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Exploring neuropsychological and socio-emotional task performance in anorexia nervosa: A cluster analytic approach

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Data availability statement

Data are available on request.

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Conflict of interest disclosure

The authors have no conflicts of interest to declare.

Ethics approval statement

The study was approved by the London-Surrey Borders Research Ethics Committee (17/LO/0271).

Patient consent statement

All participants provided written informed consent. In addition, written consent was also provided by the participant's legal guardian where participants were under the age of 18.

Abstract

Objective: The aim of this study was to characterise heterogeneity in neuropsychological and socio-emotional task performance in young women with anorexia nervosa (AN) using hierarchical cluster analysis. Further, we aimed to test whether cognitive profiles were associated with differences in clinical variables (BMI, illness duration, and age at diagnosis), psychopathology (eating disorder, autistic symptoms, anxiety, and depression), and functional impairment. Method: set-shifting, central coherence, and theory of mind abilities were measured in 118 women with acute or remitted AN. A hierarchical cluster analysis using Ward's method with a Euclidean distance measure was performed with the neuropsychological and socio-emotional variables. Differences between clusters were assessed using ANOVAs. Results: four clusters emerged, with significant differences in neuropsychological and socio-emotional task performance. There were no significant differences between clusters in clinical variables, psychopathology, or functional impairment, however these analyses lacked power due to small cluster sizes. Conclusions: our results demonstrate significant heterogeneity in cognitive profiles in AN, supporting a more personalised approach to treatment. Studies in larger samples are required to establish whether these variables map onto clinically significant differences in aetiology, clinical presentation, comorbidity patterns, and/or treatment responses.

Keywords: anorexia nervosa; set-shifting; central coherence; theory of mind; cluster analysis

Introduction

Anorexia nervosa (AN) is a severe psychiatric disorder affecting around 1-2% of females and less than 0.5% of males (Hoek, 2006). AN becomes chronic in around 20% of cases, and is associated with one of the highest mortality rates of all psychiatric disorders (Chesney et al., 2014; Harris & Barraclough, 1998). Despite the severity of the disorder, effective psychological and pharmacological treatments are lacking. For example, only around 30% of patients reach recovery at 1 or 2 year follow-up after "gold-standard" psychological interventions for AN (Byrne et al., 2017; Schmidt et al., 2016). Similarly, evidence regarding the efficacy of medications such as serotonin reuptake inhibitors and atypical antipsychotics for AN is poor (Miniati et al., 2016).

Improvements in treatment for AN will depend on advances in understanding the aetiology of the disorder. Among several genetic, sociocultural, and temperamental factors implicated in the development of AN, differences in neuropsychological functioning and social cognition have been identified as potential biomarkers for the disorder (Treasure et al., 2007; Zhou et al., 2017). For example, difficulties in areas such as set-shifting, weak central coherence, working memory, decision making, and theory of mind (ToM) have all been demonstrated in individuals with AN, both in the acute state and after recovery (Fagundo et al., 2012; Lang et al., 2015; Lindner et al., 2014; Nikendei et al., 2011; Phillipou et al., 2016; Russell et al., 2009). Difficulties in set-shifting and weak central coherence specifically are proposed to predispose individuals to developing the disorder, and maintain the illness by inhibiting flexible behaviour (Treasure & Schmidt, 2013). However, reviews of neuropsychological and social-cognitive functioning in AN have highlighted mixed findings across studies, with some reporting no differences in task performance in AN compared to healthy controls (HCs) (Lang et al., 2014; Lena et al., 2004; Leslie et al., 2020). This likely reflects the highly heterogenous presentation of AN; difficulties in these domains are not shown by all or even the majority of individuals (Rose et al., 2012). Thus, while these traits may not represent biomarkers (i.e., an objectively measured characteristic differentiating between cases and controls), they may in fact represent stratification biomarkers. These are characteristics that distinguish between subgroups of individuals with AN, mapping onto differences in aetiology, clinical presentation, comorbidity patterns, and/or treatment responses (Loth et al., 2018).

A potentially useful method for characterising neuro- and social-cognitive heterogeneity in AN is cluster analysis. A variety of cluster analytic methods are available, but generally, these methods group the most similar observations in a data set together, resulting in distinct subgroups ("clusters"). In disorders such as schizophrenia, cluster analysis has been used to define subgroups of participants based on neuropsychological and social cognition performance, with studies finding meaningful differences in outcomes and clinical characteristics (such as positive and negative symptoms) between clusters (Gilbert et al., 2014; Ohi et al., 2017; Rocca et al., 2016). These studies also find that a sizeable proportion of those with schizophrenia show no difficulties in performance, highlighting the limitations of a mean between-group differences approach.

Past research using cluster analysis in those with eating disorders has mostly focussed on characterising comorbidity (Van Alsten & Duncan, 2020), clinical presentation (Damiano et al., 2015; Errichiello et al., 2016), or personality types (Claes et al., 2006; Hopwood et al., 2010), however very few have performed clustering based on neuropsychological or social-cognitive performance. Most notably, Renwick et al. (2015) included a comprehensive assessment of neuropsychological and social function as cluster variables, including set-shifting, central coherence, and ToM tasks. They found three clusters: one with average to high performance, a second with mixed performance, and a final cluster with poor performance across measures. Interestingly, 45% of adults with AN fell within the average to high performance cluster, showing no difficulties across domains, while 17% fell within the third poor performance cluster. The authors describe this third cluster as "ASD-like"; showing similar difficulties to those with autism spectrum disorder (ASD). This is in agreement with previous research showing that around 25% of individuals with AN may also have comorbid ASD (Kerr-Gaffney et al., 2020; Kinnaird & Tchanturia, 2021).

The aim of the current study was to characterise the neuropsychological and social-cognitive profile in individuals with AN, using hierarchical cluster analysis. We chose to examine set-shifting, central coherence, and ToM performance, as difficulties in these domains appear to be the strongest candidates for biomarkers for AN in comparison to other neuropsychological and social-cognitive functions (Fuglset, 2019; Holliday et al., 2005; Kanakam et al., 2013; Kanakam & Treasure, 2013; Tchanturia et al., 2004). Given there is some evidence to suggest that adolescents with AN may not show the same cognitive

difficulties as adults (Giannunzio et al., 2018), we included a younger sample (aged 12 to 27), to explore whether we would find similar cluster solutions as in adults (Renwick et al., 2015). Secondly, we aimed to examine whether cluster membership was related to clinical characteristics (such as body mass index (BMI), medication use, and illness duration), as well as eating disorder psychopathology and comorbid psychiatric symptoms.

Methods

Participants

118 participants with a lifetime history of AN were recruited from specialist eating disorder services, online advertisement, and [INSTITUTION NAME REMOVED FOR BLINDING] participant recruitment advertisements. All participants were required to be between 12 and 27 years old, right-handed, female, and have no history of serious brain trauma, learning disability or neurological impairment. Participants were screened using the Structured Clinical Interview for DSM-5 Disorders, research version (SCID-5-RV) (First et al., 2015) to ensure they met criteria for current AN (59%) or partial or full remission (41%). No psychiatric comorbidities were excluded, and 52.5% of participants were taking psychiatric medication at the time of assessment (35.6% were taking an antidepressant, 13.6% were taking an antipsychotic, and 3.4% were taking antiepileptic medication). The study was approved by the [LOCATION REMOVED FOR BLINDING] Research Ethics Committee (17/LO/0271).

Measures

Participants completed several self-report questionnaires assessing eating disorder and comorbid psychopathology: the Eating Disorders Examination Questionnaire (EDE-Q) (Fairburn & Beglin, 1994), the Hospital Anxiety and Depression Scale (HADS) (Zigmond & Snaith, 1983), and the 10-item Autism Quotient (AQ-10) (Allison et al., 2012). The Work and Social Adjustment Scale (WSAS) (Mundt et al., 2002) measured functional impairment. IQ was measured using the National Adult Reading Test (NART) (Nelson & Willison, 1991). Participants also provided demographic and clinical information, and height and weight were measured to calculate BMI (height/weight^2). All measures and the following neuropsychological and socio-emotional tasks were taken during a single testing session.

Neuropsychological and socio-emotional tasks

The Frith-Happé animations were used to measure ToM (Abell et al., 2000). These are a series of cartoons in which two triangles move around a central open box, sometimes in a way that implies they are animate and interacting. Three types of animations are included: random movement (triangles move aimlessly across the screen, occasionally bumping into one another, but with no apparent social interaction), goal-directed interactions (triangles interact with one another, for example, chasing or following one another, but with no mentalising behaviour), and ToM interactions (triangles reacted to each other's mental state, for example, by tricking or coaxing each other). The cartoons were presented on a computer screen, and participants were required to describe aloud what is happening in the clip. Both an accuracy and a language score ranging from 0 to 2 are derived for each of the three types of animations. Higher scores indicate more accurate descriptions of the cartoons (accuracy score) or more use of mental state language (language score). In this study, only accuracy and language scores from the ToM interactions are used as our ToM variables in the cluster analysis.

The Wisconsin Card Sorting Test (WCST) computer version (Heaton, 1993) was used to measure set-shifting abilities. This task involves matching stimulus cards to one of four category cards (according to colour, number, or shape). The matching rule must be deduced by trial and error and the feedback received. The number of perseverative errors (as a proportion of total trials) was used as the set-shifting variable in the cluster analysis.

The Rey-Osterreith Complex Figure test (ROCFT) (Osterrieth, 1944) is a pen and paper task measuring global processing ability. Participants are required to copy a complex figure, and their strategy is scored according to whether they use a more global or local processing style. The central coherence index (CCI) was used in the cluster analysis, with higher scores indicating better central coherence (Booth, 2006).

Analysis

To control for the effects of age and sex on neuropsychological and socio-emotional performance, ToM language and accuracy, WCST perseverative errors, and ROCFT CCI were converted to Z scores, based on those of the control group included in a wider study (Leslie et al., 2020). Scores are therefore relative to age, sex, and IQ-matched controls,

demographic information for which is included in the supplementary material. Scores were also standardised across variables so that higher scores indicate better performance, to aid interpretation. Additionally, outliers with scores more than +-3 SD were curtailed to +-3 SD, as extreme values can unduly influence clustering.

A hierarchical cluster analysis using Ward's method with a Euclidean distance measure was performed with the four neuropsychological and socio-emotional variables: ToM accuracy, ToM language, WCST perseverative errors, and ROCFT CCI. Group differences in task performance, clinical and demographic variables, and psychopathology between clusters were analysed using one-way ANOVAs with Tukey's post hoc tests or the Kruskal-Wallis test for data with non-normally distributed residuals. α was set at <.05 and η^2p reflected effect size (small: 0.01-0.05, medium: 0.06-0.13, large: >0.14). Analyses were conducted in RStudio V1.3.1093 and SPSS V26.

Results

Demographic and clinical characteristics of the whole sample, as well as the acute and remitted AN groups separately are displayed in table 1.

[TABLE 1 HERE]

Inspection of the dendrogram and the Elbow method suggested a four cluster solution (see supplementary material). The agglomerative coefficient was 0.95, suggesting a strong clustering structure. Figure 1 shows neuropsychological and socio-emotional task performance across the four clusters. Cluster 1 showed poor performance across ToM and central coherence, but average set-shifting performance. Cluster 2 was similar, although participants in this cluster showed above average central coherence. Cluster 3, the smallest cluster, showed average ToM and central coherence, but very poor set-shifting performance. Finally, the largest cluster was cluster 4, with participants showing average to above average performance across domains.

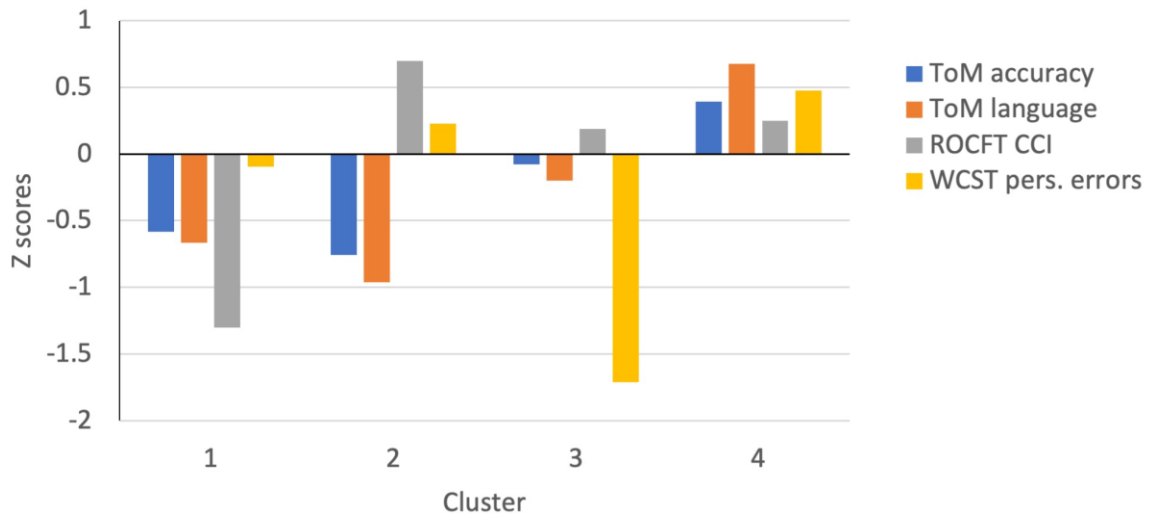

Figure 1. Mean neuropsychological and socio-cognitive task performance across clusters.

Significant differences in neuropsychological and socio-cognitive variables can be seen across clusters, with large effect sizes (Table 2).

[TABLE 2 HERE]

Demographic and clinical characteristics of each cluster are shown in Table 3. No significant differences were found between clusters, with some small effect sizes. This likely reflects lack of power from small cluster sizes.

[TABLE 3 HERE]

Discussion

This study aimed to characterise profiles of neuropsychological and socio-cognitive task performance in young women with AN using hierarchical cluster analysis. Our findings demonstrate that the cognitive profile in AN is highly heterogenous, with four distinct clusters emerging. A large cluster with average to high performance was identified, including 42% of participants. This is remarkably similar to previous research in AN (Renwick et al., 2015), but also in other disorders, such as schizophrenia (Rocca et al., 2016). This cluster did not significantly differ from the others in regard to clinical characteristics, psychopathology, or functional impairment. Similarly, we did not find an “ASD-like” cluster showing difficulties across all domains, as in Renwick et al. (2015). Although cluster 1 bears some resemblance to this profile (e.g., difficulties in ToM and central coherence),

participants in this group did not show excessive perseverative errors. Although mean AQ-10 scores were numerically highest in this cluster compared to the others, this difference did not reach significance and the effect size was small. These findings will be discussed in turn.

That almost half of participants showed no difficulties across domains highlights the importance of exploring cognitive profiles in this way, over a case-control comparison approach. Previous research has shown significant differences in mean scores between AN and HC in these domains, with small or medium effect sizes (Lang et al., 2015, 2016). However, from these studies it is not clear whether the significant *p* value reflects small difficulties across most participants with AN, or severe difficulties in a small subgroup. Our study suggests the latter option may be the case, at least in adolescents and young adults. Such findings clearly have implications for treatment. Interventions which target difficulties in central coherence and inflexible behaviour, such as cognitive remediation therapy (CRT), may be appropriate for certain patients with difficulties in these domains. This could be assessed on admission to inpatient treatment, for example. More generally, these results call for a more personalised approach to treatment, tailored to an individual's cognitive, social, and other risk and resilience factors.

No significant group differences between clusters in clinical presentation or psychopathology were found, similar to previous research in AN (Renwick et al., 2015). There are a few possible explanations for this. One is that the neuropsychological and social variables studied here are "clinically silent"; meaning that difficulties in these areas do not manifest as meaningful predictors of illness severity among young people with a relatively short duration of illness. However, our between-group analyses were quite underpowered due to small cluster sizes, a significant limitation of the study. Therefore, another possibility is that cognitive profiles may be associated with subtle differences in clinical presentation, which may be revealed in studies with much larger sample sizes. It may also be the case that the cognitive profiles found predict longer term outcomes; future studies would benefit from employing longitudinal designs to measure outcomes months or years later.

Our results support the notion that neurocognitive and socio-emotional functioning are altered in AN, even in the early stage of illness. For example, cluster 2, who had a median illness duration of 2 years, displayed the poorest ToM abilities compared to the other

clusters. This would suggest difficulties in these domains are not merely a consequence of extended period of starvation, and may constitute a risk factor for the illness for some individuals. In contrast to the previous study in adults with AN by Renwick et al. (2015), we did not find a cluster with difficulties across all domains. This might suggest some worsening of neuropsychological and socio-cognitive functioning with increasing age and/or illness duration. However, our studies are not directly comparable due to some differences in cluster variables, which likely impacted our results. Nonetheless, cluster analysis provides a promising approach for characterising heterogeneity in AN, and may be useful in moving towards a more personalised approach to treatment in this population.

Strengths and limitations

The use of cluster analysis is a significant strength of the study. Previous research examining neurocognitive and socio-cognitive functioning in AN has almost exclusively used a case-control between-group differences approach, however this approach can obscure differences *within* the AN population. We also included a rather heterogenous sample, including participants with acute AN who were not attending treatment, inpatients, and outpatients, as well as those who were in the remitted state. This has the benefit of more accurately reflecting the general population of people with AN, rather than those that gain access to specialist treatment. However, our lenient inclusion criteria may also be seen as a limitation, by introducing additional sources of variability into our analyses. For example, the inclusion of both acute and remitted participants, as well as medicated and unmedicated participants likely introduced clinical heterogeneity within clusters, possibly contributing to the non-significant results between clusters on variables such as BMI and eating disorder psychopathology. Similarly, we were unable to examine the proportion of each AN subtype (AN-R and AN-BP), or the presence of diagnosed psychiatric comorbidities, within each cluster. These factors may affect neuropsychological and socio-cognitive performance (Tamiya et al., 2018), and therefore should be taken into consideration in future research.

References

Abell, F., Happé, F., & Frith, U. (2000). Do triangles play tricks? Attribution of mental states to animated shapes in normal and abnormal development. *Cognitive Development*, *15*(1), 1–16. https://doi.org/10.1016/S0885-2014(00)00014-9

Allison, C., Auyeung, B., & Baron-Cohen, S. (2012). Toward brief "red flags" for autism screening: The short Autism Spectrum Quotient and the short Quantitative Checklist in 1,000 cases and 3,000 controls. *Journal of the American Academy of Child and Adolescent Psychiatry*, *51*(2), 202–212. https://doi.org/10.1016/j.jaac.2011.11.003

Booth, R. (2006). *Local-global Processing and Cognitive Style in Autism Spectrum Disorder and Typical Development*. King's College London.

Byrne, S., Wade, T., Hay, P., Touyz, S., Fairburn, C. G., Treasure, J., Schmidt, U., McIntosh, V., Allen, K., Fursland, A., & Crosby, R. D. (2017). A randomised controlled trial of three psychological treatments for anorexia nervosa. *Psychological Medicine*, *47*(16), 2823–2833. https://doi.org/10.1017/S0033291717001349

Chesney, E., Goodwin, G. M., & Fazel, S. (2014). Risks of all-cause and suicide mortality in mental disorders: A meta-review. *World Psychiatry*, *13*(2), 153–160. https://doi.org/10.1002/wps.20128

Claes, L., Vandereycken, W., Luyten, P., Soenens, B., Pieters, G., & Vertommen, H. (2006). Personality prototypes in eating disorders based on the big five model. *Journal of Personality Disorders*, *20*(4), 401–416. https://doi.org/10.1521/pedi.2006.20.4.401

Damiano, S. R., Reece, J. E., Reid, S., Atkins, L., & Patton, G. (2015). Empirically Derived subtypes of full and subthreshold anorexia nervosa in adolescent females: Understanding general psychopathology and treatment implications. *Eating Disorders*, *23*(3), 223–241. https://doi.org/10.1080/10640266.2014.1000106

Errichiello, L., Iodice, D., Bruzzese, D., Gherghi, M., & Senatore, I. (2016). Prognostic factors and outcome in anorexia nervosa: a follow-up study. *Eating and Weight Disorders*, *21*(1), 73–82. https://doi.org/10.1007/s40519-015-0211-2

Fagundo, A. B., de la Torre, R., Jiménez-Murcia, S., Agüera, Z., Granero, R., Tárrega, S., Botella, C., Baños, R., Fernández-Real, J. M., Rodríguez, R., Forcano, L., Frühbeck, G.,

Gómez-Ambrosi, J., Tinahones, F. J., Fernández-García, J. C., Casanueva, F. F., & Fernández-Aranda, F. (2012). Executive functions profile in extreme eating/weight conditions: From Anorexia Nervosa to Obesity. *PLoS ONE*, *7*(8). https://doi.org/10.1371/journal.pone.0043382

Fairburn, C. G., & Beglin, S. J. (1994). Assessment of eating disorders: Interview or self-report questionnaire? *International Journal of Eating Disorders*, *16*(4), 363–370. https://doi.org/10.1002/1098-108X(199412)16:4<363::AID-EAT2260160405>3.0.CO;2-%23

First, M. B., Williams, J. B., Karg, R. S., & Spitzer, R. L. (2015). *Structured clinical interview for DSM-5 disorders, research version*. American Psychiatric Association.

Fuglset, T. S. (2019). Set-shifting, central coherence and decision-making in individuals recovered from anorexia nervosa: A systematic review. *Journal of Eating Disorders*, *7*, 22. https://doi.org/10.1186/s40337-019-0251-5

Giannunzio, V., Degortes, D., Tenconi, E., Collantoni, E., Solmi, M., Santonastaso, P., & Favaro, A. (2018). Decision-making impairment in anorexia nervosa: New insights into the role of age and decision-making style. *European Eating Disorders Review*, *26*(4), 302–314. https://doi.org/10.1002/erv.2595

Gilbert, E., Mérette, C., Jomphe, V., Émond, C., Rouleau, N., Bouchard, R. H., Roy, M. A., Paccalet, T., & Maziade, M. (2014). Cluster analysis of cognitive deficits may mark heterogeneity in schizophrenia in terms of outcome and response to treatment. *European Archives of Psychiatry and Clinical Neuroscience*, *264*(4), 333–343. https://doi.org/10.1007/s00406-013-0463-7

Harris, E. C., & Barraclough, B. (1998). Excess mortality of mental disorder. *The British Journal of Psychiatry*, *173*(1), 11–53. https://doi.org/10.1192/BJP.173.1.11

Heaton, R. K. (1993). *Wisconsin Card Sorting Test: Computer Version*. Psychological Assessment Resources.

Hoek, H. W. (2006). Incidence, prevalence and mortality of anorexia nervosa and other eating disorders. *Current Opinion in Psychiatry*, *19*(4), 389–394. https://doi.org/10.1097/01.yco.0000228759.95237.78

Holliday, J., Tchanturia, K., Landau, S., Collier, D., & Treasure, J. (2005). Is impaired set-shifting an endophenotype of anorexia nervosa? *American Journal of Psychiatry*, *162*(12), 2269–2275. https://doi.org/10.1176/appi.ajp.162.12.2269

Hopwood, C. J., Ansell, E. B., Fehon, D. C., & Grilo, C. M. (2010). Personality heterogeneity in female adolescent inpatients with features of eating disorders. *Comprehensive Psychiatry*, *51*(6), 585–591. https://doi.org/10.1016/j.comppsych.2010.03.006

Kanakam, N., Krug, I., Raoult, C., Collier, D., & Treasure, J. (2013). Social and emotional processing as a behavioural endophenotype in eating disorders: A pilot investigation in twins. *European Eating Disorders Review*, *21*(4), 294–307. https://doi.org/10.1002/erv.2232

Kanakam, N., & Treasure, J. (2013). A review of cognitive neuropsychiatry in the taxonomy of eating disorders: State, trait, or genetic? *Cogntive Neuropsychiatry, 18,* 83-114. https://doi.org/10.1080/13546805.2012.682362

Kerr-Gaffney, J., Harrison, A., & Tchanturia, K. (2020). Autism spectrum disorder traits are associated with empathic abilities in adults with anorexia nervosa. *Journal of Affective Disorders*, *266,* 273-281. https://doi.org/10.1016/j.jad.2020.01.169

Kinnaird, E., & Tchanturia, K. (2021). Looking beneath the surface: Distinguishing between common features in autism and anorexia nervosa. *Journal of Behavioral and Cognitive Therapy*, *31*(1), 3–13. https://doi.org/10.1016/j.jbct.2020.09.001

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), 1–13. https://doi.org/10.1371/journal.pone.0131724

Lang, K., Roberts, M., Harrison, A., Lopez, C., Goddard, E., Khondoker, M., Treasure, J., & Tchanturia, K. (2016). Central coherence in eating disorders: A synthesis of studies using the rey osterrieth complex figure test. *PLoS ONE*, *11*(11), 1–11. https://doi.org/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. *International Journal of Eating Disorders*, *47*(4), 394–399. https://doi.org/10.1002/eat.22235

Lena, S. M., Fiocco, A. J., & Leyenaar, J. A. K. (2004). The role of cognitive deficits in the development of eating disorders. *Neuropsychology Review*, *14*(2), 99–113. https://doi.org/10.1023/B:NERV.0000028081.40907.de

Leslie, M., Halls, D., Leppanen, J., Sedgewick, F., Smith, K., Hayward, H., Lang, K., Fonville, L., Simic, M., Mandy, W., Nicholls, D., Murphy, D., Williams, S., & Tchanturia, K. (2020). Neural correlates of theory of mind are preserved in young women with anorexia nervosa. *Frontiers in Psychology*, *11,* 568073. https://doi.org/10.3389/fpsyg.2020.568073

Lindner, S. E., Fichter, M. M., & Quadflieg, N. (2014). Set-shifting and its relation to clinical and personality variables in full recovery of anorexia nervosa. *European Eating Disorders Review*, *22*(4), 252–259. https://doi.org/10.1002/erv.2293

Loth, E., Garrido, L., Ahmad, J., Watson, E., Duff, A., & Duchaine, B. (2018). Facial expression recognition as a candidate marker for autism spectrum disorder: how frequent and severe are deficits? *Molecular Autism*, *9*(1), 7. https://doi.org/10.1186/s13229-018-0187-7

Miniati, M., Mauri, M., Ciberti, A., Mariani, M. G., Marazziti, D., & Dell'Osso, L. (2016). Psychopharmacological options for adult patients with anorexia nervosa. *CNS Spectrums*, *21*(2), 134–142. https://doi.org/10.1017/S1092852914000790

Mundt, J. C., Marks, I. M., Shear, M. K., & Greist, J. M. (2002). The Work and Social Adjustment Scale: A simple measure of impairment in functioning. *British Journal of Psychiatry*, *180*(5), 461–464. https://doi.org/10.1192/bjp.180.5.461

Nelson, H. E., & Willison, J. E. (1991). *The revised national adult reading test*. NFER-Nelson.

Nikendei, C., Funiok, C., Pfüller, U., Zastrow, A., Aschenbrenner, S., Weisbrod, M., Herzog, W., & Friederich, H. C. (2011). Memory performance in acute and weight-restored anorexia nervosa patients. *Psychological Medicine*, *41*(4), 829–838. https://doi.org/10.1017/S0033291710001121

Ohi, K., Shimada, T., Nemoto, K., Kataoka, Y., Yasuyama, T., Kimura, K., Okubo, H., Uehara,

T., & Kawasaki, Y. (2017). Cognitive clustering in schizophrenia patients, their first-degree relatives and healthy subjects is associated with anterior cingulate cortex volume. *NeuroImage: Clinical*, *16*, 248–256. https://doi.org/10.1016/j.nicl.2017.08.008

Osterrieth, P. A. (1944). Test of copying a complex figure; contribution to the study of perception and memory. *Archives de Psychologie*, *30*, 206–356.

Phillipou, A., Rossell, S. L., Gurvich, C., Castle, D. J., Troje, N. F., & Abel, L. A. (2016). Body image in anorexia nervosa: Body size estimation utilising a biological motion task and eyetracking. *European Eating Disorders Review*, *24*(2), 131–138. https://doi.org/10.1002/erv.2423

Renwick, B., Musiat, P., Lose, A., Dejong, H., Broadbent, H., Kenyon, M., Loomes, R., Watson, C., Ghelani, S., Serpell, L., Richards, L., Johnson-Sabine, E., Boughton, N., Treasure, J., & Schmidt, U. (2015). Neuro- and social-cognitive clustering highlights distinct profiles in adults with anorexia nervosa. *International Journal of Eating Disorders*, *48*(1), 26–34. https://doi.org/10.1002/eat.22366

Rocca, P., Galderisi, S., Rossi, A., Bertolino, A., Rucci, P., Gibertoni, D., Montemagni, C., Sigaudo, M., Mucci, A., Bucci, P., Acciavatti, T., Aguglia, E., Amore, M., Bellomo, A., De Ronchi, D., Dell'Osso, L., Di Fabio, F., Girardi, P., Goracci, A., … De Capua, A. (2016). Social cognition in people with schizophrenia: A cluster-analytic approach. *Psychological Medicine*, *46*(13), 2717–2729. https://doi.org/10.1017/S0033291716001100

Rose, M., Frampton, I., & Lask, B. (2012). A case series investigating distinct neuropsychological profiles in children and adolescents with anorexia nervosa. *European Eating Disorders Review*, *20*(1), 32–38. https://doi.org/10.1002/erv.1095

Russell, T. A., Schmidt, U., Doherty, L., Young, V., & Tchanturia, K. (2009). Aspects of social cognition in anorexia nervosa: Affective and cognitive theory of mind. *Psychiatry Research*, *168*(3), 181–185. https://doi.org/10.1016/J.PSYCHRES.2008.10.028

Schmidt, U., Ryan, E. G., Bartholdy, S., Renwick, B., Keyes, A., O'Hara, C., Mcclelland, J., Lose, A., Kenyon, M., Dejong, H., Broadbent, H., Loomes, R., Serpell, L., Richards, L., Johnson-Sabine, E., Boughton, N., Whitehead, L., Bonin, E., Beecham, J., … Treasure, J. (2016). Two-year follow-up of the MOSAIC trial: A multicenter randomised controlled trial

comparing two psychological treatments in adult outpatients with broadly defined anorexia nervosa. *International Journal of Eating Disorders*, *49*(8), 793–800. https://doi.org/10.1002/eat.22523

Tamiya, H., Ouchi, A., Chen, R., Miyazawa, S., Akimoto, Y., Kaneda, Y., & Sora, I. (2018). Neurocognitive impairments are more severe in the binge-eating/purging anorexia nervosa subtype than in the restricting subtype. *Frontiers in Psychiatry*, *9*, 138. https://doi.org/10.3389/fpsyt.2018.00138

Tchanturia, K., Morris, R. G., Anderluh, M. B., Collier, D. A., Nikolaou, V., & Treasure, J. (2004). Set shifting in anorexia nervosa: An examination before and after weight gain, in full recovery and relationship to childhood and adult OCPD traits. *Journal of Psychiatric Research*, *38*(5), 545–552. https://doi.org/10.1016/j.jpsychires.2004.03.001

Treasure, J., Lopez, C., & Roberts, M. (2007). Endophenotypes in eating disorders: moving toward etiologically based diagnosis and treatment focused on pathophysiology. *Pediatric Health*, *1*(2), 171–181. https://doi.org/10.2217/17455111.1.2.171

Treasure, J., & Schmidt, U. (2013). The cognitive-interpersonal maintenance model of anorexia nervosa revisited: A summary of the evidence for cognitive, socio-emotional and interpersonal predisposing and perpetuating factors. *Journal of Eating Disorders*, *1*, 13. https://doi.org/10.1186/2050-2974-1-13

Van Alsten, S. C., & Duncan, A. E. (2020). Lifetime patterns of comorbidity in eating disorders: An approach using sequence analysis. *European Eating Disorders Review*, *28*(6), 709–723. https://doi.org/10.1002/erv.2767

Zhou, Z. C., McAdam, D. B., & Donnelly, D. R. (2017). Endophenotypes: A conceptual link between anorexia nervosa and autism spectrum disorder. *Research in Developmental Disabilities*, *82,* 153-165. https://doi.org/10.1016/j.ridd.2017.11.008

Zigmond, A. S., & Snaith, R. P. (1983). The hospital anxiety and depression scale. *Acta Psychiatrica Scandinavica*, *67*(6), 361–370. https://doi.org/10.1111/j.1600-0447.1983.tb09716.x

Table 1. Mean (SD) demographic and clinical characteristics of the sample.

	Acute AN (n=70)	Remitted AN (n=48)	Full sample (n=118)
Age (years)	18.73 (3.13)	19.17 (3.50)	18.91 (3.28)
IQ	111.73 (7.73)	111.69 (7.55)	111.70 (7.62)
BMI	16.57 (1.50)	20.89 (2.25)	18.34 (2.82)
Age at diagnosis	15.85 (2.77)	15.18 (3.04)	15.56 (2.90)
Illness duration (years)†	3.00 (4.00)	4.00 (3.50)	3.00 (3.00)
% on psychiatric medication	48.6	58.3	52.5
EDE-Q†	3.65 (2.60)	2.93 (3.12)	3.44 (2.61)
AQ-10	3.98 (2.38)	3.60 (2.12)	3.83 (2.27)
HADS anxiety	10.91 (3.48)	9.61 (3.92)	10.36 (3.71)
HADS depression	8.13 (4.55)	6.65 (4.20)	7.51 (4.45)
WSAS	19.11 (10.47)	15.00 (10.36)	17.42 (10.58)

AN: anorexia nervosa; AQ-10: 10-item Autism Quotient; BMI: body mass index; EDE-Q: eating disorder examination questionnaire; HADS: Hospital Anxiety and Depression Questionnaire; IQ: intelligence quotient; SD: standard deviation; WSAS: Work and Social Adjustment Scale

†Median and IQR

Table 2. Mean (SD) z scores across neuropsychological and socio-cognitive tasks.

	1 (n=23)	2 (n=29)	3 (n=17)	4 (n=49)	ANOVA F	*p*	η^2p
ToM accuracy	-0.58 (0.69)^{ab}	-0.76 (0.47)^{a}	-0.08 (0.83)^{b}	0.39 (0.62)^{c}	24.75	<.001	.39
ToM language	-0.67 (0.46)^{ab}	-0.96 (0.32)^{a}	-0.20 (0.62)^{b}	0.67 (0.66)^{c}	73.82	<.001	.63
ROCFT CCI	-1.30 (0.42)^{a}	0.70 (0.66)^{b}	0.19 (0.71)^{b}	0.25 (0.79)^{b}	75.87	<.001	.51
WCST perseverative errors	-0.10 (0.78)^{a}	0.23 (0.58)^{ab}	-1.71 (0.91)^{c}	0.48 (0.42)^{b}	31.97	<.001	.59

ANOVA: analysis of variance; ROCFT CCI: Rey-Osterreith Complex Figure test Central Coherence Index; SD: standard deviation; ToM: theory of mind; WCST: Wisconsin Card Sorting Test

Different superscripts indicate significant differences between groups.

Table 3. Mean (SD) demographic, clinical, and psychopathological characteristics.

	1 (n=23)	2 (n=29)	3 (n=17)	4 (n=49)	Test statistic	p	η^2p
Age (years)	18.43 (3.03)	18.52 (2.82)	19.24 (3.58)	19.24 (3.57)	0.52	.670	.01
IQ	108.70 (5.09)	110.86 (9.52)	113.66 (8.34)	112.88 (6.90)	1.95	.127	.05
BMI	18.47 (3.29)	17.84 (2.76)	17.74 (1.70)	18.78 (2.92)	0.98	.405	.03
Age at diagnosis	14.85 (2.58)	15.83 (2.75)	15.69 (3.67)	15.70 (2.85)	0.51	.678	.02
Illness duration (years)†	3.00 (3.50)	2.00 (4.00)	4.00 (5.00)	4.00 (3.75)	2.71	.439	.00
% on psychiatric medication	60.9%	51.7%	41.2%	53.1%	1.53	.675	.11‡
EDE-Q†	3.68 (2.34)	3.35 (3.72)	3.80 (1.69)	2.93 (2.77)	4.74	.192	.02
AQ-10	4.55 (2.37)	3.86 (2.17)	4.06 (2.16)	3.36 (2.29)	1.42	.241	.04
HADS anxiety	11.43 (3.46)	9.89 (3.99)	11.12 (3.57)	9.86 (3.66)	1.24	.300	.03
HADS depression	8.10 (3.69)	6.46 (4.19)	9.24 (5.65)	7.23 (4.33)	1.57	.200	.04
WSAS	18.00 (11.15)	16.89 (12.23)	20.24 (7.24)	16.40 (10.37)	0.58	.630	.02

AQ-10: 10-item Autism Quotient; BMI: body mass index; EDE-Q: eating disorder examination questionnaire; HADS: Hospital Anxiety and Depression Questionnaire; IQ: intelligence quotient; SD: standard deviation; WSAS: Work and Social Adjustment Scale

Different superscripts indicate significant differences between groups.

†Median and IQR

‡Cramer's V