King's Research Portal

DOI:

[10.1016/j.psychres.2017.09.005](https://doi.org/10.1016/j.psychres.2017.09.005)

Document Version

Peer reviewed version

[Link to publication record in King's Research Portal](#)

Citation for published version (APA):

Westwood, H., Mandy, W., & Tchanturia, K. (2017). The association between symptoms of autism and neuropsychological performance in females with Anorexia Nervosa. *Psychiatry Research*.
<https://doi.org/10.1016/j.psychres.2017.09.005>

Citing this paper

Please note that where the full-text provided on King's Research Portal is the Author Accepted Manuscript or Post-Print version this may differ from the final Published version. If citing, it is advised that you check and use the publisher's definitive version for pagination, volume/issue, and date of publication details. And where the final published version is provided on the Research Portal, if citing you are again advised to check the publisher's website for any subsequent corrections.

General rights

Copyright and moral rights for the publications made accessible in the Research Portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognize and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the Research Portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the Research Portal

Take down policy

If you believe that this document breaches copyright please contact librarypure@kcl.ac.uk providing details, and we will remove access to the work immediately and investigate your claim.

Author's Accepted Manuscript

The association between symptoms of autism and neuropsychological performance in females with Anorexia Nervosa

Heather Westwood, William Mandy, Kate Tchanturia

PII: S0165-1781(17)30380-3
DOI: <http://dx.doi.org/10.1016/j.psychres.2017.09.005>
Reference: PSY10815

To appear in: *Psychiatry Research*

Received date: 2 March 2017
Revised date: 18 August 2017
Accepted date: 2 September 2017

Cite this article as: Heather Westwood, William Mandy and Kate Tchanturia, The association between symptoms of autism and neuropsychological performance in females with Anorexia Nervosa, *Psychiatry Research*, <http://dx.doi.org/10.1016/j.psychres.2017.09.005>

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting galley proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

**The association between symptoms of autism and neuropsychological performance
in females with Anorexia Nervosa**

Heather Westwood^a, William Mandy^b and Kate Tchanturia^{a,c,d*}

^a King's College London, IoPPN, Psychological Medicine, London, UK

^b University College London, Clinical, Educational and Health psychology, London, UK

^c Ilia State University, Tbilisi, Georgia

^d South London and Maudsley NHS Foundation Trust National Eating Disorders Service, Psychological Medicine Clinical Academic Group

*Corresponding author: Kate Tchanturia, King's College London, SE5 8AF, Institute of Psychiatry, Psychology and Neuroscience, Psychological Medicine, 103 Denmark Hill. T: 02078480134. Kate.tchanturia@kcl.ac.uk

Abstract

The aim of this study was to investigate the relationship between symptoms of autism spectrum disorder (ASD) and performance on measures of set-shifting and central coherence in a sample of females with anorexia nervosa (AN). Ninety-nine females aged 12 to 47, recruited from inpatient and day patient eating disorder services, were assessed with the Autism Diagnostic Observation Schedule, 2nd edition (ADOS-2), as well as the Wechsler Abbreviated Scale of Intelligence, 2nd edition (WASI-II); Wisconsin Card Sorting Test (WCST); Rey-Osterrieth Complex Figure Test (ROCFT) and self-report questionnaires assessing eating disorder pathology, depression, cognitive rigidity and attention to detail. Individuals scoring above clinical cut-off on the ADOS-2 (N=35) reported significantly higher levels of cognitive rigidity than those with lower levels of

ASD symptoms but there was no difference between groups on self-reported attention to detail. The group with high levels of ASD symptoms also made significantly more perseverative errors on the WCST but there was no association between ASD symptoms and performance on the ROCFT. The group who scored above cut-off on the ADOS-2 were significantly younger than the sub-clinical groups. The presence of symptoms associated with ASD appears to be related to increased cognitive rigidity in females with AN.

Keywords: executive function; feeding and eating disorders; autism spectrum disorder; neuropsychology

1. Introduction

Anorexia Nervosa (AN) is a severe eating disorder characterised by low body weight, intense fear of gaining weight and undue influence of weight and shape on self-evaluation (APA, 2013). It is associated with high mortality rates (Fichter and Quadflieg, 2016), severe physical complications (Treasure et al., 2015) and high levels of psychiatric co-morbidity (Hudson et al., 2007). One such comorbidity, which has received recent research attention, is Autism Spectrum Disorder (ASD). ASD is a pervasive developmental, dimensional disorder defined by difficulties with social interaction and communication and repetitive, restricted behaviours and interests (APA, 2013). While ASD tends to affect more males than females (Brugha et al., 2011), the opposite gender ratio to AN (Micali et al., 2013), it has been found to be over-represented in the predominantly female AN adult populations (Huke et al., 2013).

While several studies have focused on the presence of ASD or ASD symptoms in AN (see Westwood and Tchanturia, 2017; Westwood et al., 2015 for reviews), others have

examined specific similarities, both in terms of neuropsychological profiles and socioemotional difficulties between the two disorders (Oldershaw et al., 2011). However, there is a lack of research exploring within-disorder differences in neuropsychological functioning in AN. Research on neuropsychological similarities has focused on two key neuropsychological domains in ASD, namely inefficient set-shifting (Tchanturia et al., 2012) and weak central coherence (Lang et al., 2016; Oldershaw et al., 2011). Difficulties with set-shifting may manifest as either cognitive inflexibility (e.g. concrete and rigid approaches to problem solving) or as inflexibility in responses (e.g. perseverative or stereotyped behaviours) (Roberts et al., 2007), while weak central coherence describes both difficulty using context to interpret information (poorer global processing), and a preference for detail-focused processing (Frith, 1989). Both adults and young people with AN exhibit poorer global processing than healthy controls (HC), as do the unaffected mothers of daughters with AN (Lang, Lloyd, et al., 2015; Lang et al., 2014; Lang et al., 2015), supporting the idea that weak central coherence may be an underlying trait in AN. However, to date, few studies have examined central coherence or set-shifting in young people with AN and systematic reviews and meta-analysis have reported non-significant differences between individuals with AN and healthy controls (Lang et al., 2014; Lang and Tchanturia, 2014). While this may be due to limited power, it is also possible that AN may exacerbate cognitive rigidity and weak central coherence such that younger individuals present with an intermediate profile between adults with the disorder and healthy controls.

A recent meta-analysis (Westwood et al., 2016) compared the set-shifting ability of individuals with either AN or ASD on a commonly used measure of cognitive flexibility, the Wisconsin Card Sorting Test (WCST; Heaton et al., 1993). Meta-

regression indicated no effect of diagnosis (ASD or AN) on test performance in adults, with both AN and ASD groups making significantly more perseverative errors (PEs) than HCs. In children, however, there was a non-significant trend for children with ASD to perform worse than those with AN. This suggests that there may be differences between the disorders in the way that difficulties with set-shifting develop. It could also be that the presence of other psychiatric symptoms, including depression which is highly co-morbid with AN (Blinder et al., 2006), may exacerbate poorer performance on neuropsychological tasks (Giel et al., 2012), and difficulties with set-shifting have been implicated in major depressive disorder (e.g., Austin, et al., 2001). The presence of high levels of depression in AN may also exacerbate the challenge of recognising ASD in AN, as individuals with high levels of depressive symptoms may erroneously score higher on measures of ASD (Westwood et al., 2017). Thus, controlling for depression when exploring the relationship between neuropsychological performance and ASD symptoms in AN is important.

Interestingly, studies with adults with AN (e.g., Westwood et al., 2017; Vagni, et al., 2016) have suggested higher levels of ASD or ASD symptoms than in studies with younger people (Pooni et al., 2012; Postorino et al., 2017; Rhind et al., 2014; Westwood, Mandy, Simic and Tchanturia, 2017). This suggests that the ill-state of AN may exacerbate symptoms associated with ASD, such as difficulties with social interaction or cognitive rigidity. Outcome in AN may also be poorer when ASD is present (Nielsen et al., 2015; Stewart et al., 2017).

Given the high treatment attrition and relapse rates in AN (Treasure et al., 2010), studies which identify possible barriers to treatment or sub-groups of patients who require

specifically tailored interventions are needed. Therapies such as Cognitive Remediation Therapy (CRT; Tchanturia et al., 2014; Tchanturia et al., 2017) and Cognitive Remediation and Emotion Skills Training (CREST; Tchanturia et al., 2014; Tchanturia et al., 2015) aim to specifically target the cognitive and socioemotional difficulties observed in both AN and ASD. However, it is not yet known whether individuals with both AN and elevated ASD symptoms have a unique neuropsychological profile and thus, whether interventions such as these would be particularly beneficial for this sub-group. Given the difference in findings between adults and young people in set-shifting, central coherence and ASD symptoms, examining within-group differences in these domains will help determine whether there are specific sub-groups of individuals with AN who may benefit from specifically-tailored treatment approaches.

1.1 Aim

The aim of the current study was to explore the relationship between ASD symptoms and cognitive style, particularly in the domains of set-shifting and central-coherence in females with AN. Specifically, the study aims were as follows:

- I. Investigate whether elevated ASD symptoms are associated with difficulties with cognitive functioning and whether any such findings are reflected in self-reported cognitive rigidity and attention to detail.
- II. Explore whether other factors such as age, illness duration and symptoms of depression are associated with different levels of ASD symptoms or neuropsychological performance.

2. Methods

2.1 Design and participants

A cross-sectional design was used to assess the relationship between ASD symptoms and neuropsychological performance in females with AN, recruited from specialist eating disorder inpatient or day patient treatment programmes. All participants had a DSM-5 primary diagnosis of AN, given by a consultant psychiatrist (APA, 2013) before recruitment to the study. Participants were: a) female; b) able to provide informed consent, or assent if under sixteen, to participate. For participants under the age of sixteen, parental consent was obtained. To make the participant group as representative as possible, exclusions criteria were kept to a minimum and consisted of: a) non-English speaking; b) existing neurological condition. A total of 99 participants ranging from 12 to 47 years of age were recruited over a 21-month period. The study was reviewed and approved by the National Research Ethics Service (14/LO/2131).

2.2 Measures

2.2.1. Autism Diagnostic Observation Schedule, 2nd Edition (ADOS-2; Lord et al., 2012)

The ADOS-2 is a standardised, semi-structured assessment for ASD and is the most widely-used and best validated direct observation of characteristics associated with ASD (NICE, 2012). It focuses on the domains of social interaction, communication, play and imaginative use of materials and takes approximately 40 minutes to administer. Module 4 is designed for use with verbally fluent adolescents and adults and was used for all participants in the current study. The diagnostic algorithm has recently been revised to reflect changing diagnostic criteria and to make it more comparable to other ADOS-2 modules (Hus and Lord, 2014). Therefore, for the purposes of this study, the revised algorithm score, consisting of a combined total of Social Affect and Restricted and Repetitive Behaviour scores was used as a measure of ASD symptoms. The scores yield a cut-off which can be used to aid the clinical diagnosis of ASD. For the purposes

of this study, this cut-off score was used to indicate the presence of elevated symptoms associated with ASD rather than to diagnose ASD, which requires a multimodal process.

2.2.2. Wechsler Abbreviated Scale of Intelligence – Second Edition (WASI-II; Wechsler, 2011)

The WASI-II is an individually administered assessment of intelligence, suitable for individuals aged 6-90 years of age. It provides scores that estimate intelligence in verbal and perceptual reasoning as well as full-scale IQ. The WASI-II includes four sub-tests: Matrix Reasoning, Block Design, Vocabulary and Similarities.

2.2.3. The Wisconsin Card Sorting Test (WCST; Heaton et al., 1993)

The WCST involves sorting stimulus cards into one of four categories per one of three sorting rules: colour, shape or number. The sorting rule changes after ten consecutive correct sorts but participants are not informed of the correct sorting rule, or that the rule changes during the paradigm. Out of several different outputs which can be analysed, perseverative errors is considered the best output for measuring conceptual flexibility or SS (Lezak et al., 2012) and was therefore the outcome of set-shifting used in this study. Percentage of PEs was used rather than raw scores to reflect that some participants underwent fewer trials depending on their performance, in line with standard procedures. The computerised, 128 trial version of the WCST: CV4 was used; detailed information on this testing procedure is described by Tchanturia et al (2012).

2.2.4. Rey-Osterrieth Complex Figure (ROCFT; Osterrieth, 1944)

A measure of global processing, the ROCFT is a complex figure used in the evaluation of visual-spatial memory and organisation. Participants are asked to copy the figure onto a piece of plain paper, with only limited instructions. Scoring based on Booth's (2006) method and the scoring criteria reported in detail in Lang et al (2016) was used to analyse the drawing strategy of the participant. This method yields three scores: An Order Index (OI); Style Index (SI) and Central Coherence Index (CCI), see Lang et al (2016) for more information. A higher CCI indicates a more global processing style. To check reliability, 15% of the sample was co-rated by a second rater. Interrater reliability was good with Cohens kappa = 0.92, $p = < .001$.

2.2.5. Detail and Flexibility Questionnaire (DFlex; Roberts et al., 2011)

The DFlex is a 24-item, self-report questionnaire measuring two aspects of neurocognitive functioning: cognitive rigidity and attention to detail. This measure was included to determine whether any group differences in neuropsychological performance were reflected in self-reported cognitive style. Higher scores represent greater cognitive rigidity/attention to detail. Both subscales show strong discriminant validity and differences with large effect sizes have been found between individuals with eating disorders and healthy controls, and between current and recovered AN patients (Roberts et al., 2011). Cronbach's alpha was .91 and .73 for the cognitive rigidity and attention to detail subscales, respectively.

2.2.6. Eating Disorder Examination Questionnaire (EDE-Q; Fairburn and Beglin, 1994)

The EDE-Q contains 36 items which ask respondents to rate how often they have engaged in certain eating disordered behaviours or held eating disordered concerns over

the past 28 days. The scores result in a 'global', or total score and four subscale scores: 'eating concern', 'weight concern', 'shape concern' and 'restriction'. The EDE-Q is frequently used in eating disorder research. In this study, Cronbach's alpha was .84, indicating good internal reliability. The EDE-Q was used to determine whether level of ASD symptom was associated with eating disorder pathology.

2.2.7. Hospital Anxiety and Depression Scale (HADS; Zigmond and Snaith, 1983) for adult participants

The HADS is a widely used 14-item self-rating instrument for anxiety and depression in patients with both physical and mental health problems. The maximum possible score on either subscale (anxiety/depression) is 21 and the clinical cut-off is 10. Cronbach's alpha was .90 for this study.

2.2.8. Mood and Feelings Questionnaires (MFQ; Angold et al., 1995) for participants aged 18 and under, recruited from child and adolescent services

The MFQ is a 33-item self-report measure assessing symptoms of major depressive disorder in young people. Participants answer on a three-point scale, indicating whether a statement is not true, sometimes true or true. In this study, Cronbach's alpha was .91. Measures of depression were included in an attempt to control for the effect that symptoms of depression may have on neuropsychological performance.

2.3. Procedure

Participants attended a testing session in which they completed the ADOS-2, the neuropsychological assessments and self-report questionnaires. All assessments were conducted by the first author, who was a trained and certified researcher, reliable in the

administration of the ADOS-2, and were video-recorded for ease of scoring.

Assessments were all completed in the following order: ADOS-2; WASI-II; ROCFT; WCST and self-report questionnaires. When assessments had to be split over two sessions due to participant fatigue or other commitments, the same order was maintained. In addition to the assessments, demographic information and weight, height and eating disorder duration were also recorded. For participants recruited from child and adolescent services (N=39), percentage of ideal body weight (%IBW) rather than BMI was calculated, which expresses proportion of an individual's optimal body weight, corrected for age and gender (Frampton and Wilkinson, 1999).

2.4. Statistical Analysis

ADOS-2 scores were not normally distributed and could not be transformed. They were therefore treated as categorical and participants were split into three groups: high autistic symptoms (at or above suggested clinical cut-off), sub-clinical autistic symptoms (below clinical cut-off but above 0) and no autistic symptoms (scored 0 on ADOS-2). Other variables were assessed for normality using histograms and the Shapiro-Wilk test. Eating disorder duration, age of illness onset, age and EDE-Q global scores were not normally distributed across all autistic symptom groups and were therefore transformed, as needed. As there was a significant correlation between years of education and age, $r = .64$, $p = <.001$, the decision was made to only include age in analyses.

To investigate any group differences in eating disorder or general psychopathology and demographic variables, one-way ANOVAs were run between the three ASD symptom groups. An ANOVA was performed to assess for group differences on %PE on the WCST. While age was considered as a potential covariate, the data did not meet assumptions for an ANCOVA, so the potential impact of age on the association between

ASD symptoms and performance on the WCST could not be controlled for. Despite the data not being normally distributed it was not transformed, as one-way ANOVAs are considered robust to deviations from normality, particularly with relatively equal sample sizes (Lix et al., 1996). To examine whether elevated ASD symptoms were associated with lower CCI scores on the ROCFT, an ANCOVA was performed with age as the covariate.

Differences in self-reported cognitive style, as assessed by the DFlex, were also assessed using one-way ANOVAs. Cognitive rigidity scores were moderately negatively skewed so were transformed.

Effect sizes were calculated using partial η^2 , with the following interpretation: small (0.01), medium (0.09) and large (0.25) (Cohen, 1988). As symptoms of depression were measured on two different questionnaires, namely the HADS from adult participants and the MFQ for younger participants, standardised Z scores were calculated to create one standardised “depression” variable. An alpha value of .05 was applied for all tests of statistical significance. Data was analysed using the statistical package IBM SPSS version 22.00.

3. Results

3.1. Clinical comparison between groups

Clinical and demographic information for the three autistic symptom groups are displayed in Table 1. The groups differed significantly on %IBW with the no autistic symptom group having a higher %IBW than the sub-clinical autistic symptom group. The high autistic symptom group were significantly younger than the no autistic symptom group. There was no association between psychiatric medication use and ASD classification, as assessed using Chi-Squared.

[Insert Table 1 here]

3.2 Associations between variables

To examine whether factors such as age, BMI or duration of AN were associated with ASD symptoms, Spearman's rank order correlations were performed between each variable. Age was significantly positively correlated with ADOS-2 scores and was therefore considered a potential confounding variable in the relationship between ASD symptom and cognitive functioning. ADOS-2 scores were also significantly positively correlated with depression scores and with %PE on the WCST. The ROCFT CCI was significantly negatively correlated with %PEs so that an increase in %PEs was associated with a decrease in CCI on the ROCFT. All correlation coefficients can be viewed in the supporting file that accompanies this paper.

3.3. Neuropsychological outcomes

Table 2 displays the mean and standard deviations for the WCST and ROCFT outcomes. As not all participants completed both the WCST and the ROCFT, due to some individuals choosing not to participate in all parts of the assessment, the exact number of participants in each group for both neuropsychological assessments are indicated in Table 2.

[Insert Table 2 here]

3.2.1 WCST

To examine whether elevated ASD symptoms were associated with difficulties with set-shifting, a one-way ANOVA was conducted, with %PE as the dependent variable. The %PE score was statistically significantly different for different levels of ASD symptoms, Welch's $F(2,59.77) = 3.77, p = .029$. Games-Howell post hoc analysis revealed that an increase in %PE score from 8.70 ± 3.94 in the no autistic symptom group to 13.35 ± 8.94 in the high autistic symptom group, an increase of 4.65 (95% CI, 0.5 to 8.7) was statistically significant, $p = .$

023. There were no other statistically significant differences between groups. Percent PEs, plotted against ADOS-2 scores in the three ASD symptom groups are displayed in Figure 1. While it was not possible to conduct an ANCOVA, Spearman's rank order correlations were performed between age and %PEs for each ASD symptom group. There were no significant correlations between age and %PEs across any of the ASD symptom groups.

[Insert Figure 1 here]

3.2.2 ROCFT

To examine whether elevated ASD symptoms were associated with difficulties with central coherence, an ANCOVA was performed with age as the covariate. After adjusting for age, there was no statistically significant difference between groups, $F(2,90) = .25, p = .782, \text{partial } \eta^2 = .005$.

3.3. Self-reported cognitive style

One-way ANOVAs were run to examine group differences in cognitive rigidity and attention to detail scores on the DFlex. Results are displayed in Table 3. Tukey's post hoc analysis revealed that the difference between the no autistic symptom group and the sub-clinical autistic symptom group and between the sub-clinical autistic symptom group and the high autistic symptom groups were not statistically significant. However, the increase in cognitive rigidity scores between the no autistic symptom and high autistic symptom groups was statistically significant, $p = .018$.

[Insert Table 3 here]

4. Discussion

This study aimed to examine the association between ASD symptoms and cognitive style in females with AN, specifically focusing on difficulties with set-shifting and central-coherence. Despite previous studies (Oldershaw et al., 2011; Westwood et al., 2016) examining similarities between AN and ASD in terms of cognitive style, this is the first study to directly examine within-disorder differences between individuals with elevated, sub-clinical and no ASD symptoms, as defined by the recommended clinical cut-off on the ADOS-2. This is the largest study to use the ADOS-2 within an AN population and found that a third of participants score above clinical cut-off, suggestive of the presence of ASD symptoms. Individuals who scored at or above the clinical cut-off on the ADOS-2 made significantly more PEs on the WCST, indicating that individuals with both AN and elevated ASD symptoms have greater difficulties with set-shifting than individuals without these ASD symptoms. Participants scoring above and below cut-off on the ADOS-2 performed similarly on the central-coherence task (ROCFT).

The age of the participants differed significantly between the three groups, with the HAS group being significantly younger. This may have important implications on the potential relationship between set-shifting ability and age in AN. In typically-developing individuals, set-shifting ability improves through adolescence, into adulthood (Kalkut et al., 2009). The recent meta-analysis and meta-regression (Westwood et al., 2016) comparing both adult and child/adolescent groups with either AN or ASD with HCs on performance on the WCST found that while the performance of adults with either disorder was statistically comparable, there was a trend for younger people with ASD to perform worse than those with AN. This suggests that whereas set-

shifting may be impaired even in younger people with ASD, the presence of AN may cause a developmental delay or exacerbate inefficiencies in set-shifting ability.

In individuals who have both AN and elevated ASD symptoms, set-shifting difficulties may be exacerbated beyond those caused by the presence of either ASD or AN alone. However, it could also be that individuals who scored above the clinical cut-off on the ADOS-2 represent a subgroup of individuals with extreme cognitive rigidity and social difficulties, rather than having co-morbid ASD. Controlling for age in analysis would help account for the normal developmental trajectory of set-shifting ability. Longitudinal studies using full ASD diagnostic criteria are needed to further examine the relationship between symptoms of ASD and neuropsychological functioning in people with AN across the lifespan.

This study did not reveal an association between the ROCFT and levels of ASD symptoms in females with AN. This may be due to the inclusion of a solely female sample. There is a clear gender disparity between ASD and AN, which may make the cognitive style associated with the two disorders less comparable. ASD is more prevalent in males (Brugha et al., 2011) whereas the opposite is true of AN (Micali et al., 2013). Consequently, most research examining cognitive style in ASD is conducted in males, so conclusions regarding the cognitive profile of females with ASD cannot be drawn. Limited research (Bolte et al., 2011) suggests that females with ASD may have fewer difficulties with executive function than their male counterparts, and may also be less detailed-focused. This highlights the need for studies directly comparing females with ASD and AN, in addition to examining disorder-specific gender differences.

The self-report findings of this study, namely individuals with elevated ASD symptoms report significantly higher levels of cognitive rigidity but not attention to detail compared to those with lower levels of these symptoms, mirror the neuropsychological results. Although self-report cognitive rigidity, as measured by the DFlex was thought to reflect difficulties with SS (Roberts et al., 2011), in the current study, there was no significant relationship between performance on the WCST and the cognitive rigidity subscale of the DFlex. This was also the case for the CCI of the ROCFT, which was not significantly associated with the attention to detail subscale of the DFlex. These findings suggest that experimental SS and self-reported cognitive styles may be different constructs (Lounes et al., 2011).

4.1 Limitations

While information on medication use was obtained, the possible effect of medication on test performance was not controlled for in analysis. As psychotropic medication may impact upon neuropsychological test performance (Helmes, 2016), future research should attempt to control for this. However, the percentage of medication use was similar in all ASD symptom groups and previous research using the both the WCST and ROCFT with young people with AN found no difference in performance between participants on medication and those who were medication-free (Lang et al., 2015).

Given the cross-sectional design of this study, assumptions about the causal relationship between ASD and AN (Hiller and Pellicano, 2013) cannot be made. In addition, questions over the validity of using assessments tools such as the ADOS-2 with adults with co-morbid mental health problems (Lai et al., 2011) limit the generalisability of the findings of this study. As discussed, it could be that the individuals who scored above

the ADOS-2 cut-off represented a subgroup of individuals with AN characterised by extreme cognitive rigidity or difficulties with social interaction, rather than having ASD. It is possible that other co-occurring symptoms, commonly found in individuals with AN, such as obsessive-compulsive disorder or alexithymia (Cederlof et al., 2015; Courty et al., 2015) may increase the likelihood of scoring above clinical cut-off on the ADOS-2, leading to “false-positive” results on its current diagnostic algorithm. In this study, ADOS-2- scores were significantly positively correlated with depression scores. While it could be that ASD symptoms increase the likelihood of experiencing symptoms of depression (Matson and Williams, 2014), however, the opposite could also be true. The aim of this study was to assess observable symptoms associated with the ASD rather than to diagnose the disorder. However, until such a time that ASD can be confidently assessed in AN populations, the findings should be interpreted with caution.

4.2 Clinical implications

The findings of this study have important clinical implications. Given that research suggests that prognosis is poorer for individuals with co-occurring eating disorders and elevated ASD traits, (Nielsen et al., 2015; Stewart et al., 2017), services may benefit from tailoring specific treatments to the needs of individuals who present with elevated ASD symptoms. Certain interventions, such as CRT (Tchanturia et al., 2013; Tchanturia et al., 2014) and CREST (Tchanturia et al., 2014; Tchanturia et al., 2015) have been specifically designed to target the inefficient cognitive and emotional style of individuals with AN. If individuals with both AN and elevated ASD traits have a more inefficient cognitive style, they may benefit from a higher dose of these therapies or from treatments being tailored to account for cognitive rigidity (Tchanturia et al., 2016). Specifically, given the finding from this study that individuals with elevated ASD

symptoms may have particular difficulties with set-shifting, targeting this inefficiency within treatment may be beneficial. However, as this is the first study to examine within-disorder differences in cognitive style, further studies are needed before specific recommendations can be made. This line of research would benefit from future studies comparing treatment outcomes in individuals with high and low levels of characteristics associated with ASD.

Acknowledgements

The authors would like to thank the MRC/IoPPN excellence studentship, The Psychiatry Research Trust and the Swiss Anorexia Foundation (58-16) for their support. KT would like to acknowledge financial support from the MRC and MRF - *child and young adult mental health –the underpinning aetiology of self-harm and eating disorders*.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

References

- Anckarsater, H., Hofvander, B., Billstedt, E., Gillberg, I. C., Gillberg, C., Wentz, E., Rastam, M. 2012. The sociocommunicative deficit subgroup in anorexia nervosa: autism spectrum disorders and neurocognition in a community-based, longitudinal study. *Psych Med*, 42(9), 1957-1967. doi: 10.1017/s0033291711002881
- Angold, A., Costello, E. J., Messer, S. C., Pickles, A., Winder, F., Silver, D. 1995. The development of a short questionnaire for use in epidemiological studies of depression in children and adolescents. *Int J Methods in Psychiatr Res*, 5, 237 - 249.

- American Psychiatric Association. 2013. Diagnostic and statistical manual of mental disorders (5th ed.). Arlington, VA: American Psychiatric Publishing.
- Austin, M. P., Mitchell, P., Goodwin, G. M. 2001. Cognitive deficits in depression: possible implications for functional neuropathology. *Br J Psychiatry*, 178, 200-6. doi: 10.1192/bjp.178.3.200
- Blinder, B. J., Cumella, E. J., Sanathara, V. A. 2006. Psychiatric Comorbidities of Female Inpatients With Eating Disorders. *Psychosom Med*, 68, 454-462. doi: 10.1097/01.psy.0000221254.77675.f5
- Bolte, S., Duketis, E., Poustka, F., Holtmann, M. 2011. Sex differences in cognitive domains and their clinical correlates in higher-functioning autism spectrum disorders. *Autism*, 15(4), 497-511. doi: 10.1177/1362361310391116
- Booth, R, D, L. 2006. Local-global processing and cognitive style in autism spectrum disorder and typical development. (Doctor of Philosophy), King's College London.
- Brugha, T. S., McManus, S., Bankart, J., Scott, F., Purdon, S., Smith, J., . . . Meltzer, H. 2011. Epidemiology of autism spectrum disorders in adults in the community in England. *JAMA Psychiatry*, 68(5), 459-465. doi: 10.1001/archgenpsychiatry.2011.38
- Cederlof, M., Thornton, L. M., Baker, J., Lichtenstein, P., Larsson, H., Ruck, C., Bulik, C. M., Mataix-Cols, D. 2015. Etiological overlap between obsessive-compulsive disorder and anorexia nervosa: a longitudinal cohort, multigenerational family and twin study. *World Psychiatry* 2015, 14:333-338. doi: 10.1002/wps.20251
- Cohen, J. 1988. Statistical power analysis for the behavioral sciences (2nd ed.). Hillsdale, NJ: Erlbaum.

- Courty, A., Godart, N., Lalanne, C., Berthoz, S. 2015. Alexithymia, a compounding factor for eating and social avoidance symptoms in anorexia nervosa. *Comp Psych*, 56, 217-228. doi: 10.1016/j.comppsy.2014.09.011
- Fairburn, C. G., Beglin, S. J. 1994. Assessment of Eating Disorders - Interview or Self-Report Questionnaire. *Int J Eat Disord*, 16(4), 363-370.
- Fichter, M. M., Quadflieg, N. 2016. Mortality in eating disorders - results of a large prospective clinical longitudinal study. *Int J Eat Disord*, 49(4), 391-401. doi: 10.1002/eat.22501
- Frampton, I., Wilkinson, A. 1994. W4H weight for height commercial software, v5.03 UK. Retrieved from: <http://www.awilkinson.eclipse.co.uk/w4h.html>
- Frith, U. 1989. *Autism: Explaining the enigma*. Oxford: Wiley-Blackwell.
- Giel, K. E., Wittorf, A., Wolkenstein, L., Klingberg, S., Drimmer, E., Schönenberg, M., Rapp, A. M., Fallgatter, A. J., Hautzinger, M., Zipfel, S. 2012. Is impaired set-shifting a feature of "pure" anorexia nervosa? Investigating the role of depression in set-shifting ability in anorexia nervosa and unipolar depression. *Psychiatry Res*, 30;200(2-3), 538-543. doi: 10.1016/j.psychres.2012.06.004
- Heaton, R. K., Chelune, G. J., Talley, J. L., Kay, G. G., Curtiss, G. 1993. *Wisconsin Card Sorting Test manual*. Odessa, Florida: Psychological Assessment.
- Helmes, E. 2016. Influence of Psychotropic Drugs upon Neuropsychological Test Performance. *Int Neuropsychiatr Dis J*, 5(3), 1-10. doi 10.9734/INDJ2016/20422
- Hiller, R., Pellicano, L. 2013. Anorexia and Autism – A Cautionary Note. *The Psychologist*, 26(11), 780.
- Hudson, J. I., Hiripi, E., Pope, H. G., Jr., Kessler, R. C. 2007. The prevalence and correlates of eating disorders in the National Comorbidity Survey Replication. *Biol Psychiatry*, 61(3), 348-358. doi: 10.1016/j.biopsych.2006.03.040

- Huke, V., Turk, J., Saeidi, S., Kent, A., Morgan, J. F. 2013. Autism spectrum disorders in eating disorder populations: a systematic review. *Eur Eat Disord Rev*, 21(5), 345-351. doi: 10.1002/erv.2244
- Hus, V., Lord, C. 2014. The autism diagnostic observation schedule, module 4: revised algorithm and standardized severity scores. *J Autism Dev Disord*, 44(8), 1996-2012. doi: 10.1007/s10803-014-2080-3
- Kalkut, E. L., Han, S. D., Lansing, A. E., Holdnack, J. A., Delis, D. C. 2009. Development of set-shifting ability from late childhood through early adulthood. *Arch Clin Neuropsychol*, 565-74. doi: 10.1093/arclin/acp048
- Lai, M-C., Lombardo, M. V., Pasco, G., Ruigrok, A. N., Wheelwright, S. J., Sadek, S. A., ...Baron-Cohen, S. 2011. A behavioral comparison of male and female adults with high functioning autism spectrum conditions. *PLoS One*, 6(6), doi: 10.1371/journal.pone.0020835
- Lang, K., Lloyd, S., Khondoker, M., Simic, M., Treasure, J., Tchanturia, K. 2015. Do Children and Adolescents with Anorexia Nervosa Display an Inefficient Cognitive Processing Style? *PLoS One*, 10(7), e0131724. doi: 10.1371/journal.pone.0131724
- Lang, K., Lopez, C., Stahl, D., Tchanturia, K., Treasure, J. 2014. Central coherence in eating disorders: An updated systematic review and meta-analysis. *World J Biol Psychiatry*, 15(8), 586-598. doi: 10.3109/15622975.2014.909606
- Lang, K., Roberts, M., Lopez, C., Goddard, E., Khondoker, M., Treasure, J., Tchanturia, K. 2016. An investigation of central coherence in eating disorders: A synthesis of studies using the Rey Osterrieth Complex Figure Test; *Plos One*: doi: 10.1371/journal.pone.0165467

- Lang, K., Stahl, D., Espie, J., Treasure, J., Tchanturia, K. 2014. Set shifting in children and adolescents with anorexia nervosa: an exploratory systematic review and meta-analysis. *Int J Eat Disord*, 47(4), 394-399. doi: 10.1002/eat.22235
- Lang, K., Tchanturia, K. 2014. A Systematic Review of Central Coherence in Young People with Anorexia Nervosa. *J Child Adolesc Behav*, 2:140. doi:10.4172/2375-4494.1000140
- Lang, K., Treasure, J., Tchanturia, K. 2015. Is inefficient cognitive processing in anorexia nervosa a familial trait? A neuropsychological pilot study of mothers of offspring with a diagnosis of anorexia nervosa. *World J Biol Psychiatry*, 1-8. doi: 10.3109/15622975.2015.1112035
- Lezak, M.D., Howieson, D. B., Bigler, E. D., Tranel, D. 2012. *Neuropsychological Assessment*, 5th Edition. Oxford: Oxford University Press.
- Lix, L. M., Keselman, J. C., Keselman, H. J. 1996. Consequences of assumption violations revisited: A quantitative review of alternatives to the one-way analysis of variance F test. *Rev Edu Res*, 66, 579-619. doi: 10.3102/00346543066004579
- Lord, C., Rutter, M., DiLavore, P. C., Risi, S., Gotham, K., Bishop, S.I. 2012. *Autism Diagnostic Observation Schedule, Second Edition (ADOS-2) Manual (Part 1) Modules 1-4*. Torrance, CA: Western Psychological Services.
- Lounes, N., Khan, G., Tchanturia, K. 2011. Assessment of cognitive flexibility in Anorexia Nervosa – self-report or experimental measure? A brief report. *J Int Neuropsychol Soc*. 17(5), 925-8: doi.1017/S1355617711000671.
- Matson, J. L., Williams, L. W. 2014. Depression and mood disorders among persons with autism spectrum disorders. *Res Dev Disabil*, 35(9), 2003-2007. doi: 10.1016/j.ridd.2014.04.020

- Mandy, W., Tchanturia, K. 2015. Do women with eating disorders who have social and flexibility difficulties really have autism? A case series. *Mol Autism*, 6. doi: Artn 6 Doi 10.1186/2040-2392-6-6
- Micali, N., Hagberg, K. W., Petersen, I., Treasure, J. L. 2013. The incidence of eating disorders in the UK in 2000-2009: findings from the General Practice Research Database. *BMJ Open*, 3(5). doi: 10.1136/bmjopen-2013-002646
- National Institute for Health and Care Excellence. 2012. Autism: recognition, referral, diagnosis and management of adults on the autism spectrum. National Institute for Health and Clinical Excellence.
- Nielsen, S., Anckarsater, H., Gillberg, C., Gillberg, C., Rastam, M., Wentz, E. 2015. Effects of autism spectrum disorders on outcome in teenage-onset anorexia nervosa evaluated by the Morgan-Russell outcome assessment schedule: a controlled community-based study. *Mol Autism*, 6, 14. doi: 10.1186/s13229-015-0013-4
- Oldershaw, A., Treasure, J., Hambrook, D., Tchanturia, K., Schmidt, U. 2011. Is Anorexia Nervosa a Version of Autism Spectrum Disorders? *Eur Eat Disord Rev*, 19(6), 462-474. doi: 10.1002/Erv.1069
- Osterrieth, P. 1994. The test of copying a complex figure: A contribution to the study of perception and memory. *Archives de Psychologie*. 30, 206–356.
- Pooni, J., Ninteman, A., Bryant-Waugh, R., Nicholls, D., Mandy W. 2012. Investigating autism spectrum disorder and autistic traits in early onset eating disorder. *Int J Eat Disord*, 45(4), 583-91. doi: 10.1002/eat.20980
- Postorino, V., Scahill, L., De Peppo, L., Fatta, L. M., Zanna, V., Castiglioni, M. C., Gillespie, S., Vicari, S., Mazzone, L. 2017. Investigation of Autism Spectrum

- Disorder and Autistic Traits in an Adolescent Sample with Anorexia Nervosa. *J Autism Dev Disord*. doi: 10.1007/s10803-016-3023-y
- Rhind, C., Bonfioli E., Hibbs, R., Goddard, E., Macdonald P., Gowers, S., Schmidt, U., Tchanturia, K., Micali, N., Treasure, J. 2014. An examination of autism spectrum traits in adolescents with anorexia nervosa and their parents. *Mol Autism*, 5:56. doi: 10.1186/2040-2392-5-56
- Roberts, M. E., Barthel, F. M., Lopez, C., Tchanturia, K., Treasure, J. L. 2011. Development and validation of the Detail and Flexibility Questionnaire (DFlex) in eating disorders. *Eat Behav*, 12(3), 168-174. doi: 10.1016/j.eatbeh.2011.04.001
- Roberts, M. E., Tchanturia, K., Stahl, D., Southgate, L., Treasure, J. 2007. A systematic review and meta-analysis of set-shifting ability in eating disorders. *Psychol Med*, 37(8), 1075-1084. doi: 0.1017/S0033291707009877
- Stewart, C.S., McEwen, F. S., Konstantellou, A. Eisler, I., Simic, M. 2017. Impact of ASD Traits on Treatment Outcomes of Eating Disorders in Girls. *Eur Eat Disord Rev*. 25(2), 123-128. doi: 10.1002/erv.2497.
- Tchanturia, K., Davies, H., Roberts, M., Harrison, A., Nakazato, M., Schmidt, U., Treasure, J., Morris, R. 2012. Poor Cognitive Flexibility in Eating Disorders: Examining the Evidence using the Wisconsin Card Sorting Task. *PLoS One*, 7(1): e28331. doi:10.1371/journal.pone.0028331.
- Tchanturia, K., Doris, E., Fleming, C. 2014. Effectiveness of Cognitive Remediation and Emotion Skills Training (CREST) for Anorexia Nervosa in Group Format: A Naturalistic Pilot Study. *Eur Eat Disord Rev*, 22(3), 200-205. doi: 10.1002/Erv.2287

- Tchanturia, K., Doris, E., Mountford, V., Fleming, C. 2015. Cognitive Remediation and Emotion Skills Training (CREST) for anorexia nervosa in individual format: self-reported outcomes. *BMC Psychiatry*, 15, 53. doi: 10.1186/s12888-015-0434-9
- Tchanturia, K., Larsson, E., Adamson, J. 2016. How anorexia nervosa patients with high and low autistic traits with respond to group Cognitive Remediation Therapy, *BMC Psychiatry*. doi: 10.1186/s12888-016-1044-x
- Tchanturia, K., Lloyd, S., Lang, K. 2013. Cognitive remediation therapy for anorexia nervosa: current evidence and future research directions. *Int J Eat Disord*, 46(5), 492-495. doi: 10.1002/eat.22106
- Tchanturia, K., Lounes, N., Holttum, S. 2014. Cognitive remediation in anorexia nervosa and related conditions: a systematic review. *Eur Eat Disord Rev*, 22(6), 454-462. doi: 10.1002/erv.2326
- Tchanturia, K., Giombini, L., Leppanen, J., Kinnaird, E. 2017. Evidence for Cognitive Remediation Therapy in young people with anorexia nervosa: Systematic Review and Meta-analysis of the literature. *Eur Eat Disord Rev* 25(4), 227-236. doi: 10.1002/erv.2522
- Treasure, J., Claudino, A. M., Zucker, N. 2010. Eating disorders. *Lancet*, 375(9714), 583-593. doi: 10.1016/S0140-6736(09)61748-7
- Treasure, J., Zipfel, S., Micali, N., Wade, T., Stice, E., Claudino, A., . . . Wentz, E. 2015. Anorexia nervosa. *Nature Review Disease Primers*, 1, 15074. doi: 10.1038/nrdp.2015.74
- Vagni, D., Moscone, D., Travaglione, S., Congtugno, A. 2016. Using the Ritvo Autism Asperger Diagnostic Scale-Revised (RAADS-R) disentangle the heterogeneity

- of autistic traits in an Italian eating disorder population. *Res. Autism Spectr. Disord.* 32, 143-155. doi: 10.1016/j.rasd.2016.10.002
- Wechsler, D. 2011. Wechsler Abbreviated Scale of Intelligence - Second Edition (WASI-II). San Antonio, TX: NCS Pearson.
- Westwood, H., Eisler, I., Mandy, W., Leppanen, J., Treasure, J., Tchanturia, K. 2015. Using the Autism-Spectrum Quotient to Measure Autistic Traits in Anorexia Nervosa: A Systematic Review and Meta-Analysis. *J Autism Dev Disord.* doi: 10.1007/s10803-015-2641-0
- Westwood, H., Mandy, W., Tchanturia, K. 2017. Clinical evaluation of autistic symptoms in women with anorexia nervosa. *Mol Autism*, 8:12. doi: 10.1186/s13229-017-0128-x
- Westwood, H., Mandy, W., Simic, M., Tchanturia, K. 2017. Assessing ASD in Adolescent Females with Anorexia Nervosa using Clinical and Developmental Measures: a Preliminary Investigation. *J Abnorm Child Psychol.* doi: 10.1007/s10802-017-0301-x
- Westwood, H., Stahl, D., Mandy, W., Tchanturia, K. 2016. The set-shifting profiles of anorexia nervosa and autism spectrum disorder using the Wisconsin Card Sorting Test: a systematic review and meta-analysis. *Psych Med*, 1-19. doi: 10.1017/S0033291716000581
- Westwood, H., Tchanturia, K. 2017. Autism Spectrum Disorder in Anorexia Nervosa: An Updated Literature Review. *Curr Psychiatry Rep*, 19. doi: 10.1007/s11920-017-0791-9
- Zigmond, A. S., Snaith, R. P. 1983. The hospital anxiety and depression scale. *Acta Psychiatr Scand*, 67(6), 361-370

Table 1. Participant demographics and one-way ANOVA results with effect sizes.

	HAS mean (SD) N = 35	SCAS mean (SD) N = 37	NAS mean (SD) N = 27	<i>p</i>	Partial η^2 effect size	Tukey post hoc tests		
						HAS vs SCAS	SCAS vs NAS	HAS vs NAS
Age	20.43(9.33)	22.27(7.59)	23.12(7.51)	.042	.06	<i>p</i> = .143	<i>p</i> = .784	<i>p</i> = .047
Eating disorder duration	4.82(8.82)	5.74(6.46)	6.29(7.57)	.554	.01			
BMI (adults)	N = 14 15.51(2.19)	N = 24 15.80(2.02)	N = 22 14.71(2.08)	.209	.05			
%IBW (young people)	N = 21 88.51(7.19)	N = 13 84.14(6.11)	N = 5 94.45(9.47)	.032	.18	<i>p</i> = .224	<i>p</i> = .028	<i>p</i> = .234
EDE-Q Global Score	3.99(1.40)	3.95(1.71)	3.45(1.53)	.205	.03			
Age of illness onset	15.76(5.99)	16.94(4.27)	16.89(5.26)	.145	.04			
HADS depression (adults)	N = 14 12.29(5.09)	N = 24 9.46(4.83)	N = 22 8.41(4.27)	.166	.04			
MFQ score (young people)	N = 21 71.11(14.24)	N = 13 71(12.95)	N = 5 69(24.26)					
Full-scale IQ (4 subtests)	106.23(16.32)	109.97(11.22)	113.54(13.38)	.139	.04			
Ethnicity (% White British)	66.7	84.2	77.8					
Psychiatric Medication Use (%)	33.3	38.9	27.8	$\chi^2(2) = 0.25$, <i>p</i> = .883.				
Antidepressants (%)	7.6	8.6	6.8					
Antipsychotics (%)	3.3	3.7	3					
Antidepressant and antipsychotic (%)	6.6	7.5	5.9					

BMI = body mass index; EDE-Q = Eating Disorder Examination Questionnaire, global score; HADS = Hospital Anxiety and Depression Scale, depression subscale; HAS = high autistic symptoms; %IBW = percentage of ideal body weight for height (for participants recruited from child and adolescent services); NAS = no autistic symptoms; SCAS = sub-clinical autistic symptoms. For age, eating disorder duration, age of illness onset and EDE-Q global score, analysis was conducted using transformed scores. For depression, analysis was conducted using standardised Z scores. Statistically significant results are highlighted in bold.

Table 2. One-way ANOVA results for WCST and ROCFT outcomes with effect sizes.

	HAS mean (SD) N = 34	SCAS mean (SD) N = 34	NAS mean (SD) N = 27	<i>p</i>	Partial η^2 effect size
<i>WCST outcomes</i>					
Number of trials administered	97.74(21.98)	91.53(16.07)	84.19(15.47)	.021	.08
Total correct responses	68.44(12.16)	71.50(7.62)	67.37(5.71)	.061	.04
Total response errors	29.29(25.07)	20.03(13.85)	16.81(14.61)	.061	.08
Total response errors %	26.68(17.34)	20.41(9.38)	18.07(10.24)	.065	.07
Total perseverative errors	14.56(12.49)	9.68(8.00)	7.89(5.61)	.027	.09
Total perseverative errors %	13.35(8.84)	10.00(5.68)	8.70(3.94)	.029	.08
<i>ROCFT outcomes</i>					
Order Index	1.95(0.69)	1.75(0.84)	1.90(0.67)	.515	.01
Style Index	1.81(0.48)	1.13(0.52)	1.23(0.52)	.739	.01

Central Coherence Index	1.20(0.43)	1.14(0.50)	1.21(0.42)	.814	.01
-------------------------	------------	------------	------------	------	-----

HAS = high autistic symptoms; NAS = no autistic symptoms; SCAS = sub-clinical autistic symptoms;
 ROCFT = Rey Osterrieth Complex Figure Test; SD = standard deviation; WCST = Wisconsin Card
 Sorting Test. For WCST results, *p* values for Welch ANOVA are reported due to homogeneity of
 variance being violated; statistically significant results are highlighted in bold

Accepted manuscript

Table 3. Self-reported cognitive style one-way ANOVA results with effect sizes.

	NAS mean (SD)	SCAS mean (SD)	HAS mean (SD)	<i>p</i>	Partial η^2 effect size
Cognitive rigidity	47.65(12.59)	51.09(12.49)	55.72(10.58)	.031	.07
Attention to detail	1.44(0.25)	46(1.44)	3.94(1.34)	.309	.03

HAS = high autistic symptoms; NAS = no autistic symptoms; SCAS = subclinical autistic symptoms; SD = standard deviation. Cognitive rigidity analysis was conducted using transformed scores.

Accepted manuscript

Figure 1: Grouped scatter plot of ADOS-2 revised algorithm scores against WCST percentage of perseverative errors for the no autistic symptom (NAS), sub-clinical autistic symptom (SCAS) and high autistic symptom (HAS) groups.

Highlights

- Autistic symptoms are associated with increased cognitive rigidity in Anorexia Nervosa
- No association between autism and measures of attention to detail
- Age may affect the relationship between autistic symptoms and cognitive functioning