# A longitudinal study of autism spectrum disorder characteristics in adolescents with restrictive type anorexia nervosa during and after underweight

TITLE

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ABSTRACT

Objectives: This prospective, longitudinal study aims to compare the prevalence of autism spectrum disorder (ASD) characteristics in adolescents with anorexia nervosa (AN) during and after underweight in order to help unravel the complex link between both conditions.

Methods: 24 adolescents with AN completed the youth self-report, autism spectrum quotient (AQ) or autism spectrum quotient adolescent version (AQ – adolescent) and a questionnaire designed by the researchers during a state of underweight and after weight recovery.

Results: AQ total score and several AQ subscale scores at the time of underweight are significantly higher than after weight recovery with medium to large effect sizes. Linear modelling cannot prove a significant effect of weight gain, internalizing problems or medication use of AQ score, but it does show an association between AQ at underweight and AQ after weight recovery.

Conclusions: The results highlight the complexity of the link between AN and ASD characteristics. Although a clear change in AQ score is seen in part of the participants, this effect cannot be generalized and a link with weight change cannot be demonstrated. It seems likely that ASD characteristics in AN are a combination of trait and state: underweight and starvation might exacerbate potentially present traits. Part of our results may indicate the existence of subgroups based on AQ score during underweight. Our study supports the theory that more ASD characteristics at T1 may result in a poorer outcome and a higher need for specified and intensive treatment.

KEY WORDS

anorexia nervosa, autism spectrum disorder, autism spectrum quotient, internalizing problems, longitudinal design

HIGHLIGHTS

- Autism Spectrum Quotient scores in adolescents with Anorexia Nervosa are significantly higher during a state of underweight than after weight recovery, but a reliable change is seen in only 50% of participants.
- A significant effect of weight change, internalizing problems or use of medication on AQ score or AQ subscale score cannot be demonstrated.
- it might be too simple to speak of state of trait, a complex interplay of factors is presumably present. Subgroups based on AQ score in underweight may play a role and could be explored in further research.

## INTRODUCTION

Anorexia nervosa (AN) is an eating disorder defined as a combination of restriction of energy intake relative to requirements, fear of gaining weight/becoming fat and a disturbance in body image, which is heavily influenced by one's weight (1). The specifier "restrictive type" refers to the fact that there has not been any binge-eating or purging over the last three months. "Binge-eating/purging type" refers to these activities being present over the past three months. The disorder is more often found in women than in men, with a usual onset in adolescence (2). Autism Spectrum Disorder (ASD) is a dimensional condition characterized by ongoing challenges in social communication and the presence of restricted, repetitive, and sensory behaviors and interests (1). Both difficulties must be present at a young age, even if not recognized until later. More males than females are diagnosed with ASD (3). Even though both conditions don't resemble each other at first sight, clinicians have reported behavioral overlap. Gillberg was the first to address this issue in 1983 (4). He wondered if a common disturbance in biochemicals could cause ASD in young boys and AN in young girls. Since then research has shown that on the one hand a lot of subjects with ASD experience eating problems (5) and that on the other hand a higher prevalence of ASD diagnosis or ASD characteristics is found in patients with AN (6). A recent review from Nickel et al. (6) describes a prevalence of 25.4% for ASD characteristics and a prevalence of 4.7% for an ASD diagnosis in subjects with AN; both in adults and adolescents. Other studies also found a higher score on the Autism Spectrum Quotient (AQ), a self-reported questionnaire measuring characteristics of ASD, in adults with AN than in healthy controls (7). Individuals with ASD and AN face common challenges in cognitive tasks, including abilities such as set-shifting (shifting attention between tasks), theory of mind (understanding others' mental states), and central coherence (processing information contextually rather than focusing on details) (8-12).

Specific differences between adult and adolescent populations are found. Several studies showed that while elevated levels of ASD characteristics and ASD diagnoses are present in adolescents with AN, the rate is lower than in adult studies (13-15). These characteristics are often not recognized by parents in early childhood (16), suggesting that they appear later on. The link between both conditions is complex, even more so in adults than in adolescents.The presence of features from an early age is currently required to make a diagnosis of ASD and this information is often missing in adult research (1). Additionally, emerging evidence suggests that females might receive ASD diagnoses later than males and that certain traits, more prevalent in females, only become apparent during adolescence (17). Because AN samples predominantly include females, this could potentially account for the variations in trait prevalence and diagnoses among different age groups. Moreover, in adults there often is a longer duration of AN and underweight, which possibly affects the ASD characteristics.

Previous research has shown that underweight and even short-time fasting in itself lead to increased rigidity and more social withdrawal (18-20). This is further supported by the studie of Oldershaw (21), showing ASD characteristics in severely underweight patients, but not in recovered patients. Contrarily, lasting ASD characteristics have been reported in patients who have already recovered from an eating disorder (22). This may indicate the presence of traits, but it may also be a consequence of long-term illness.
Research specifically in young adolescents is valuable as the effect of long-term illness can be minimized and because of the opportunity to collect information about earlier development. Little prospective longitudinal research, however, is available. In addition, several studies focus on adult patients or include both adults and adolescents as one group. Further prospective longitudinal research evaluating the effect of underweight on the occurrence of ASD characteristics in young adolescents with AN is therefore indicated.

Internalizing problems such as anxiety, depression, and compulsion have been suggested to play a role in the occurrence and impact of ASD characteristics in subjects with AN (16, 23). An analysis from Pender et al. shows that increasing social difficulties during adolescence are associated with escalating internalizing problems(24). On one hand internalizing problems are often accompanied by weight change (1), on the other hand underweight can lead to increased internalizing complaints (20, 25). Furthermore, in a qualitative study of Bele et al. women with ASD and AN reported struggling with identifying, regulating, and communicating their emotions, leading to emotional confusion and overwhelm (26). Specific eating behaviours are reported to be used to numb or channel these emotions, whereby internalizing difficulties may exacerbate eating difficulties in women with ASD. Further investigation into the link between internalizing difficulties and the occurrence of ASD characteristics in adolescents with AN is warranted. It stands to reason that other factors influencing cognitive functioning may also impact ASD characteristics in AN patients. One of these factors is the use of psychotropic medication, such as antidepressants and antipsychotics which are sometimes used in the treatment of AN and its comorbidities. Evaluating their impact therefore seems valuable. To date, no studies have been known to show the impact of the use of psychotropic medication on the occurrence of ASD characteristics in patients with AN.

The aim of this prospective, longitudinal study in an adolescent, Flemish population is to compare the prevalence of ASD characteristics in adolescents with restrictive AN during and after underweight. Additionally, correlations for possible confounders such as internalizing problems and use of medication will be taken into account.

## METHODS AND MATERIALS

### Ethics

The study was approved by the ethical committee/institutional review board of Antwerp University Hospital on May 13th 2020. An insurance policy was taken out that covered any damage or negative consequences that participants could experience as a result of participating in the study. (Insurer: Allianz Global Corporate & Specialty SE - Policy number: EL000862). Written informed consent was obtained from all participants and their parents prior to participation.

### Participants

Participants were recruited, during the acute phase of the illness while underweight, at the inpatient and daypatient eating disorder service of the University hospital for Child and Adolescent Psychiatry Antwerp and at the outpatient eating disorder service Care in Balance in Antwerp. All adolescents (12-18 years) with AN, restrictive type, who consulted there between August 2020 and November 2021 were invited to participate in the study. Diagnosis of AN was made by a child and adolescent psychiatrist (in training) based on anamnesis and clinical examination. A minimum healthy weight was determined by a specialist pediatrician. Patients were included if they had at least 5 kg underweight in comparison to this minimum healthy weight. Patients with a known intelligence quotient of <75 were excluded, since some of the questionnaires used are not suitable for this target group. After recruitment patients completed the following questionnaires: The Autism Spectrum Quotient (AQ), the Youth Self-report 11-18 (YSR) and a clinical questionnaire designed by the researchers. For patients younger than 16 years of age, the Autism Spectrum Quotient Adolescent Version (AQ-adolescent) was used instead of the AQ. When they had reached a stable healthy weight for at least one month, they were invited to complete all three questionnaires again. The follow-up period ran between February 2021 and February 2023. In this article the first study moment (while underweight) and the second study moment (after weight recovery) are referred to as T1 and T2.

### Materials

*Autism Spectrum Quotient and Autism Spectrum Quotient Adolescent (AQ – adolescent)*
The AQ is a self-report questionnaire, developed in 2001 by Baron-Cohen et al. (27), designed to easily measure ASD characteristics in individuals of normal intelligence of 16 years or older.

The AQ–adolescent, a version for adolescents (12-15 years of age) to be completed by the parents, was developed by Baron-Cohen et al. in 2006 (28). The AQ was translated and validated in a Dutch population in 2008 by Hoekstra et al. (29). The test-retest reliability is good (r = 0.78). The questionnaire is not intended as a diagnostic instrument, but as a screening instrument within scientific research. The questionnaire consists of 50 questions, each with four options: “Completely agree”, “somewhat agree”, “somewhat disagree” and “completely disagree”. The Dutch version uses a 4-point system for which scores vary between 50 and 200. A higher score correlates with a higher degree of ASD characteristics. The questionnaire is further divided into five subscales with a score between 10 and 40: attention to detail, attention switching, imagination, communication and social skills and behavior. Official norm scores are not yet available for the Dutch AQ. However Hoekstra et al. (29) presented the questionnaire to a group of people with ASD diagnosis (n=127) and a control group (n=302). The reported averages and standard deviations from this study can be used as a reference point. Spek (30) suggests a cut-off score of 110 for the Dutch AQ (30). As the adult and the adolescent versions have comparable scoring, means and standard deviation, the data can be analyzed together. From now on “AQ score” in this article refers to the scores of all participants.

*The* Achenbach system of empirically base assessment *(ASEBA) youth self-report 11-18 (YSR)*

The YSR is part of the ASEBA questionnaires developed by Achenbach and colleagues (31). The self- reported questionnaire evaluates competences, emotional and behavioral problems in the adolescent. There are always three options: “0 not applicable at all”, “1 somewhat or sometimes applicable” and “2 clearly or often applicable”. The questionnaire has three skill scales (social, school, activities), three problem summary scales (internalizing problems, externalizing problems, and total problem score), eight syndrome scales (anxiety/depressed, withdrawn/depressed, somatic complaints, social problems, thinking problems, attention problems, rule-breaking behavior and aggressive behavior) and six DSM-oriented scales (affective problems, anxiety problems, physical problems, attention deficit/hyperactivity problems, oppositional defiant problems, and behavioral problems). The questionnaire was translated into Dutch by Verhulst and Van den Ende (32). The scoring of the questionnaire is done via a computer program which contains norm scores for a Dutch-speaking population (33). The scores distinguish three areas: a normal area, a subclinical area and a clinical area.

*Clinical questionnaire designed by the researchers*

This questionnaire collects a number of additional data about the patient at the time of completing the questionnaires, unless otherwise specified: sex, age, weight, height, use of medication, age at onset of AN, family history of ASD, completed counseling process for AN

(outpatient, inpatient, daypatient). At T1 data is measured by healthcare professionals, at T2 data is patient and parent reported.

Primary and secondary outcomes

Body mass index (BMI) is computed using the available data about length and weight. Since weight and BMI naturally vary with age in adolescence, these variables are less suitable as a comparative parameter in this young age group. BMI percentile is comparable across different ages and is therefore used as variable in the further analyses.
As selective serotonin reuptake inhibitors (SSRI) and antipsychotics are the main drugs of interest when investigating AN, use of medication is redefined to a binary parameter: use/no use of SSRI and/or antipsychotics. Use of other medication is not taken into account.
Change in BMI percentiles and YSR internalizing scale scores are computed as new variables, using the formula: T2 minus T1.

Statistical analysis

All statistical analyses are performed with the software package SPSS Statistics version 28. The normality of continuous variables is evaluated with Shapiro-Wilk tests, and inspection of histograms and QQ-plots. Alpha is set to 0.5 by default, but since multiple tests are performed, the Holms correction is applied. Significant p values after correction are indicated in bold. All tests are two-tailed. Cohen's d and hedges g are used as standardized effect size measures. All linear regression models are checked for linearity, normal distribution of residues, independence from the variance of residues, interdependence and influencing factors.
Comparisons between paired groups (T1 – T2) are performed with a paired t-test (normal distribution) or a Wilcoxon test (deviation of normal distribution). A standardized change score (for AQ total score) is calculated for each participant using the formula of Jacobson (34). Cut-off for reliable change is set at 1.96. One sample t-tests are used to compare mean AQ scores of study population to the reference scores.
If the paired t-tests show a significant difference in AQ scores between T1 and T2, a multiple linear regression model is fitted with dependent variable AQ score at T2 and independent variables AQ score at T1, change in BMI percentile, change in YSR internalizing scale score and use of medication. Multiple regression models are also used to examine the effect on AQ subscale scores at T2.
Lastly the data set is split into two subgroups: AQ score at T1 above/below threshold of 110 as suggested by spek (30). Comparisons between paired groups (T1-T2) are than repeated.

## RESULTS

### Descriptive statistics

Twenty-nine patients participated in T1: 27 girls, two boys. Twenty-four patients participated in both T1 and T2: 23 girls, one boy. Four patients were not included for follow-up because they did not reach a healthy weight by the end of the study period. One patient did not wish to participate further in the study. None of the participants had AN for more than 2 years. All patients had restrictive type AN. None had a known diagnosis of ASD, nine had a positive family history for ASD. Eleven participants used an SSRI or an antipsychotic (Risperidone) at T1, 18 did not. Other used drugs were Methylfenidate, laxative, vitamin supplements and inhalation corticoids. These were not further investigated. Table 1 shows the remaining characteristics of the study population at T1 and T2. Seven participants (29.2%) completed an outpatient treatment, seven (29.2%) a daypatient treatment and 10 (41.7%) an inpatient treatment.

### AQ scores

Mean BMI percentile is significantly lower at T1 than at T2 (**p< .001**, d = -1.66). Total AQ scores and AQ subscale scores for T1 and T2 are reported in Table 2, along with representation of the significance level and the standardized effect size for the comparison between T1 and T2. AQ score at T1 is significantly higher than AQ score at T2. More specific, AQ subscale scores at T1 are significantly higher than AQ subscale scores at T2 for attention switching and imagination, but not for social skills, communication and attention to details. Standardized effect sizes for significant differences are all medium or large.

Standardized change scores for all participants are reported in Table 4. A reduced AQ score is seen in in 11 participants (45.83%), an increased score is seen in one participant (4.17%) and non-reliable change is seen in 12 participants (50%).

Mean AQ score at T1 is significantly higher than the mean AQ score of the general population reported in the study of Hoekstra (29) (**p< .001**, g= .84). Mean AQ score at T2 does not differ from this mean AQ score (p=.54, g= -.15). The mean AQ score at T1 does not differ significantly from the cut-off point of 110 suggested by Spek et al. (p=.127) (30), while the mean AQ score at T2 is significantly lower than this cut-off point (**p=.01**). Ten patients score below and nineteen patients score above the threshold at T1. Eighteen patients score below and six patients score above the threshold at T2.

AQ score ranks at T1 are significantly higher for those who did not recover a healthy weight and were thus excluded from T2 (mean rank 22.8) than for those who did recover a healthy

weight and participated in T2 (mean rank 13.38) (**p= .023**). This is also the case for AQ subscale scores social skills (**p= .037**), and attention to details (**p= .032**), but not for AQ subscale scores communication (p=.845), attention switching (p=.027) and imagination (p=.414).

Regression models

A multiple linear regression is fitted to evaluate effect of AQ score at T1, change in BMI percentile, change in YSR internalizing scale score and use of medication on AQ score at T2. This is repeated for all AQ subscale scores with a significant difference between mean scores at T1 and T2. No deviations from the model assumptions are found and no highly influential observations are detected. Results of all four models are reported in Table 4. Only AQ score at T1 added significantly to the prediction of AQ score at T2. The other models are not statistically significant after application of Holms correction.

Subgroups

The data set is split into two subgroups: AQ score at T1 above/below threshold of 110. No significant differences between T1 and T2 for AQ (subscale) scores are seen in the subgroup AQ score at T1 below threshold. The same pattern as in the whole group is seen in the subgroup AQ score at T1 above threshold: a significant difference between T1 and T2 for AQ total score and AQ subscale scores imagination and attention switching, but not for AQ subscale scores communication, social skills and attention to details. Total AQ scores and AQ subscale scores for the subgroup with AQ T1> 110 are reported in Table 3, along with representation of the significance level and the standardized effect size for the comparison between T1 and T2 in this subgroup.

## DISCUSSION

The aim of this prospective, longitudinal study was to compare the prevalence of ASD characteristics in adolescents with restrictive AN during and after underweight. This report is the only recent longitudinal study concerning this topic. The main outcome of our study is that the AQ score at T1 is significantly higher than the AQ score at T2 and the effect size of this difference is large. This might indicate that ASD characteristics in AN should be viewed as a phase rather than a trait, however the reality is presumably more complex. It is in line with the findings of Oldershaw et al. (21) and Kerr-Gaffney et al. (11) that the emotion recognition ability, the emotional theory of mind and social attention are impaired in underweight patients with AN, but not in recovered patients. ASD characteristics as a state in AN is further supported by earlier research that ASD characteristics are not continuously present in patients with AN: While elevated ASD characteristics are seen in AN patients, these characteristics are often not recognized by parents in earlier development (16, 35). A recent longitudinal study from Susanin (36) also observed fluctuations in ASD characteristics in adolescent patients before and after treatment. Thus, these studies do not advocate for ASD diagnosis despite ASD characteristics. This signifies that caution should be exercised when interpreting studies conducted with underweight AN patients. It also supports the notion that a diagnosis of ASD should not be made before patients have reached a stable healthy weight. However, our findings partially contrast with several other studies reporting persistent problems in adult AN patients after recovery (7, 14). In several studies with adolescents with AN the rate of reported ASD characteristics is lower than in adult studies, but it often remains elevated in comparison to the general population (14, 35, 37). Since AN usually starts during adolescence, adult patients often have a history of long term underweight. It is possible that the duration of the underweight affects patients to such an extent that recovery of ASD characteristics with weight gain does not ensue as easily as in younger patients. The review and meta-analysis by Saure and colleagues (38) substantiates this theory: they found that long-term illness is associated with an increase in ASD characteristics. This may result in ASD characteristics reflecting a combination of state ánd trait features in AN patients with a long history of underweight. The combination of state and trait is also suggested by Kerr-Gaffney (7). This duplicity is also found in our study. The reliable change index scores indicate that in 50% of the participants changes in AQ score are associated with effective change. Despite the clear reduction in ASD characteristics in part of our study group, 25% still scores above the AQ score threshold at T2 and 33% scores below the AQ score threshold at T1. Thus there are patients in which ASD characteristics remain despite weight gain and there are patients without ASD characteristics despite underweight. This further supports the notion of a complex interplay of both traits and states.

The results of the multiple regression model, which shows that AQ score at T2 is significantly influenced by AQ score at T1, and the reliable change index scores advocate for the presence of subgroups, presumably based on baseline AQ score. Multiple subgroup analyses are not possible, due to our small sample size. However future research might benefit from further mapping of baseline AQ score subgroup analysis to investigate whether this can account for some of the inconsistency between studies. If this theory holds, it would be interesting to investigate potential risk- and protective factors such as developmental issues, age of onset, speed of weight loss, family history of certain psychiatric disorders and/or strength of the available social network.

A significant change in both BMI percentile and AQ (subscale) score between T1 and T2 is seen, suggesting that weight gain might influence the presence of ASD characteristics. However the regression model is unable to prove a significant effect of weight gain. This is not what we expected, but is in line with the findings from Rhind (37), Bentz (22) and Pruccoli (39) that ASD characteristics in adolescents with AN are not correlated to BMI. This raises the question of how to understand the difference in AQ scores between both measurement moments. The lack of a significant correlation in our study is presumably due to the limited power of the analyses because of our small study population. The earlier discussed possibility of subgroups may also help explain this. However, it is also possible that there is another, as yet unknown factor that influences change both in weight and in ASD characteristics. Literature suggests internalizing problems such as compulsion, anxiety and depression might be a confounding factor (16, 23, 40). It also stands to reason that the use of psychotropic medication will have an impact on cognitive functions such as flexibility and attention. Both possible confounders are entered into the regression model, but no evidence for effect is seen. This is in line with the results from Bentz that neither found a significant correlation with internalizing problems (22). Our study is the first to examine the effect of psychotropic medication on the link between weight and ASD characteristics in adolescent patients with AN. Though an association was found for one of the AQ subscales it might be worth further exploring the possibility that use of psychotropic medication is a predictor of a higher AQ score after weight recovery. Due to our small study population we are unable to incorporate other possible confounders, but future research with larger patient groups should consider the following: age of onset of AN, developmental problems, duration of AN.

Interestingly, the difference between T1 and T2 is significant for those subscales of the AQ focusing on cognitive flexibility and attention functions, but not for those subscales focusing directly on social skills and communication. This is in line with the findings of Courty et al. (41) that revealed similarities between participants with ASD and participants with AN in a few

cognitive domains (attention switching, perspective taking and fantasy, lack of emotional introspection) but not in social skills and with the findings of Kerr-Gaffney (7) reporting similar scores for repetitive behavior and restricted interests but not for other ASD characteristics in patients with AN. Ghiotto also reported that lower BMI is associated with poorer executive functioning in patients with AN (12). This is an important observation as it indicates that when examining ASD characteristics in patients with AN focus should not solely be on social and communicative measures.

We see that participants who did not recover to a minimum healthy weight within the time period of the study (two years), achieve a significantly higher AQ score at T1 than patients who did recover. The first multiple regression model shows that the AQ score at T1 is relevant to the further evolution of ASD characteristics and thus suggests that subgroups based on AQ score at T1 might exist. This could indicate that a higher AQ score at T1 might predict a less favorable outcome. Our sample was too small to investigate association between AQ score and treatment intensity, but this is in line with a bulk of recent research that showed that patients with more ASD characteristics often need a more intensive treatment and may show a lower satisfaction with treatment (42-44). Although the numbers in our study are too small to draw strong conclusions, this is an important observation as it suggests that measuring ASD characteristics at T1 might help to make a more correct estimate of the need for intensive treatment and to facilitate early specific intervention for this vulnerable patient group. Both Tchanturia (45) and Loomes (46) suggested specific treatment adaptations for AN patients with elevated ASD characteristics. The evaluation of ASD characteristics at the start of treatment, may therefore remain clinically relevant.

Participants were recruited from inpatient, daypatient and outpatient facilities and thus received different levels of treatment intensity. It was decided to include participants of all treatment intensities in order to become results that are as generalizable as possible. Vision and treatment program were similar across all settings. All participants and their environment received system-oriented therapeutic guidance from both a psychologist and a child and adolescent psychiatrist. Frequency and intensity of therapy were higher for daypatient and inpatient participants, who also received group support. It is possible that these settings influenced the scoring of certain AQ subscales and that differences between the groups might be found. However, the relationship between these two parameters was not the focus of this study. The sample size is too small to make well-founded statements and running more tests would drastically increase the change of a type 1 error, especially in the regression models.

## Limitations

The most important limitation of the current study is the sample size. This must be taken into account when interpreting all statistical results. As only one male participant is included in T1 and T2, gender-specific comparisons were not possible. This comparison would have been particularly interesting as more and more research shows that ASD characteristics differ between the genders (17, 47). In the regression analyses the effective sample sizes were small, which increased the risk for an overfitted model. To reduce this risk, recommendations by Babyak (48) were followed: pretesting of candidate predictors and dichotomization of continuous variables were avoided. All decisions were theory-driven. Despite the risk of overfitting, YSR internalizing scale score and use of medication were included in the last model as they were suggested to be confounding factors by literature. Another limitation was the lack of official norm scores for the AQ Dutch. Future research into this topic would benefit from reliable regional data based on the 1 to 4-point scoring system. In our study results from both the parent-reported AQ-ado and the participant-reported AQ are analyzed together. Analyzing both groups separately would result in an even smaller sample size, loss of power and less reliable results. It was decided not to reduce to participant-reported data only by working with the AQ for all, as it is estimated that the young age might lead to a different assessment, especially when underweight.

Strengths of this study were the prospective, longitudinal design, the focus on adolescents specifically and the inclusion of patients from all over the Flemish region and with all treatment intensities. Taking into account the limited available longitudinal research into this topic, the results of this report remain relevant, despite the small study cohort.

## Conclusions

The results of our study highlight the complexity of the link between AN and ASD characteristics. Although a clear change in AQ score is seen in part of the participants, this effect cannot be generalized and a link with weight change cannot be demonstrated. It seems likely that ASD characteristics in AN are a combination of trait and state: underweight and starvation might exacerbate potentially present traits. Part of our results may indicate the existence of subgroups based on AQ score during underweight. Our study supports the theory that more ASD characteristics at T1 may result in a poorer outcome and a higher need for specified and intensive treatment. So despite a call for caution when diagnosing ASD in AN patients, we advocate further evaluation of these characteristics. Application of this study

procedure in a larger, multicenter study is appropriate to further unravel the link between ASD characteristics and underweight in patients with AN. Further exploration of the subgroup theory would be valuable. Future studies should also focus more on outcome and treatment intensity measures.

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**Table 1**

*Characteristics of the study population*

| | Age T1 (years) | Age T2 (years) | Time between T1 and T2 (years) | BMI T1 (kg/m²) | BMI T2 (kg/m²) | BMI percentile T1 | BMI percentile T2 | Percent underweight with respect to MHW | Age at start eating disorder (years) |
|---|---|---|---|---|---|---|---|---|---|
| N valid | 29 | 24 | 24 | 29 | 24 | 29 | 24 | 29 | 29 |
| Missing | 0 | 5 | 5 | 0 | 5 | 0 | 5 | 0 | 0 |
| Mean | 15.0 | 16.40 | 1.20 | 16.03 | 19.49 | 8.10 | 35.00 | 15.10 | 16.80 |
| Median | 14.6 | 16.10 | 1.20 | 15.81 | 19.34 | 3.00 | 26.50 | 13.50 | 13.70 |
| Standard deviation | 1.20 | 1.20 | 0.30 | 1.67 | 1.41 | 10.30 | 22.40 | 4.80 | 1.40 |
| Minimum | 12.75 | 14.50 | 0.05 | 12.40 | 17.37 | 1.00 | 10.00 | 8.00 | 8.83 |
| Maximum | 17.75 | 18.83 | 1.84 | 19.84 | 22.95 | 37.00 | 80.00 | 31.00 | 16.75 |

T1: time/moment one, start of the study, during underweight
T2: time/moment two, end of the study, after weight recovery
BMI: body mass index
MHW: minimal healthy weight

**Table 2**

*Mean and standard deviation of AQ scores and AQ subscale scores, with representation of the significance level and the standardized effect size for the comparison between T1 and T2*

| | T1: M (SD) | T2: M (SD) | P value | Cohen's d |
|---|---|---|---|---|
| Total AQ score | 113.3 (3.3) | 102.5 (5.6) | **< .001** | .89 |
| AQ score social skills | 22.2 (1.1) | 20.7 (4.2) | .21 | .26 |
| AQ score attention switching | 26.3 (4.3) | 22.2 (4.6) | **< .001** | .87 |
| AQ score Communication | 21.3 (4.8) | 20.4 (3.4) | .374 | .18 |
| AQ score imagination | 26.0 (4.8) | 23.2 (3.3) | **.009** | .58 |
| AQ score attention to detail | 22.7 (4.5) | 20.8 (2.7) | .028 | .48 |

AQ: autism spectrum quotient
T1: time/moment one, start of the study, during underweight
T2: time/moment two, end of the study, after weight recovery
M (SD): Mean (standard deviation)

**Table 3**

*Mean and standard deviation of AQ scores and AQ subscale scores for subgroup with AQ at T1>110, with representation of the significance level and the standardized effect size for the comparison between T1 and T2*

| | T1: M (SD) | T2: M (SD) | P value | Cohen's d |
|---|---|---|---|---|
| Total AQ score | 123.00 (7.55) | 107.56 (11.30) | **< .001** | 1.52 |
| AQ score social skills | 24.56 (4.91) | 21.69 (4.24) | .072 | .49 |
| AQ score attention switching | 28.63 (2.96) | 23.63 (4.81) | **.002** | .96 |
| AQ score Communication | 23.56 (3.27) | 21.38 (2.90) | .075 | .48 |
| AQ score imagination | 27.75 (3.21) | 24.19 (3.25) | **.002** | .92 |
| AQ score attention to detail | 24.13 (4.59) | 21.69 (2.33) | .051 | .53 |

AQ: autism spectrum quotient
T1: time/moment one, start of the study, during underweight
T2: time/moment two, end of the study, after weight recovery
M (SD): Mean (standard deviation)

**Table 4**

*Reliable change index scores*

| Participant | Standardized change score | Classified as reliable change ($p < .05$) |
|---|---|---|
| 1 | -1.55 | No |
| 2 | -.80 | No |
| 3 | 4.21 | Yes |
| 4 | -3.99 | Yes |
| 5 | -.93 | No |
| 6 | .44 | No |
| 7 | -.66 | No |
| 8 | .44 | No |
| 9 | .00 | No |
| 10 | -.27 | No |
| 11 | -2.40 | Yes |
| 12 | -2.67 | Yes |
| 13 | -2.14 | Yes |
| 14 | -2.66 | Yes |
| 15 | .53 | No |
| 16 | .13 | No |
| 17 | -6.64 | Yes |
| 18 | -2.54 | Yes |
| 19 | -3.74 | Yes |
| 20 | -4.87 | Yes |
| 21 | -1.87 | No |
| 22 | -3.20 | Yes |
| 23 | -3.47 | Yes |
| 24 | -1.87 | No |

**Table 5**

*Coefficients and p values of the four linear regression models*

| Model 1, dependent variable: total AQ score at T2 | | |
|---|---|---|
| Adjusted $R^2$ = .519 F = 7.215 **p = .001** | | |
| Independent variable | Unstandardized beta coefficient | P value |
| Constant | 55.675 | **.001** |
| Change in BMI percentile | -.198 | .105 |
| AQ score at T1 | .483 | **<.001** |
| Use of medication | 4.618 | .250 |
| Change in YSR internalizing scale score | .436 | .083 |
| Model 2, dependent variable: AQ subscale score attention switching at T2 | | |
| Adjusted $R^2$ = .172 F = 2.198 p = .108 | | |
| Independent variable | Unstandardized beta coefficient | P value |
| Constant | 14.578 | .024 |
| Change in BMI percentile | -1.316 | .108 |
| AQ subscale score attention switching T1 | .500 | .027 |
| Use of medication | .-.388 | .836 |
| Change in YSR internalizing scale score | .085 | .441 |
| Model 3, dependent variable: AQ subscale score imagination at T2 | | |
| Adjusted $R^2$ = .208 F = 2.508 p = .076 | | |
| Independent variable | Unstandardized beta coefficient | P value |
| Constant | 17.312 | .<.001 |
| Change in BMI percentile | -.430 | .449 |
| AQ subscale score imagination T1 | .282 | .044 |
| Use of medication | 2.679 | .049 |
| Change in YSR internalizing scale score | .108 | .179 |
| Model 4, dependent variable: AQ subscale score attention to details at T2 | | |
| Adjusted $R^2$ = .339 F = 3.943 p = .017 | | |
| Independent variable | Unstandardized beta coefficient | P value |
| Constant | 15.358 | <.001 |
| Change in BMI percentile | -.193 | .645 |
| AQ subscale score attention to details T1 | .253 | .025 |
| Use of medication | 2.317 | .023 |
| Change in YSR internalizing scale score | .059 | .323 |

AQ: autism spectrum quotient
$R^2$: coefficient of determination
BMI: body mass index
T1: time/moment one, start of the study, during underweight
T2: time/moment two, end of the study, after weight recovery