

RESEARCH ARTICLE

Autistic Traits and Social Responsiveness: The Relationship Between Autistic Traits and Comorbid Psychiatric Symptoms in Adolescents with Anorexia Nervosa

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ABSTRACT

Introduction: It is known that patients with anorexia nervosa (AN) display social difficulties like social responsiveness and high levels of autistic behaviors such as rigidity, narrow interests of food and weight; however it is not clear whether they have comorbid Autism Spectrum Disorders (ASD) or it is about acute phase of illness. In this study it is aimed to investigate autistic traits and social responsiveness in adolescents with AN.

Methods: Study group was consisted of 39 female AN patients aged between 12-18 years. Control group was consisted of 34 female adolescents who did not have any psychiatric disorder. K-SADS-PL was applied to all participants in order to detect the psychiatric disorders. Autism traits and social responsiveness were evaluated using Social Responsiveness Scale. All adolescents of the study were administered The Eating Attitude Test, Beck Depression Inventory, Screen for Child Anxiety and Related Disorders, Maudsley Obsesive Compulsive Inventory.

Results: Results of the study indicated that adolescents with AN had higher symptoms of depression, anxiety and autism-like symptom clusters; and lower social responsiveness. Psychiatric comorbidities were not associated with these difficulties.

Conclusion: The results show that AN patients have an impairment of social responsiveness, the impairment seems to be associated with AN regardless of psychiatric comorbidities. Despite these two disorders are considered unrelated, they have several traits in common. These results suggest that there may be a common pathogenesis between ASD and AN.

Keywords: Anorexia nervosa, autistic traits, autism, adolescents, social responsiveness, comorbidity

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INTRODUCTION

Anorexia Nervosa (AN) is characterized by a significantly low body weight due to restricted food intake, an intense fear of gaining weight, and a disturbance in self perceived body image (1). The onset of AN is usually during adolescence, between the age of 13 and 20 years, but studies in recent years have reported that age of onset has gradually decreased (2). It is one of the leading psychiatric disorders that severely impairs social functioning (3) and is more common in females [female-to-male (F: M) ratio is 10:1] (4). Autism spectrum disorder (ASD) is a pervasive developmental disorder with an early onset characterized by difficulties with social interaction and communication and repetitive, stereotyped interests and behaviours (1). In contrast to AN, ASD is more prevalent in males (M: F ratio of 4:1) (5) and differences in social communication can be observed even in the first year of life (1). Despite these distinct clinical features, it is known that patients with AN display difficulties in social responsiveness and high levels of autistic traits such as cognitive rigidity, restrictive/repetitive patterns of behavior, narrow interests in food and weight (6); however it is not clear whether patients have comorbid ASD or it is about the acute phase of the illness (7).

There have been many studies over the past few years documenting the relationship between AN and ASD, first identified by Gillberg in 1983

(8). Both conditions share a common profile of resistance to changes, social withdrawal and social disengagement, and show similar patterns of neurocognitive dysfunction including impaired set-shifting, weak central coherence, and impaired theory-of-mind (ToM) abilities (6, 9). Patients with AN have also poor social and emotional functioning (10, 11), including interpersonal relationship problems (7), reduced facial emotion expression (12), impaired facial emotion recognition (13), difficulties identifying emotions (10) and social anhedonia (3). As a result, the studies based on experimental data and clinical observations show that these cognitive, socio-emotional and interpersonal problems may be both a cause and a contributing factor in the course of the disease (14). It is therefore possible that the presence of underlying ASD traits effectively maintains AN (7, 11). On the other hand, deterioration in social and emotional functioning in the course of AN is also associated with longer duration of disease, increase in disease severity, and poorer treatment outcome (3, 15, 16).

Recent studies have emphasized the overlap between these conditions with the hypothesis that ASD could be a risk factor for females to develop AN (17). Another thought supporting this idea is that ASD may present with different clinical symptoms in females than in males

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like better social skills, less stereotyped behaviors or restricted interests (18, 19), so that females may be under-diagnosed or misdiagnosed as having other disorders (20). An important challenge in investigating the relationship between AN and ASD is the presence of starvation and comorbid psychopathologies such as obsessive-compulsive disorder (OCD) symptoms, anxiety or depression in AN which might also have more contribution to above-mentioned cognitive and socio-emotional problems, rather than the underlying neurodevelopmental disorder (7, 21, 22).

In the light of this information, the objective of this study was to investigate the social responsiveness and autistic traits in adolescent girls with AN and to examine the relationships of these variables with comorbid psychiatric symptoms. Because a well-documented but poorly understood relationship between AN and ASD is associated with longterm morbidity and increased mortality. It also remains unclear whether this relationship is independent of comorbid psychiatric symptoms. Adolescents with AN were assumed to have less social responsiveness and more autistic traits when compared to healthy counterparts, even though the effect of comorbid depressive, anxiety and obsessive compulsive symptoms on these variables were controlled. In the studies performed in patients with autism, Social Responsiveness Scale (SRS) was frequently used to assess various difficulties in the area of social reciprocity such as understanding social messages or engaging in social interactions and increased SRS scores were associated with impairment in social responsiveness and social functioning. Although the SRS has been validated and widely used as a quantitative measure of autistic traits in different psychopathologies (23-26), to our knowledge it has not been used in the studies of adolescents with AN. The majority of the studies investigating autistic traits in AN have used the Autism-Spectrum Quotient (AQ). Thus, the another aim of the present study was to investigate the social responsiveness and austistic traits in adolescent girls with AN by using SRS.

METHODS

Participants

The research group was recruited from the patients who were diagnosed with AN at the Department of Child and Adolescent Psychiatry, or the Division of Adolescent Medicine at Hacettepe University. The research group consisted of female adolescents between the ages of 12 and 18 years, with normal mental development according to psychiatric evaluation, and without any chronic medical disease. AN and other psychopathologies were diagnosed by applying Schedule for Affective Disorders and Schizophrenia for School-Age Children, Present and Lifetime Version, DSM-5 November 2016-Turkish Adaptation (K-SADS-PL-DSM-5-T). Among the 40 participants assessed with the provisional diagnosis of AN, one was excluded from the study due to the presence of accompanying ulcerative colitis and remaining 39 female adolescents made the study group. All patients in the research group received a restrictive type of AN diagnosis, were in the acute phase of the disorder and medically stable during the psychiatric evaluation. The patients who required hospitalization for medical stabilization were evaluated within one month after discharge from the hospital. The control group was created by pairing the patients with voluntary adolescents who had no complaints and history of psychiatric, neurologic or chronic medical diseases, with regard to age, gender and socio-economic status. Thirtyfour female adolescents between the ages of 12 and 18 years constituted the control group. The adolescents and their parents who participated in the study gave written informed consent after briefing them on the details of the study. The research protocol was approved by the Ethics Committee of Non-Interventional Clinical Researches of Hacettepe University with the decision number GO 15/355-17.

Measures

Socio-demographic and Clinical Information Form. It is the information form prepared by the researchers in order to determine socio-demographic, developmental and medical histories of the participants. This form included questions on the socio-demographic variables, developmental milestones, clinical course of the symptoms, medical problems, medications, interventions, and family history of psychiatric and medical disorders.

Hollingshead-Redich Scale. The Turkish translation of the scale which is formed to determine the socio-economic level of the families (27) was used. The scale produces a general measurement that reflects the highest level reached for a period of time, based on the occupation and educational status of the parents.

Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version, DSM-5 November 2016-Turkish Adaptation (KSADS-PL-DSM-5-T). The K-SADS-PL is a semi-structured clinical interview form developed by Kaufman et al. (28) to determine the past and the present psychopathologies of children and adolescents. The validity and reliability study of the Turkish sample of the scale which is based on the DSM-5 diagnostic criteria (KSADS-PL-DSM-5-T) was conducted (29). K-SADS-PL-DSM-5-T was applied to both groups and their parents to confirm the diagnosis of AN and to identify the accompanying psychiatric disorders in the research group, and to exclude those with psychiatric disorders in the control group.

Eating Attitudes Test-40 (EAT-40). The EAT-40 is a self-report scale that assesses the changes in eating behaviours in both healthy populations and patients with eating disorders (EDs) (30). The scale consists of 6-point Likert-type 40 items. The Cronbach alpha index of the internal consistency was found as 0.70 in the validity and reliability study of the Turkish form of the EAT-40 (31).

Social Responsiveness Scale (SRS): The SRS is a 65-item parent questionnaire asking about the child's social behavior in the past six months, particularly focusing on the parent's perception of the child's ability to process social information and respond appropriately in interpersonal interactions (32). The measure represents the three criterion domains for autism and multiple publications have shown that the SRS correlates strongly with a gold standard diagnosis of ASD, based on the Autism Diagnostic Interview (32). The scale includes 39 items on reciprocal social behaviors and communication, six items on social usage of language and 20 items on autistic traits. Based on a previous study that identified five separate factors through principal components analysis of the SRS (33), the total score is often broken down into five subscales: receptive awareness, cognition, expressive communication, motivation, and autistic mannerism. As the overall score obtained from the scale increases, the severity of the social impairment also increases. Although the Turkish reliability and validity study of the scale has not been published yet, in a large scale study of school-age children, it was employed by Unal et al. (34). In this study, the Cronbach's alpha value of the SRS was found to be 0.86 and, based on a factor analysis, it was decided that the test would be used as a single factor. The test-retest reliability of the Turkish version of the SRS was determined to be high, based on the data that were obtained six months apart (Pearson's r=0.53, P=0.001) (34).

Beck Depression Inventory (BDI). Beck and his colleagues developed BDI in 1961 to measure the behavioural symptoms of depression in adolescents and adults (35). It is used to describe the disorder, to measure its severity and to monitor changes with the treatment. The total score of 0-9 is interpreted as minimal symptoms, 10-16 as mild, 17-29 as moderate and 30-63 as severe. The Turkish validity and reliability study of the BDI was conducted by Tegin (36) and Hisli (37) and the cut-off point was determined as 17.

Screen for Child Anxiety and Related Disorders (SCARED). SCARED was developed by Birmaher et al. (38) to screen anxiety disorders during childhood and adolescence. The Turkish validity and reliability study of the scale was carried out by Çakmakçi (39). The scale can be used in children and adolescents between the ages of 8 and 18 years and consists of 41 items. Each item is scored between 0 and 2, and the total score of 25 or more qualifies a warning sign for an anxiety disorder. The Cronbach's alpha coefficients were reported to vary between 0.74 and 0.93 for the general scale and subscales obtained from the original scale, while test-retest reliability coefficients were reported to be between 0.70 and 0.90 (38). Cronbach's alpha coefficients of the scale for general scale and subscales ranged between 0.88 and 0.91 in the Turkish validity and reliability study (39).

Maudsley Obsessive-Compulsive Inventory (MOCI). The scale which was developed by Hodgson and Rachman (40) aims to evaluate the type and severity of obsessive-compulsive symptoms. It can be applied to children aged 9 and over. In the validity and reliability study which was conducted by Erol and Savaşir (41), seven new items were added to the scale, and the scale was rearranged as 37 items. The total score from the scale varies from 0 to 37, and the higher score indicates an increase in obsessive-compulsive symptoms.

BDI, SCARED, and MOCI were applied to the all adolescents in the study in order to evaluate relationships between the psychiatric symptoms and social responsiveness/autistic traits and to control the effects of psychiatric symptoms on these assessed areas of social functioning.

Procedure

The details of the study were explained and appointments were set for psychiatric evaluation for the adolescents and their families. The patients who required hospitalization for medical stabilization were evaluated within one month after discharge from the hospital. After obtaining socio-demographic and clinical data from the parents, K-SADS-PL-DSM-5-T was applied by interviewing adolescents and their parents, separately. The adolescents were informed about the self-report scales and asked to fill them in.

Data Analysis

The Statistical Program for Social Sciences (SPSS) 17.0 was used for the statistical analyses. The statistical analyses of the data indicated by measurements were conducted using the Student's t-test or the Mann-Whitney U test according to whether the parametric test assumptions were met or not, respectively. The Chi-square (χ^2) test or Fisher's exact Chi-square test was used in the evaluation of the nominal data. The Pearson's correlation analysis was used to assess the relationship between the two continuous variables. The Analysis of Covariance (ANCOVA) was used to statistically control the effects of psychiatric symptoms on the social responsiveness in the two groups. To examine the differences between the two groups in the SRS subscales, multivariate analysis of variance (MANOVA) was conducted. In all analyses, two-tailed p values less than 0.05 were considered as statistically significant. Effect sizes were given for each statistical analysis.

RESULTS

Socio-Demographic And Clinical Characteristics

A total of 73 female adolescents between the ages of 12 and 18 years were included in the study, 39 of them were in the AN group and 34 adolescents were in the control group. There were no significant differences between the two groups in terms of age, duration of education, socio-economic status, age of parents and duration of education of parents (Table 1). The mean ages were 14.2±1.5 years and 14.8±1.4 years for the onset of the symptoms and the referral to the hospital in the AN group, respectively. Eleven adolescents (28.2%) in the AN group had received a psychiatric treatment (mean duration 9.8±4.1 months) for AN. At least one comorbid psychiatric disorder was observed in 23 (59%) patients with AN and there were more than one comorbid psychiatric disorder in five of the patients (12.8%). Mood disorders were diagnosed in 14 (35.9%), anxiety disorders in five (12.8%), attention deficit hyperactivity disorder (ADHD) in three (7.7%), OCD in two (5.1%) patients and enuresis nocturna in one (2.6%) patient. All of the patients with mood disorders had a major depressive disorder; three of the patients with anxiety disorders (60%) had a generalized anxiety disorder, one (20%) had a social anxiety disorder and one (20%) had a separation anxiety disorder. After the Bonferroni correction was applied, in the AN group, the mean total scores of EAT, BDI and SCARED were found to be significantly higher than the control group (Table 1). There was no statistically significant difference between the mean total scores of MOCI in the two groups (Table 1).

Scores of Social Responsiveness and Autistic Traits

The adolescents in the AN group obtained significantly higher total SRS scores than the control group which points out lower social functioning (AN group, 54.8 ± 19.3 ; control group, 36.3 ± 15.9 ; t=4.420; p<0.000; Cohen's d: 1.046). It was also found that adolescents in the AN group had significantly higher receptive awareness, cognition, expressive communication and motivation subscale scores, however there was no significant difference between the two groups in the autistic mannerism subscale score (Table 2).

Age (years)	AN group (N=39) Mean ± SD 15.2±1.6	Control group (N=34) Mean ± SD 14.9±1.8	Statistics*		Cohen's d
			t=0.800 NS	p=0.426	0.176
Duration of education (years)	9.8±1.5	9.7±1.7	t=0.244 NS	p=0.808	0.062
Mother age	43.3±5.9	40.7±4.9	t=1.985 NS	p=0.051	0.479
Father age	47.5±6.3	45.6±4.8	t=1.395 NS	p=0.168	0.339
Education of mother (years)	10.7±5.0	10.0±4.4	t=0.601 NS	p=0.550	0.148
Education of father (years)	11.6±4.1	12.9±3.4	t=-1.444 NS	p=0.153	0.345
BMI	16.6±1.4	20.6±1.4	t=12.340	p=0.000	2.857
EAT	43.3±17.2	14.7±5.8	t=9.258	p=0.000	2.228
BDI	20.5±12.3	7.8±5.3	t=5.552	p=0.000	1.341
SCARED	31.3±16.0	21.8±10.9	t=2.940	p=0.004	0.693
MOCI	13.8±5.8	13.5±6.1	t=0.288 NS	p=0.774	0.050

*Bonferroni correction was applied. AN, anorexia nervosa; SD, standard deviation; BMI, body mass index; EAT, eating attitudes test; BDI, Beck depression inventory; SCARED, screen for child anxiety and related disorders; MOCI, Maudsley obsessive compulsive inventory; NS, not significant.

Receptive awareness	AN group Mean ± SD	Control group Mean ± SD 5.5±2.5	Statistics		Effect size
	7.7±3.4		F=9.86	p=0.002	Partial η ² : 0.122
Cognition	11.4±4.8	7.3±3.9	F=15.29	p=0.000	Partial η²: 0.177
Communication	17.5±7.3	9.9±6.7	F=21.11	p=0.000	Partial η²: 0.229
Motivation	11.6±5.9	8.0±4.2	F=8.66	p=0.004	Partial η²: 0.109
Autistic mannerism	5.8±3.9	5.09±3.0	F=0.80 NS	p=0.375	Partial η ² : 0.011

Multiple variance analysis (MANOVA); AN, anorexia nervosa; SD, standard deviation; SRS, social responsiveness scale; NS, not significant; Partial q², partial eta squared.

When the SRS scores of the participants in both groups were examined categorically according to the cut-off point of the scale, it was found that 14 (35.9%) of the adolescents in the AN group and 1 (3%) of the adolescents in the control group scored higher than 60, which is the cut-off point for social dysfunction and this result was found to be statistically significant (χ^2 =25.3, p<0.000).

Relationships between Social Responsiveness/Autistic Traits and Socio-Demographic and Clinical Data

It was found that total SRS scores were not related to the age of the patients, socio-economic status, BMI/EAT scores, age at the onset of the disorder, duration of the disorder and previous psychiatric treatment status in the AN group.

There was only a positive correlation between the total social responsiveness scores and the anxiety scores in the AN group (r=0.323, p=0.045), which shows as the anxiety increases the social responsiveness decreases. There were no significant correlations between the total social responsiveness scores and the depression or OCD scores in both AN and control groups.

When the effects of depression, anxiety and OCD symptoms on the total SRS scores of the adolescents in the study were controlled, the difference between the study and the control groups was maintained as statistically significant (AN group, 53.0 \pm 3.2; control group, 38.4 \pm 3.5; F=7.545; p=0. 008; Partial η^2 : 0.100).

DISCUSSION

This study examined the presence of autistic traits in adolescent females with AN during the acute phase of illness using the SRS. The results of this study showed that female adolescents with AN had a higher level of autistic traits and less social responsiveness. In addition, there were no relationships between the autistic traits/social responsiveness and comorbid psychiatric symptoms, except for anxiety also, it was found that adolescents with AN had lower functionality in the areas of social awareness, social cognition, social communication and social motivation that represents the characteristics of autistic traits.

Numerous researchers have evaluated the prevalence of autistic features in patients with AN in order to investigate the relationship between AN and ASD. It has been reported that adolescents with AN have elevated ASD traits (7, 20), in particular, repetitive stereotyped behaviors, elevated difficulties with reciprocal social interaction (42), similar to the results of this study. In systematic review studies, it is reported that the prevalence of ASD is higher in patients with AN than in healthy controls (43, 44). In these studies, 40% of adolescents with AN had broader autism phenotype (45) and 26% of adults with AN had autistic features (46). It is thought that there may be a common pathogenesis between the AN and ASD, because some symptoms of ASD are observed in AN, such as misunderstanding social clues, difficulties in processing social information and providing appropriate response in interpersonal communication, and obsessivecompulsive features (9, 47). Similar to those results in the literature, the findings of this study showed that the social awareness, social cognition, communication and social motivation are impaired in adolescents with AN, indicating that there may be a common pathogenesis between AN and ASD.

Another key finding of this study is that although adolescents with AN were found to score significantly higher than HCs on the SRS, the scores were not high enough to meet the indicated cut-off point for ASD. While these difficulties may not be severe enough to diagnose ASD, they could still leave an individual vulnerable to the development of AN (48) and may have impact on treatment outcome, making them clinically relevant (7, 11, 49). Although the SRS, has been established to have high reliability and validity, to be significantly correlated with the diagnosis of autism made using the Autism Diagnostic Interview-Revised and can be used with the aim of evaluating autism-like symptom clusters (32, 50, 51), it has not previously been used to determine autistic traits in adolescents with AN. The fact that the adolescents with AN received a higher score from the SRS supports the results of studies showing that there may be a common pathogenesis between AN and ASD. Although SRS has been used in many different studies to determine the features of ASD, it is the first study used in evaluating social responsiveness/autistic traits in adolescents with AN.

In this study social responsiveness/autistic traits were not related to the BMI of patients. In the literature, some of the studies investigating the relationship between social functioning/autistic traits and BMI in patients with AN noted that the starvation impairs the social functions by affecting brain (52). Because adolescence is a critical period for the brain development, it is thought that neurodevelopmental disorders due to starvation in adolescence may have negative effects on social functioning (53). However, there are also studies indicating that the factor causing social dysfunction is not starvation, since the impairment of social functioning in AN patients is seen in the pre-disease period and continues after treatment (6, 47). There is a lack of consensus about whether autistic traits, including social communication and flexibility, are present prior to the onset of the AN or they are state dependent, resulting from prolonged starvation and thus not truly autistic in origin (7). Therefore, although the results of this study point out elevated levels of autistic traits in adolescents with AN, the aetiology of these apparent traits remains unknown.

Many studies have highlighted the impairment in social skills and communication abilities in AN patients (7, 11, 15), however, these characteristics could be attributed to comorbid psychopathologies (44, 54), and do not necessarily reflect a phenotypic autistic trait. Calderoni et al. suggested that aspects of depression such as low mood, social withdrawal, and social anhedonia could have a major role in increasing autistic traits in AN (22). In this study when the effects of depression, anxiety and OCD scores on the social responsiveness/autistic traits of adolescents in both AN and control groups were controlled, the difference between the AN and HC groups was maintained as statistically significant. In contrast to previous studies, these findings suggest that autistic traits observed in adolescents are associated with AN, regardless

of the presence of depressive and other psychiatric symptoms. However, while evaluating this finding, it should be kept in mind that psychiatric diagnoses other than depression are found to be very few in the study group and this may lead to misleading results.

The results of this study should be interpreted with caution. All of the patients included in the study were in the acute illness period in which BMI was below the normal limits and had moderate AN compared to the average BMI. In this case, it is not clear whether the difficulties in social provision exist in the pre-disease period, and these symptoms may be increasing with starvation. In addition, although there are few studies in the literature, it is reported that autistic traits may be lower in children and adolescents with AN than adults (7, 22), but it is emphasized that this may be due to the methodological differences of the studies. At present, the available data are insufficient to understand the relationship between the severity and duration of the disease and autistic symptoms, and do not allow conclusive differences between children and adolescents with AN and adults. Whatever it is, social difficulties and interpersonal problems should be taken as reasonable targets for intervention and treatment because they may be both risk and maintaining factors for AN. Also patients with high levels of autistic behaviors have been found less responsive to the psychological treatments (47, 55). Recent studies have suggested that interpersonal problems at the beginning of the therapy could influence treatment outcome. Therefore, further studies are needed using clinical evaluation tools that can help us to understand the presence of ASD characteristics in children and adolescents with AN.

This study has some strengths and limitations. Including only female adolescents with AN from a single institution has critical importance in understanding of the disease that often begins in adolescent girls by increasing the homogeneity of the research group. However, this prevents the generalization of the results to all patients with AN and to those from other centers. Also including younger people with both early onset and short duration is the strength of the recent study to control the impact of starvation and duration of AN on the ASD symptoms. The cross-sectional nature of the study makes it difficult to understand the direction of the relationship between the AN and autistic traits, although useful for generating hypotheses, these hypotheses need to be confirmed by longitudinal investigations. Future studies investigating the issue of trait or state differences in autistic features in AN would benefit from using clinical tools such as the autism diagnostic observation schedule (ADOS) and eating disorder diagnostic interview (EDDI) along with developmental history in order to figure out whether any social or cognitive difficulties associated with ASD are present prior to the onset of the EDs. In this study alexithymia was not evaluated. Alexithymia is a common co-occurrence in not only AN but also ASD. There are studies reporting that alexithymia, which has difficulty in defining emotional states seen in both AN and ASD (10), may be responsible for the relationship between AN and ASD. The evaluation of alexithymia in future studies will help reveal the mechanism of the assumed relationship between AN and ASD. Another limitation of the study is the sample size. In future studies, whether autistic traits observed in adolescents are associated with AN, regardless of the presence of depressive and other psychiatric symptoms should be confirmed with larger patient groups. The results may also be affected by our dependence on self-report measures as those may be subject to shared method variance and recall and reporting bias.

As conclusion, in this study female adolescents with AN have a higher level of autistic traits and less social responsiveness and autistic traits observed in adolescents are associated with AN, regardless of the presence of depressive and other psychiatric symptoms. Social difficulties may not be severe enough to diagnose ASD, they could still leave an individual vulnerable to the development of AN. Based on these results social difficulties and interpersonal problems should be taken as reasonable targets for intervention and treatment because they may be both risk and maintaining factors for AN. Interpersonal problems at the beginning of the therapy could influence treatment outcome. Determination of autistic traits in patients may enhance the use of treatment methods targeting social-emotional difficulties and change the course of the disease.

Ethics Committee Approval: The research protocol was approved by the Ethics Committee of Non-Interventional Clinical Researches of Hacettepe University with the decision number GO 15/355-17.

Informed Consent: The adolescents and their parents who participated in the study gave written informed consent after briefing them on the details of the study.

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