

**Title: Alexithymia and autism diagnostic assessments: evidence from twins at genetic risk of autism and adults with anorexia nervosa**

Authors: Hannah Hobson<sup>a,b\*</sup>, Heather Westwood<sup>c</sup>, Jane Conway<sup>d</sup>, Fiona S. McEwen<sup>e, f, g</sup>,  
Emma Colvert<sup>f</sup>, Caroline Catmur<sup>h</sup>, Geoffrey Bird<sup>f,i</sup>, Francesca Happé<sup>f</sup>

<sup>a</sup> Department of Psychology, Social Work & Counselling, University of Greenwich, Old Royal Naval College, Park Row, London SE10 9LS

<sup>b</sup> Department of Psychology, University of York, York, YO10 5DD

<sup>c</sup> Psychological Medicine, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, SE5 8AF, United Kingdom

<sup>d</sup> Institute for Advanced Study in Toulouse, Manufacture des Tabacs 21, Allée de Brienne, 31015 Toulouse Cedex 6, France

<sup>e</sup> Biological & Experimental Psychology, School of Biological & Chemical Sciences, Queen Mary University of London, London, E1 4NS, United Kingdom

<sup>f</sup> Social, Genetic and Developmental Psychiatry Centre, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, SE5 8AF, United Kingdom

<sup>g</sup> Child & Adolescent Psychiatry, Institute of Psychiatry, Psychology and Neuroscience, King's College London, SE5 8AF, United Kingdom

<sup>h</sup> Department of Psychology, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, SE5 8AF, United Kingdom

<sup>i</sup> Department of Experimental Psychology, University of Oxford, New Radcliffe House, Radcliffe Observatory Quarter, Oxford, OX2 6GG, United Kingdom

\*Corresponding author: [hannah.hobson@york.ac.uk](mailto:hannah.hobson@york.ac.uk)

### **Abstract**

**Background:** Alexithymia, a difficulty identifying and communicating one's own emotions, affects socio-emotional processes, such as emotion recognition and empathy. Co-occurring alexithymia is prevalent in Autism Spectrum Disorder (ASD) and underlies some socio-emotional difficulties usually attributed to autism. Socio-emotional abilities are examined during behavioural diagnostic assessments of autism, yet the effect of alexithymia on these assessments is not known. This study aimed to examine the associations between alexithymia and Autism Diagnostic Observation Schedule (ADOS) assessment scores.

**Method:** Two previously collected samples of ADOS assessments were used to examine the relationship between alexithymia and ADOS scores. Participants included 96 women with anorexia, and 147 adolescents who were either high in autistic symptoms, or whose twin had high autistic symptoms. We examined 1) the impact of alexithymia on meeting the criteria for autism/ASD, 2) correlations between alexithymia and ADOS subscales, and 3) whether alexithymia predicted scores on specific ADOS items, selected a priori based on existing literature.

**Results:** In the adolescent group, parent-reported (but not self-reported) alexithymia correlated with both ADOS sub-scales, predicted scores on ADOS items, and predicted meeting clinical cut-offs for an ASD/autism diagnosis. Few associations were observed in the anorexic sample between self-reported alexithymia and ADOS subscale and item scores, but the presence of alexithymia predicted the likelihood of meeting diagnostic criteria for autism/ASD in this sample.

**Conclusions:** Alexithymia does show relationships with ADOS assessment scores. We discuss potential clinical and research implications, particularly in studies of autism where the ADOS is often the only diagnostic measure used.

**Keywords:** ADOS, alexithymia, diagnosis, autism, anorexia nervosa.

### **Highlights**

- Alexithymia has been argued to contribute to some deficits associated with autism
- As several of these alexithymia-related deficits are examined during diagnosis, it is possible alexithymia affects scores on instruments such as the ADOS
- The relationships between alexithymia and ADOS scores were investigated in two samples: women with anorexia nervosa, and adolescent twins with high autistic traits/whose twin had high autistic traits
- Parent-reported alexithymia in the adolescent sample was associated with ADOS outcome, sub-scale scores and items on the ADOS that consider socio-emotional processes
- In the anorexia sample, alexithymic women were more likely to meet ADOS diagnostic thresholds, but there were few associations between ADOS items scores or subscale scores and alexithymia

## **Alexithymia and autism diagnostic assessments: evidence from twins at genetic risk of autism and adults with anorexia nervosa**

Alexithymia, a sub-clinical trait characterised by a difficulty identifying and describing one's own emotional states, is elevated in Autism Spectrum Disorder (ASD; hereafter referred to as "autism"), and several other psychiatric and neuropsychiatric conditions such as substance abuse, schizophrenia and eating disorders (Berthoz, Lalanne, Crane, & Hill, 2013; Pinard, Negrete, Annable, & Audet, 1996; van 't Wout, Aleman, Bermond, & Kahn, 2007; Westwood, Kerr-Gaffney, Stahl, & Tchanturia, 2017), as well as in acquired brain damage or neurodegenerative disease (Sturm & Levenson, 2011; Wood & Williams, 2007). Despite evidence that alexithymia may be relevant to understanding socio-emotional difficulties (such as impaired emotion recognition and empathy) across a broad range of clinical conditions, there has been little attempt to investigate the potential impact of alexithymia on diagnostic practices. We focus here on the role of alexithymia in the diagnosis of autism.

Recent studies have argued that alexithymia, rather than autism, is responsible for several socio-emotional difficulties commonly attributed to autism, including emotion recognition, eye contact and empathy (Bird & Cook, 2013; Bird, Press & Richardson, 2011; Grynberg, Luminet, Corneille, Grèzes, & Berthoz, 2010; Oakley, Brewer, Bird, & Catmur, 2016). As yet, the causal relationship between autism and elevated rates of alexithymia are unclear, but autism and alexithymia are conceptually distinct. Although between 40 and 65% of the autistic<sup>1</sup> population are thought to be alexithymic (Berthoz & Hill, 2005; Hill, Berthoz, & Frith, 2004), a figure significantly above the rate of 10% observed in the general population (Franz et al., 2008), alexithymia is neither necessary nor sufficient for a diagnosis

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<sup>1</sup> To respect the wishes of autistic individuals and report the study in line with scientific parlance, we use language preferred by clinical professionals (e.g., 'individuals with autism'), as well as the term 'autistic', a term endorsed by many individuals with ASD (see Kenny et al., 2016).

of autism: there exist autistic individuals with and without alexithymia, and alexithymic individuals who do not meet the diagnostic criteria for autism. Therefore, while certainly autistic individuals are more likely to be alexithymic than non-autistic individuals, alexithymia is not always a characteristic of autism, and it has similarly increased prevalence across other psychiatric populations.

However, the findings regarding the association between alexithymia and socio-emotional difficulties have important implications for diagnostic practice. A key piece of evidence clinicians may draw upon when making a diagnosis of autism is behavioural assessment, most commonly the Autism Diagnostic Observation Schedule (ADOS; Lord, Rutter, DiLavore & Risi, 1999; ADOS-2; Lord et al., 2012). The ADOS is considered by many to be a ‘gold standard’ test for the presence of autism, however, elements of this assessment involve socio-emotional processes known to be associated with alexithymia. Given recent findings that some socio-emotional impairments usually thought to be a feature of autism are attributable to alexithymia, it is important to investigate the impact that alexithymia has on autism diagnostic assessments.

If ADOS scores in part reflect several processes now known to be associated with alexithymia, it could be expected that alexithymic individuals would appear to demonstrate greater autistic symptomatology in ADOS assessments than non-alexithymic individuals. Hypothetically, in the extreme, an individual may receive a diagnosis of autism when in fact they simply have a high degree of alexithymic traits (a false positive). Another possibility is that if scores on ADOS assessments are highly confounded by alexithymia, and ADOS cut-off scores were determined in populations of autistic individuals with a high degree of co-occurring alexithymia, then individuals who have autism but low levels of alexithymia may not meet ADOS cut-offs and therefore not receive a diagnosis (a false negative). While diagnosis should not be based on any single instrument, in practice the diagnosis of autism in

adults, or where a caregiver cannot provide developmental history, may rely heavily on behavioural assessments including the ADOS. As adult diagnosis of autism becomes increasingly common (see Bastiaansen et al., 2011), examining factors that potentially confound behavioural assessments is important. Furthermore, in research, the ADOS is often the only measure administered to confirm diagnosis (Falkmer, Anderson, Falkmer, & Horlin, 2013).

### **Alexithymia and autism symptomatology**

The ADOS comprises four modules, administered dependent upon the verbal ability and age of the individual. Scoring algorithms for use with the latest edition of the ADOS (ADOS-2) yield two subscale scores for Modules 1 to 3: social affect (SA), and restricted and repetitive behaviours (RRB) (Gotham, Risi, Pickles, & Lord, 2007). Published algorithms also allow these same subscale scores to be derived for Module 4 of the ADOS (Hus & Lord, 2014). The symptoms assessed in the ADOS have not been investigated for their association with alexithymia before now. However, based on existing literature, it is possible to predict that alexithymia likely impacts at least a subset of the items included in the ADOS assessment.

### **Alexithymia and the social affect ADOS subscale**

For adolescents and adults with fluent verbal ability, the ADOS includes an item which assesses the ability to communicate one's own emotions. Specifically, individuals are asked to identify times that they felt a given emotion, and to describe what that emotion feels like. This clearly requires an ability that is by definition impaired in alexithymia. Indeed, previous research shows that, when asked similar interview questions to those contained in the ADOS, alexithymic individuals (without autism) produce fewer emotion words, and more null responses ("I don't know"), than individuals with fewer alexithymic traits (Wotschack &

Klann-Delius, 2013). Thus, alexithymic individuals would be expected to show greater impairment on this ADOS item than those without alexithymia.

The ADOS also assesses whether an individual comments on others' emotions or displays empathy. Although empathy deficits are often assumed in autism, research suggests it is alexithymia rather than autism that predicts reduced empathy (Bird et al., 2010; Bird & Cook, 2013). In the general population, alexithymia is inversely related to empathy, and alexithymic individuals report lower scores on empathy questionnaires, and demonstrate atypical neural responses to others' pain compared to non-alexithymic people (Grynberg et al., 2010; Guttman & Laporte, 2002; Moriguchi et al., 2007). Alexithymic individuals also perform worse than typical individuals on tasks requiring the recognition of emotion from faces (Grynberg et al., 2012; Jongen et al., 2014) and voices (Heaton et al., 2012), and alexithymia, rather than autistic traits, accounts for the difficulties in facial and vocal emotion recognition in the autistic population (Cook, Brewer, Shah, & Bird, 2013; Heaton et al., 2012). Such deficits would likely lead to a reduced ability to interpret accurately, and presumably a reduced propensity to comment upon, others' emotions (Coll et al., 2017).

An ADOS assessor will consider unusual eye-contact, and whether appropriate facial expressions are directed to the assessor. Eye-tracking investigations have shown that alexithymia, rather than autism symptom severity, predicts fixation of the eye region in autism (Bird et al., 2011). Production of emotional facial expressions has also been shown to be affected in alexithymic individuals, and reduced emotional expression has been linked to alexithymic traits rather than autistic traits in groups with and without autism (Brewer et al., 2016; McDonald & Prkachin, 1990; Trevisan, Bowering, & Birmingham, 2016). Limited or abnormal facial expressions and eye contact may thus be a feature of alexithymia and contribute to higher scores on these ADOS items.



Individuals' insight into typical social situations (e.g. what it means to be a friend versus an acquaintance, why people might seek romantic relationships) is examined during an ADOS assessment. At present there is limited evidence about alexithymic individuals' social insight, *per se*. Nonetheless, alexithymic individuals experience difficulties in their interpersonal lives, including cold social functioning (Spitzer, Siebel-Jürges, Barnow, Grabe, & Freyberger, 2005; Vanheule, Desmet, Meganck, & Bogaerts, 2007), and reduced satisfaction in intimate relationships (Humphreys, Wood, & Parker, 2009). Alexithymia also impacts social reward (Foulkes, Bird, Gökçen, McCrory, & Viding, 2015) and the ability to draw typical inferences about others' character (Brewer, Collins, Cook, & Bird, 2015), which could underpin some of the interpersonal problems reported by alexithymic individuals. Interpersonal difficulties and abnormal social responses could feasibly reflect and/or contribute to atypical insights into social situations and roles as measured by the ADOS.

### **Alexithymia and the restricted and repetitive behaviours ADOS subscale**

The association between alexithymia and RRBs has received comparably less research interest than social abilities. Nonetheless, alexithymia appears to be related to unusual sensory abilities, both in non-autistic (Kano, Hamaguchi, Itoh, Yanai, & Fukudo, 2007; Nyklíček & Vingerhoets, 2000) and autistic populations (Milosavljevic et al., 2016), and is related to hypersensitivity to touch and pain and self-reported sensory processing sensitivity (Liss, Mailloux, & Erchull, 2008; Nyklíček & Vingerhoets, 2000; Sivik, 1993). Thus, there may be some overlap between the sensory issues reported in autism and those experienced by individuals with alexithymia, but at present there is limited evidence concerning the rest of the RRB scale.

### **Alexithymia and emotional difficulties outside of the autism spectrum – anorexia nervosa**

Alexithymia does not only co-occur with autism, and it is important to consider the impact of alexithymia on autism assessments in groups for which assessment for co-occurring autism is sometimes indicated. One group that may be of particular interest is individuals with eating disorders, and specifically anorexia nervosa (AN).

Research into socio-emotional functioning in AN has reported deficits in recognising emotion from faces (Kucharska-Pietura, Nikolaou, Masiak, & Treasure, 2004; Zonneville-Bendeck, van Goozen, Cohen-Kettenis, van Elburg, & van Engeland, 2002), reduced empathy (Morris, Bramham, Smith, & Tchanturia, 2014), and poor theory of mind (Russell, Schmidt, Doherty, Young, & Tchanturia, 2009; Tchanturia et al., 2004). Poor social-cognitive functioning may be in part the result of generally diminished cognitive function due to starvation; though some social difficulties appear to begin before the onset of eating disorders (and thus before the effects of malnourishment) (Gillberg & Råstam, 1992; Westwood, Lawrence, Fleming, & Tchanturia, 2016).

These deficits have been commented upon by some as being similar to the difficulties seen in autism (Treasure, 2013). Indeed, autism is overrepresented in populations with eating disorders (Huke, Turk, Saeidi, Kent, & Morgan, 2013; Westwood et al., 2017; Westwood et al., 2015; Westwood, Mandy, & Tchanturia, 2017), with some studies reporting a rate of ASD in AN of up to 52.5% (see Westwood & Tchanturia, 2017). Individuals with AN also score higher on self-report measures of autistic traits (Westwood et al., 2015). Thus, the evidence suggests that autistic-like behaviours, indexed by experimental tasks, self-report measures and clinical behavioural assessments, occur in a sizeable proportion of individuals with AN.

Alexithymia may play an important role in the heterogeneity of the emotional problems and autistic-like difficulties observed in AN. Alexithymia has been linked to both

eating disorder symptomatology and social difficulties in anorexia (even after depression, anxiety and state of starvation are accounted for; Brewer et al., 2018; Courty, Godart, Lalanne, & Berthoz, 2015). Emotion recognition deficits may arise in cases of eating disorder where there is co-occurring alexithymia (Brewer, Cook, Cardi, Treasure, & Bird, 2015), and emerging evidence suggests that alexithymia in AN accounts for the autistic symptoms in some of these individuals (Westwood, Ker-Gaffney, et al., 2017). The presence of alexithymia in AN may also have important implications for how to assess autism in this group; indeed, some reports have indicated that autism assessments based on developmental data versus current self-report symptoms yield different findings regarding whether rates of autism are higher than would be expected in AN samples (see Stewart et al. 2017). However, it has also been argued that the association between eating disorders and alexithymia may largely be driven by joint associations with depression (Marchesi, Ossola, Tonna, & De Panfilis, 2014; Montebanocci, Surcinelli, Rossi, & Baldaro, 2011); whether this can also account for the association between AN and autism is unclear.

### **Aims of the current paper**

Understanding the impact of alexithymia on autism diagnostic measures will yield important insights for both research and clinical practice. Considering the relationship between alexithymia and ADOS scores in populations with and without autism, including populations known to have high rates of alexithymia (e.g. AN) would illuminate whether high alexithymic traits increase ADOS scores. This paper thus examined the association between ADOS scores and alexithymia, using previously collected data from two groups: AN patients, and adolescents with autism or with increased likelihood of showing subthreshold autistic traits due to having a co-twin with autism. The extent to which alexithymia predicted ADOS scores was examined, and our predictions were that individuals with alexithymia would: a) be more likely to meet criteria for an autism/ASD diagnosis; b) score higher on the

ADOS than those without alexithymia, and c) score higher on certain ADOS items that tap processes previously linked to alexithymia. To test the latter prediction, in order to avoid an increased risk of Type I error due to multiple comparisons, the decision was made not to examine all items included in the ADOS, but to focus selectively on a subset of items for which previous research predicted an association. These included: a) Comments on others' emotion; b) Unusual eye contact; c) Facial expressions directed to examiner; d) Communication of own affect (recorded for Module 4 participants only); e) Insight into typical social situations.

## **Method**

### **Participants**

Data from two sources were used in the analyses (participant characteristics are summarised in Table 1). The first was a sample of adolescent and adult patients diagnosed with AN, who undertook the ADOS-2 Module 4. All were either day patients or inpatients (and thus not in disease remission phase). For 59 of the participants from this sample, BMI information was available for the day of ADOS assessment: 89.8% of these participants had a BMI of below 18.5 (Mean BMI =15.42, SD =2.12), indicating that many of the sample were underweight at the time of the assessment. None of the sample had a previous diagnosis of autism/ASD and were undergoing the ADOS-2 as part of a research project as opposed to part of standard clinical practice. Comorbidities with other mental conditions were frequent: 18 of the participants had depression, 12 had OCD, and 11 had anxiety. Other comorbidities included ADHD ( $N=1$ ), substance or alcohol abuse ( $N=1$ ), PTSD ( $N=3$ ) and personality disorders ( $N=5$ ). Further details about this sample can be found in Westwood, Mandy and Tchanturia (2017).

The second sample consisted of a set of adolescents with autism and their co-twins. This dataset forms part of the Social Relationship Study (SRS), a sub-study of the Twins Early Development Study (TEDS) (Haworth, Davis, & Plomin, 2013). Those assessed with the ADOS in this study represented children originally in the TEDS sample where one or both twin(s) scored above cut-off on the Childhood Autism Spectrum Test (CAST) (Allison et al., 2007; Scott, Baron-Cohen, Bolton, & Brayne, 2002) or where a parent reported that one or both twin(s) had a diagnosis of ASD. These families then completed the Development and Well-being Assessment (Goodman, Ford, Richards, Gatward, & Meltzer, 2000), and if one or both twin(s) met the criteria for autism, ASD or Asperger's Syndrome, the family were invited to take part in the SRS. Both twins were assessed with the ADOS-G (ADOS- Generic; Lord et al., 2000) and ADI-R (Autism Diagnostic Interview-Revised; Rutter, Le Couteur, & Lord, 2003), and diagnosis confirmed by expert review. Thus, this sample includes adolescents with ASD or subthreshold autistic traits, and their co-twins. Further details about the recruitment and data collection for the SRS population can be found in Colvert et al. (2015). In this analysis, adolescents who were assessed using the ADOS-G Module 3 were selected, to limit the heterogeneity of the sample (as participants who had completed Modules 2 or 1 were likely to have language or intellectual impairment)<sup>2</sup>. After this criteria was applied, along with the requirement that an alexithymia measure had been completed for a participant, there were 147 adolescents identified from the larger SRS sample. We refer to this sample throughout as the SRS sample.

For each respective dataset, ethical approval had been granted by the relevant local ethics board, and informed consent was obtained from adult participants. In the case of

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<sup>2</sup> Although all SRS participants would have needed to be verbally fluent to complete the Module 3 assessment, there are 11 participants whose FSIQ score was below 80. Similarly, for the AN sample, 2 participants had FSIQ scores of below 80. To check whether the inclusion of these individuals altered the pattern of results, the analyses were re-run with these participants removed. The changes to the results were minimal, but are noted where relevant in the Results and Supplementary Materials sections.

participants being minors, parental consent was obtained, and the participants themselves gave their assent to take part.

### **Alexithymia measures**

The Toronto Alexithymia Scale (TAS-20) is a widely used self-report measure of alexithymic traits, which asks respondents to rate to what extent they struggle to identify and communicate their emotions (Parker et al., 1993). It has previously been used in autistic and eating disorder populations, and its reliability and validity for use in adult autistic populations has been confirmed (Berthoz & Hill, 2005; Gaigg, Cornell, & Bird, 2016). Both the SRS sample and AN samples completed the TAS-20; the SRS sample completed a child-friendly version, with a reduced reading age making it more accessible for younger respondents (Rieffe, Oosterveld, & Terwogt, 2006). Both samples used a 5-point Likert scale to respond to the TAS-20. Cronbach's alpha for both samples suggested that the internal reliability of the TAS was sufficient: for the anorexia sample,  $\alpha = 0.79$ , for the SRS sample:  $\alpha = 0.78$ .

The Observer Alexithymia scale (OAS) (Haviland, Louise Warren, & Riggs, 2000) is a parent-report measure of alexithymia, containing 5 subscales, including Distant, Uninsightful, Somatizing, Humorless and Rigid scales. The Uninsightful subscale corresponds best to the traits assessed via the TAS-20 (e.g. "Has trouble finding the right words to describe his or her feelings", "Has strong emotions that he or she cannot explain") and so was the only subscale used. These responses were collected using a 5-point Likert scale. Responses to the Uninsightful subscale were available for the SRS sample, but not the AN sample. Cronbach's alpha suggested that the internal reliability of the OAS was good:  $\alpha = 0.84$ . The correlation between these two measures of alexithymia was significant, but small:  $r_s(144) = .19, p = .009$  (one-tailed).

### **Analytic approach**

Given that the two samples are not comparable on a number of factors (e.g. age, gender), direct comparison of the two groups would be inappropriate. Therefore, we analysed the data from each sample separately. Results for the SRS sample are presented first, followed by the results for the AN sample. For each dataset we examined a) the impact of alexithymia on meeting criteria for autism or ASD, b) the correlations between ADOS scale scores (SA and RRB) and alexithymia measures, and c) associations between alexithymia and scores on individual ADOS items. We also conducted analyses that controlled for the potential confounding influence of depressions and/or anxiety; these analyses are reported in the Supplementary Materials, in addition to analyses considering the effects of age and IQ.

For the SRS dataset, participants were considered for a diagnosis, not just based on ADOS scores, but via clinical consensus (drawing on the ADI and other diagnostic information). Unsurprisingly given the centrality of the ADOS assessment to most diagnostic decisions, there is generally good agreement between the individuals who surpassed threshold on the ADOS and those awarded a diagnosis by the clinical team. Nonetheless, diagnostic decisions were not in 100% agreement: of the 74 participants considered by clinical consensus to have ASD, 12 did not meet the ADOS ASD threshold. Conversely, of the 69 participants that met criteria for ASD on the ADOS, 7 were not considered to have sufficient autistic symptomatology to warrant a diagnosis. These cases represent an interesting test regarding the potential influence of alexithymia on diagnostic outcomes, as it is possible that even if the ADOS scores are inflated in the presence of alexithymia, other information/clinical judgement may mean that such individuals do not receive a diagnosis. We therefore compared these small groups on their alexithymia scores.

## **Results**

### **SRS sample (autistic adolescents and their co-twins)**

### **Does being alexithymic predict meeting diagnostic thresholds on the ADOS?**

We examined whether being alexithymic predicted meeting ASD or autism thresholds on the ADOS. For this sample, the most recent algorithms published in the ADOS-2 were used to determine the groups meeting or not meeting diagnostic cut-offs. Alexithymia as judged by the TAS-20 may be used as a continuous factor, but a standard cut-off of a score of 61 or higher is usually judged to deem a person as “alexithymic”. No such cut-off exists for the OAS. Three logistic regressions were conducted: two using the TAS-20, first as a continuous measure and secondly using the categorical cut-off to examine whether being “alexithymic” or “not alexithymic” predicted meeting the criteria for a diagnosis of autism/ASD. The third regression used the OAS as a predictor.

Neither continuous TAS-20 nor alexithymia group as determined by TAS-20 score was not predictive of meeting ADOS cut-offs. Continuous OAS score was predictive of meeting ASD/autism criteria: Wald  $\chi^2(1) = 17.86, p < .001$  (two-tailed), Nagelkerke R Square = .194, OR = 1.15 (95% CI: 1.08, 1.23).

### **Are alexithymic traits associated with higher ADOS subscale scores?**

The correlations between the two alexithymia measures and the subscales of the ADOS were examined, summarized in Table 2. As the ADOS subscale scores were skewed (because non-autistic twins generally scored 0, or close to 0), one-tailed Spearman’s rank was used<sup>3</sup>.

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<sup>3</sup> Correlations were also conducted using Kendall’s tau as it is possible that by including a moderate number of individuals who are not autistic, and who score 0 or close to 0 on the ADOS, we would have a high number of tied ranks which can impact upon the accuracy of Spearman’s Rank coefficients and p-values. Comparing the correlations for both forms of non-parametric correlation, there were very minimal differences in coefficients (in no instances were changes in correlations greater than 0.15) and no effect on patterns of significance.



No significant correlations were found for the TAS-20 (see Table 2). The OAS was moderately correlated with both the SA ( $r_s(137) = .40, p < .001$ ) and RRB ( $r_s(137) = .25, p = .003$ ) scales.

### **Are alexithymic traits associated with performance on individual ADOS items?**

The association between alexithymia and scores on individual ADOS items was examined using ordinal regression, in which the scores for items in the ADOS (scored between 0 and 3) were the dependent variables, and alexithymia scores the independent variable. Eye contact was examined using a logistic regression, as scoring this item only allows examiners to rate participants as either “0” or “2”. With the exception of the TAS regression for social insight, all ordinal regressions met the assumption of proportional odds. For this exception, follow-up binomial logistic regression was conducted, with scores dichotomized.

For the TAS-20 regressions, the only ADOS item score that was significantly predicted was social insight (see Table 3)<sup>4</sup>. However, because the ordinal regression for social insight did not meet the assumption of proportional odds, scores on this item were dichotomized to examine the predictive effect of TAS-20 scores on: scores of 0 versus 1 or more; scores of 0 or 1 versus 2 or more; and scores of 0-2 versus 3. TAS-20 scores were only significant when predicting whether a score of 0 or 1 versus 2 or more was given: Wald  $\chi^2 = 9.56, p = .001$  (one-tailed), OR = 1.07 (95% CI: 1.03, 1.12).

Regarding analyses with the OAS however, all items were significantly predicted by OAS scores (summarized in Table 4).

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<sup>4</sup> When the 11 participants with low FSIQ were removed, standardised TAS score was examined with ordinal regression as the assumption of proportional odds was no longer violated: standardised TAS not a significant predictor of social insight item scores for this reduced sample. All other results remained the same.

Analyses were repeated controlling for age, IQ, and then anxiety / depression symptoms; results were not substantially changed (see Supplementary Materials).

### **Alexithymia and discrepant diagnostic decisions**

We compared cases where the diagnosis according to the ADOS and the diagnosis according to clinical judgement did not agree. Individuals who scored at or above threshold on the ADOS but who were not considered by the clinical team to have autism had significantly lower levels of alexithymia according to the OAS (Mean = 19.00,  $SD = 5.29$ ) than those who did not meet the ADOS threshold scores but were considered by the diagnostic team to warrant a diagnosis (Mean = 25.36,  $SD = 4.59$ ):  $t(16) = -2.71, p = .016$  (two-tailed). Differences in the TAS were not significant, though showed the same pattern.

### **AN sample (anorexic adults)**

#### **Does being alexithymic predict meeting diagnostic thresholds on the ADOS?**

We considered whether, in the AN sample, continuous TAS-20 score, or meeting or surpassing the cut-off of 61 on the TAS-20 was predictive of meeting ASD or autism criteria on the ADOS (using the algorithm detailed by Hus and Lord, 2014), using a logistic regression. Continuous TAS-20 score was not predictive of meeting ASD/autism criteria. Being above the TAS-20 threshold for alexithymia was predictive of meeting ADOS criteria: Wald  $\chi^2 = 4.20, p = .04$  (two-tailed), Nagelkerke R Square = .06, OR = 2.67 (95% CI: 1.04, 6.81).

#### **Are alexithymic traits associated with higher ADOS subscale scores?**

The correlations between alexithymia and the subscales of the ADOS (calculated using the method outlined in Hus and Lord, 2014) were examined, summarized in Table 5. As for the SRS sample, ADOS subscale scores were skewed and so (one-tailed) Spearman's rank was used. The correlations between the ADOS and alexithymia measures and depression

were also considered (see Supplementary Materials). TAS-20 score correlated significantly with SA, though this association was small ( $r_s(94) = .19, p = .031$ ) and was no longer significant when controlling for depression (Supplementary Materials).

### **Are alexithymic traits associated with performance on individual ADOS items?**

As with the SRS sample, the association between alexithymia and scores on individual ADOS items was examined using ordinal regression. All ordinal regressions met the assumption of proportional odds.

Items' relationships with TAS-20 scores are summarized in Table 6. Alexithymia was not predictive of scores on items measuring eye contact (examined using logistic regression), facial expression, comments on own emotions, or comments on others' emotions/empathy item. TAS-20 scores predicted scores on insight into social relationships, and this remained significant when controlling for depression (see Supplementary Materials).<sup>5</sup>

## **Discussion**

This paper provides a first examination of the relationship between alexithymia, a deficit in recognizing and communicating one's affective states, and ratings on a standardised diagnostic instrument for autism. This relationship was examined in a sample of adolescents who were autistic or at genetic risk for autism, and a sample of patients with anorexia, a condition in which alexithymia is also prevalent and in which there are increased rates of autism. Different patterns of results emerged for the two groups. For the autistic adolescents and their co-twins, associations between parent-reported alexithymia and ADOS measures were found: parent-reported alexithymia was associated with increased scores on the SA and RRB subscales, and scores on pre-selected ADOS items (though the effect sizes were small).

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<sup>5</sup> With the 2 participants who had low FSIQ scores removed, TAS score was a significant predictor for the facial expressions item.

No associations were found with child-reported alexithymia. For the AN group, self-reported alexithymia correlated with the SA subscale score, and predicted scores on social insight. Being above threshold on self-reported alexithymia increased the likelihood of meeting diagnostic cut-offs, which suggests that co-occurring alexithymia may be a potential explanation for the high proportion of patients with AN who exhibit symptoms of ASD.

Two features of the results complicate the relationship between alexithymia and ADOS scores; firstly, the differential relationships between ADOS scores and parent- and child-reported alexithymia in the SRS sample. Although the OAS and the ADOS are both observer-rated measures, parents complete the OAS while trained researchers administer and score the ADOS. Thus, it seems unlikely that the positive findings for the OAS but not the TAS for the SRS sample are due to an effect of observer bias. The differential predictive ability of the self- and parent-report alexithymia are in keeping with other reports suggesting that self-reported alexithymia measures may be problematic for children. Indeed, only a small correlation between the OAS and TAS-20 was found. Similarly, Griffin et al (2016) did not find a significant correlation between their child self-report and parent-report measures of alexithymia. This could indicate problems in self-reporting alexithymia in developing populations, given that parent-reported alexithymia showed almost all of the predicted relationships while self-report did not. Furthermore, the SRS sample reported a fairly low rate of alexithymia (just 15% above the standard TAS cut-off); even if we just consider the proportion of the sample who met the criteria for an ASD/autism diagnosis, only 13% surpassed the threshold on the TAS. This is much lower than previous estimates of the rate of alexithymia in autism (48% according to Hill, Berthoz, & Frith, 2004). The low rate of alexithymia in this sample might also be reflective of the discrepancy between parent and child reports of alexithymia, with adolescents potentially underreporting their alexithymic difficulties. However previous estimates of the prevalence of alexithymia in autism were

predominantly in adults, and the threshold typically used to determine high alexithymic traits was not developed with younger samples in mind.

Indeed, at present we cannot assume that parents are more accurate reporters of their children's alexithymia than children themselves; as alexithymia taps into private processes regarding one's own emotions, the weak correlation between parent and children reports may reflect limited insight on the part of the parents. The shared association between the ADOS and parent-report scores could reflect children's difficulties with expressing their emotions, which represents one part, but not the whole, of the alexithymic concept. The discrepancy between self and parent-rated alexithymia in children (both typically developing and those with developmental disorders) warrants further study, given the very different conclusions that would have been reached in the current study had we only had either child or parent reports for the SRS sample.

The second issue is the different pattern of findings in the SRS and AN samples. The AN group were included to examine the relationship between alexithymia and ADOS scores in a second population in which alexithymia and autistic symptoms are prevalent and where it is of benefit to explore the extent to which alexithymia may bias autism assessment, as there is ongoing discussion about whether there is an increase of comorbid autism in AN, or whether increased autistic symptoms arise in this group for other reasons (Tchanturia et al., 2013). However, though alexithymia predicted whether women in the AN group would surpass diagnostic thresholds on the ADOS, limited associations between ADOS subscales and items and alexithymia were found for the AN group. As opposed to a difference in diagnostic group, this may be a reflection of the different alexithymia measures that were available for either sample. Observer report scores were not available for the AN group, and as noted above few associations were found between the self-report TAS-20 and ADOS scores for the SRS sample. Previous studies have found significant but modest correlations

between self- and observer-reported alexithymia in eating disorder populations (Berthoz, Perdureau, Godart, Corcos, & Haviland, 2007), indicating that a large amount of variance in the OAS does not overlap with the TAS-20. The inclusion of observer-reported alexithymia measures in future studies would help to clarify whether issues with self-report affected the associations reported in the current study.

Several potential reasons for why few associations emerged between self-reported alexithymia and the ADOS in the AN sample can nonetheless be ruled out. First, as a group, the anorexia patients rated themselves as highly alexithymic, with the majority of patients surpassing the TAS-20 cut-off. Thus, it seems unlikely that few associations emerged because anorexic patients were not aware of their emotional difficulties. However, it is possible that scores may have been inflated by low self-esteem which may produce negative biases on any self-report measure relating to impaired functioning. Indeed, this may be why only using the TAS-20 cut-off to categorize AN patients into “alexithymic” and “non-alexithymic” was predictive of ADOS criteria being met. Although controlling for depression may account for some of this potential effect (see additional analyses included in the Supplementary Materials), depression is an imperfect measure of self-esteem.

In addition, all of the AN group were inpatients, while the SRS sample included some individuals who, while at higher genetic risk of autism symptoms due to their twin being high in autistic symptoms, were not autistic, nor suffering from any psychiatric condition. Arguably this may be expected to lead to an increased range of ADOS scores in the SRS sample, which may have allowed associations to emerge for this group only. However, the range and standard deviations of ADOS scores was similar between the two samples (although it should be noted that they undertook different ADOS modules). Increased range of ADOS scores therefore cannot explain why greater associations emerged for the SRS

sample, although it should be noted that the SRS sample represents a more heterogeneous sample in other respects.

Indeed, differences in results between these two groups could be due to differences in gender and age: the AN group was exclusively female, and included adults as well as adolescents, while the SRS sample included predominantly male adolescents aged up to 16 years. Both age and gender have been shown to be related to levels of alexithymic traits (Honkalampi et al., 2009; Joukamaa et al., 2007; Levant, Hall, Williams, & Hasan, 2009; Murphy, Brewer, Catmur & Bird, 2017). When age was partialled out of the correlations between ADOS scale scores and alexithymia there were no changes to the results (see Supplementary Materials). Proper exploration of the impact of gender however was more problematic in the current dataset: for the SRS sample (of which 43 were female), being female was highly confounded by also being under the diagnostic threshold for autism/ASD. This meant that by controlling for gender the very relationships with autism symptomatology were essentially removed. It has been argued that women are less likely to meet the diagnostic threshold, and face under-diagnosis (Bargiela, Steward, & Mandy, 2016; though see Tillmann et al., 2018). Potentially, the current data are affected by these issues. Future studies should ideally match samples on age and gender to differentiate the impact of diagnostic group and sample demographics.

Another limitation of the current study is that we did not have clinical diagnoses available for the AN group that included alongside observational measures a developmental history; this would have helped highlight which of our sample likely had comorbid autism, as opposed to increased autistic symptoms due to alexithymia. Ideally, autism diagnoses should rely not only on observational measures such as the ADOS but also a developmental history (usually with a parent). Our study is reflective of many others in which the ADOS is only measure used to for autism diagnosis (Falkmer et al., 2013).

However, we also compared small groups of the SRS participant group for whom the clinical judgment and ADOS threshold-based diagnoses were in disagreement. We found that actually the participants who scored below threshold on the ADOS but were deemed by clinical judgement to meet the criteria for autism were more alexithymic than those who met the ADOS threshold but were not considered autistic by the clinicians. This finding provides counter evidence to our suggestion that alexithymia could increase rates of false positives on ADOS assessments. Of course, these results are based on data from a small sub-sample of the larger SRS dataset, and while these results are useful for research studies relying on the ADOS, this sample does not represent a population drawn from a clinical setting; rather, these participants were included in the SRS sample following research-led screening for ASD symptoms.

One point that must be raised here is the issue of causality: the data analysed here show a relationship between alexithymia and autism assessment scores. We interpret these relationships as alexithymia leading to increased scores, but we cannot rule out that individuals with more severe autism symptoms display higher levels of alexithymia. Indeed, perhaps the AN patients who score above ADOS thresholds have undiagnosed autism, and their autism increases their risk of high alexithymic traits. The predictions as to which ADOS items would be likely to be impacted by alexithymia were based on studies which directly contrasted the impact of autism and alexithymia. These studies found that alexithymia, not autism, best explained socio-affective impairment, and given these results, we suggest here that it is likely that alexithymia causes the increase in ADOS scores reported here. However, the field is currently lacking strong evidence for direction of causality, which requires longitudinal studies. Indeed, in order to conduct this ambitious programme of research, it will be necessary to develop measures of alexithymia, or postulated precursors to alexithymia, for use with quite young children. Our current data suggest that the correlation between parent



and self-reports of alexithymia is weak, so alternative methods of assessment, such as observational measures or experimental tasks, may be required. This will pose a major challenge to collecting alexithymia data longitudinally in order to explore the developmental relationships with emerging psychopathology.

## Implications

Although this paper has focused on the role of alexithymia in the ADOS assessment specifically, other assessment tools used to diagnose autism may also show associations with alexithymia. Co-occurring alexithymia only occurs in approximately 50% of the autistic population, yet the symptoms used to consider whether or not an individual meets the diagnostic criteria for an autism diagnosis are overlapping with alexithymia. Indeed, this is arguably not surprising: if alexithymia is present in half of individuals with autism, the inclusion of items that tap into alexithymia may contribute to making instruments like the ADOS better at discriminating autistic individuals from controls. Given that alexithymia may represent an important factor on which autistic individuals are heterogeneous, the frequency of symptoms such as difficulty with social insight, difficulty empathizing, flat affect and atypical eye contact in autism in the *absence* of alexithymia warrants further study to ascertain to what extent they can arise in autism independently of alexithymia.

More broadly, alexithymia is a risk factor for a number of other mental health conditions, and has recently been shown to mediate between autism symptoms and anxiety (Maisel et al., 2016). Knowing whether an individual presents with alexithymia may guide clinicians in their decisions about what other support a recently diagnosed individual with autism might need. Being able to disentangle symptoms of autism from characteristics of alexithymia is therefore an important part of the diagnostic process. The results also highlight

the need to assess the impact of alexithymia in other groups, and for conditions other than autism.

## **Summary**

This paper is the first to examine the role of alexithymia in ADOS assessments. Using data from autistic adolescents and their co-twins, and an anorexia nervosa population, we examined the extent to which alexithymia predicted meeting the diagnostic threshold for autism, whether alexithymia correlated with ADOS scores, and whether alexithymia predicted individual item scores. Parent-reported alexithymia predicted ADOS scores at all levels of analysis in the group of autistic adolescents and their co-twins. Self-reported alexithymia was not predictive of ADOS scores in this group, and our results indicate discrepancy between parent and child reports of alexithymia. Few associations arose for the AN group, although self-reported alexithymia did predict surpassing diagnostic thresholds. These findings have implications for research practices that rely on the ADOS to establish diagnosis in research participants, and suggest the need for more controlled investigations into the impact of alexithymia on autism diagnostic practices.

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