risk of having an eating disorder). In the study by Russell et al. [33] the HC group had a mean BMI of 26.2, and no test to check for potential eating disorders was administered to this group.

Table 3. Pearson correlations in the AN group. Significant correlations are shown in bold.

	вмі	Onset	Duration	uration BDI-II		TAS-20	EQ	MSPSS
	DIVII	Oliset	Duration	BDI-II	RME	143-20	EQ	IVISESS
BMI	-							
Onset	r = .103 p = .589	-						
Duration	r = .013 p = .947	r =136 p = .474	-					
BDI-II	r = .172 $p = .363$	r =277 p = .138	r =063 p = .740	-				
RME	r = .020 $p = .917$	r =178 p = .347	r = .301 p = .106	r = .102 $p = .591$	-			
TAS-20	r = .173 p = .361	r = .146 p = .441	r =249 p = .185	r=.523 p=.003	r =059 p = .755	-		
EQ	r = .038 p = .840	r =139 p = .464	r = .302 p = .104	r =038 p = .844	r = .172 p = .365	r=471 p=.009	-	
MSPSS	r =270 p = .149	r = .084 p = .658	r = .200 p = .290	r=−.436 p=.016	r = .135 p = .478	r= −.587 p=.001	r=.539 p=.002	-

BMI = Body Mass Index, BDI-II = Beck Depression Inventory-II, RME = Reading the Mind in the Eyes, TAS-20 = Twenty-item Toronto Alexithymia Scale, EQ = Empathy Quotient, MSPSS = Multidimensional Scale of Perceived Social Support.

A further variable that may contribute to explain discrepancies between our results on the ToM task and those of previous studies is the duration of illness. While in our group of participants with AN the mean duration of illness is well below four years, in the study by Russell et al. [33] this variable exceeds nine years, as well as in the studies by Harrison et al. [35-36] in which a statistical difference to the RME was found. As suggested by Harrison et al. [35], it is possible that their findings may be secondary to severe weight loss and the starvation effects associated with AN and that it would be a good idea to explore this question using a sample with a shorter illness duration. We have followed this suggestion. To the best of our knowledge, no previous studies have investigated the ToM ability in an AN group with a shorter duration of illness and thus the present findings contribute to extend our knowledge on the relationship between this latter dimension and the level of ToM ability in patients with AN. We suggest that this relationship should be further investigated in longitudinal studies that could properly test the hypothesis proposed by Zucker et al. [52] according to which individuals with AN are characterised by a chronic avoidance of salient social cues (such as facial ones) that leads to increased dysfunction over

We interpret our results also in light of the evidence of the crucial role played by the amygdala in the neurobiology of AN. In fact, numerous structural and functional neuroimaging studies [68-77] point to the role of this cerebral region in emotional processing and to its alterations in people with AN, supporting our hypothesis of impaired performance among these people in the tasks we used to assess emotional functioning. While the role of the amygdala in determining the capacity to share emotional experiences and to recognize emotions in oneself and others is well known and acknowledged [55-56,66-67], the role of this brain structure in ToM is very controversial and highly debated. Indeed, although Baron-Cohen et al. [93] proposed the 'amygdala theory' to explain autism (a neurodevelopmental disorder characterised by ToM impairments), this theory has been subsequently revisited by Dziobek et al. [63], who show that in autism the amygdala is not crucially involved in social functioning, and by Paul et al. [64] who by assessing two rare individuals with developmental bilateral amygdalar lesions demonstrated that the amygdala is not essential for the aspects of social behavior that are diagnostically characteristic of autism. Furthermore, investigating by means of a factorial design the interaction between the emotional and perspective-tacking (ToM) factors, Ruby and Decety [65] come to the conclusion that the amygdala is not necessary for ToM expression. Anyway, it is worth noting that with only one exception [94] none of the functional imaging studies that have to date investigated the ToM brain areas involved in solving the RME task report amygdala activations [91,95–98] and that a lesion study examining two patients with bilateral amygdalar damage reported impaired performance to the RME in only one patient [99]. Overall, these findings seem to support the hypothesis originally proposed by Gallagher and Frith [62] according to which the amygdala is not involved in

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mentalising *per se*, as well as our hypothesis of a preserved ToM ability in patients with AN on the RME task.

Our results concerning perceived social support deserve attention. They are in accordance with previous findings reporting lower levels of perceived social support in patients with AN than in an HC group [100] and showing no correlation between social support and duration of illness [53]. Furthermore, to the best of our knowledge, the present study is the first to demonstrate a correlation between social support as perceived by AN patients and emotional functioning. Although the nature of the present study does not permit inference of cause and effect, this latter result is particularly relevant, as it seems to suggest a potential role of social support in the treatment and recovery of AN, and it supports previous indications according to which interventions designed to encourage patients to broaden their social networks may be a useful addition to standard approaches based on a good therapeutic relationship [53,101]. In particular, interventions based on helping the patient to reflect on the impact her behaviors have on the feelings of her carers and, contextually, based on developing more effective methods for eliciting social support might be recommended.

The present study has several limitations, however. First, compared with other studies in this area, we enrolled a greater number of patients with AN, but nonetheless, our study is still limited by a relatively small sample size. Second, although there is a strong amount of structural and functional evidence supporting the crucial role of the amygdala in the neurobiology of AN, we conducted no direct measurement of activity in this brain structure in the patients of our sample. Third, the experimental tasks we used elicit mainly reflective processes of social cognition. Further studies should integrate this kind of task with others able to elicit more automatic processes as well: as face regions outside from the eyes can convey a number of socially relevant information, of particular interest are the tasks concerning the evaluation of faces expressing basic and social emotions [102-106]. Despite these limitations, we believe the findings presented here may be useful to help us better understand the social-cognitive profile of patients with AN and to contribute to the development of effective interventions based on the ways in which patients with AN actually perceive their social environment.

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Author Contributions

Conceived and designed the experiments: MA PT RBA. Performed the experiments: MA PT RBA. Analyzed the data: MA RBA. Contributed reagents/materials/analysis tools: MA PT RBA. Wrote the paper: MA RBA. Collection of medical data: PT. Participant recruitment: MA PT RBA.

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