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Modeling the Cognitive Mechanisms Linking Autism Symptoms and Anxiety in Adults

Max E. Maisel, Kevin G. Stephenson, Mikle South

Brigham Young University

Jacqui Rodgers and Mark H. Freeston

University of Newcastle

Sebastian Gaigg

City University London

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Corresponding author information:

Mikle South, PhD Brigham Young University 245 TLRB, Provo, Utah, USA 84602 email: <u>south@byu.edu</u>; phone: 801-422-4058 Modeling the Cognitive Mechanisms Linking Autism Symptoms and Anxiety in Adults
Abstract

Emotional acceptance, alexithymia, and intolerance of uncertainty (IU) contribute to anxiety disorders in neurotypical populations. Their association with anxiety in people diagnosed with autism spectrum disorder (ASD) has not been studied. We aimed to model the contributions of these constructs on the relationship between dimensional measures of autism and anxiety. Participants were 151 adults recruited from two sites, including those diagnosed with ASD (n=76) and a matched comparison group (n=75). All participants completed a battery of questionnaires measuring core autism symptoms, anxiety, emotional acceptance, alexithymia, and intolerance of uncertainty. Structural equation modeling with mediation was used to examine directional relationships among these variables. Autism symptoms directly predicted less emotional acceptance and increased alexithymia and IU. Alexithymia and acceptance were shown to explain 64% of the effect between autism symptom severity and anxiety level. This suggests that people with ASD experience increased levels of anxiety because they are more likely to react aversively to their emotional experiences, while lacking the ability to identify and understand their emotions. Developing and implementing mindfulness-based interventions aimed at assuaging alexithymia and IU, while increasing emotional acceptance, may be especially helpful in treating anxiety in ASD.

Keywords: autism, anxiety, emotional acceptance, alexithymia, intolerance of uncertainty

General Scientific Summary: This study suggests that people with ASD experience increased levels of anxiety because they are more likely to react aversively to their emotional experiences, while lacking the ability to identify and understand their emotions. This suggests that the

development and utilization of interventions targeting these constructs may be especially helpful in the treatment of anxiety disorders for people diagnosed with ASD.

Introduction

It is estimated that around 50% of individuals diagnosed with autism spectrum disorder (ASD) also demonstrate significant levels of anxiety that causes individuals much dysfunction in their day-to-day functioning (Bejerot, Eriksson, & Mörtberg, 2014; Lugnegård, Hallerbäck, & Gillberg, 2011; Luke, Clare, Ring, Redley, & Watson, 2012; South, Newton, & Chamberlain, 2012). Anxiety is closely linked to poor quality of life (van Steensel, Bögels, & Dirksen, 2012) and thought to compound the core clinical symptoms of ASD because of a bi-directional link between social-cognitive skills and anxiety (White, Oswald, Ollendick, & Scahill, 2009). Developing effective interventions for anxiety is therefore a research priority in ASD and the present paper contributes to this issue by developing a theory-driven model about the cognitive mechanisms that link ASD symptoms to anxiety.

Recent studies regarding the underlying mechanisms of anxiety in ASD have investigated the relevance of constructs that are known to play a role in the etiology of anxiety in non-ASD populations, including *intolerance of uncertainty* (IU), *alexithymia* and *emotional acceptance*. IU is a transdiagnostic risk factor for the development of a broad range of anxiety disorders (Carleton, 2012; Carleton et al., 2012; McEvoy & Mahoney, 2012) and in studies of children diagnosed with ASD, IU has been shown to mediate the relationship between ASD symptoms and anxiety (Boulter, Freeston, South, & Rodgers, 2014). IU and anxiety together also appear to account for the co-occurrence of sensory processing difficulties and repetitive behaviors in ASD (Wigham, Rodgers, South, McConachie, & Freeston, 2014) and a potentiated startle study has suggested a role for IU in the physiological arousal responses that are associated with anxiety (Chamberlain et al., 2013). Alexithymia is formally defined as a difficulty in identifying and describing internal emotional states (Cameron, Ogrodniczuk, & Hadjipavlou, 2014; Nemiah, Freyberger, & Stifneos, 1976) and in non-ASD samples it is well known to relate strongly to symptoms of generalized anxiety disorder, social anxiety, and depression (Grabe, Spitzer, & Freyberger, 2004; Karukivi et al., 2010; Mennin, Holaway, Fresco, Moore, & Heimberg, 2007; Mennin & Fresco, 2009; O'Toole, Hougaard, & Mennin, 2013). Its role in the etiology of anxiety in ASD has not been formally assessed, but its high prevalence in ASD, together with evidence linking alexithymia with many of the social-cognitive impairments of the disorder (Bernhardt et al., 2014; Bird & Cook, 2013; Bird et al., 2010) leads to the prediction that alexithymia also plays a significant role in mediating the association between ASD symptoms and anxiety.

Finally, the third factor suspected to play a role in anxiety in ASD is impaired psychological mindedness, especially *emotional acceptance*, which describes the ability to allow one's internal experience to be as it is and not to push feelings away (Harris, 2009). In non-ASD populations poor emotional acceptance is well-known to be a contributor to anxiety (Baer, Smith, Hopkins, Krietemeyer, & Toney, 2006; Campbell-Sills, Barlow, Brown, & Hofmann, 2006; Douglas S. Mennin, McLaughlin, & Flanagan, 2009). It is one of the primary mechanisms of action targeted by mindfulness based therapies that have proven very successful in alleviating anxiety (Dan-Glauser & Gross, 2015; Kohl, Rief, & Glombiewski, 2012; Roemer, Orsillo, & Salters-Pedneault, 2008). Four small studies of mindfulness/acceptance-based psychotherapies have shown some reductions in anxiety in ASD samples of adults or adolescents (de Bruin, Blom, Smit, van Steensel, & Bögels, 2014; Kiep, Spek, & Hoeben, 2014; Pahnke, Lundgren, Hursti, & Hirvikoski, 2014; Spek, van Ham, & Nyklíček, 2013), suggesting that impairments in emotional acceptance may indeed be a factor mediating anxiety in ASD. Ongoing work in our lab has shown that adults diagnosed with ASD report the largest level of impairment on the mindfulness facet of "nonreactivity to inner experience." Extant research in neurotypical samples shows that when people react aversively to thoughts and feelings, as opposed to gentle acceptance, they are much more likely to experience distress and anxiety (Mennin et al., 2007; Mennin, McLaughlin, & Flanagan, 2009).

Although current research supports a role for IU, alexithymia, and emotional acceptance as mechanisms mediating the association between ASD symptoms and anxiety, the relative importance of these constructs has never been formally modeled. The aim of the current study, therefore, was to model the interactions of IU, alexithymia and emotional acceptance for explaining the relationship between autism symptoms and anxiety. We expected to extend evidence of a mediating role of IU between autism and anxiety symptoms to adult samples and hypothesized that diminished capacity for emotional introspection (i.e., alexithymia) and emotional acceptance would explain additional variance in the relationship between ASD symptoms and anxiety. The focus on adult samples was an important feature of the current study and is motivated by the recognition that the needs of adults with ASD have been relatively neglected in the literature, resulting in a dearth of autism-specific support mechanisms for individuals with ASD after they leave school (Binnie & Blainey, 2013; Spain, Sin, Chalder, Murphy, & Happé, 2015; Vasa et al., 2014). Another important aspect of this study was the use of dimensional measures of both autism symptoms and anxiety in ASD and neurotypical samples, with the aim to describe these relationships generally in typical as well as ASD adults.

Method

Sample

All procedures were approved by local ethics committees and participants signed informed consent forms. Basic demographic information is shown in Table 1. Participants for 6

this study included 76 cognitively able adults with ASD and 75 neurotypical controls (CON group) with similar age and IQ. While we refer to the participants in the sample as adults, it is important to note that we included data from 4 ASD participants and 2 CON participants who were 17 years old at the time of data collection. Participants were recruited from two separate sites: City University London (London, UK; n=77) and Brigham Young University (Utah, USA; n=74). Participants from both sites were recruited from existing databases of volunteer research participants. Moreover, to assist in the recruitment of neurotypical control participants, the US site recruited participants from a university-based volunteer research program offering class credit.

The only noticeable between-sites difference was older age for the UK sample. All ASD participants at the US site and many at the UK site (28 out of 40) completed the ADOS-G (Lord et al., 2000) administered by a researcher trained to research reliability. All participants who received an ADOS met diagnostic criteria for ASD. While 12 ASD participants did not formally complete an ADOS in the UK site, all of the ASD participants recruited there had medical records from qualified clinicians within the UKs' National Health Service confirming that a diagnosis of ASD was established according to the DSM-IV criteria at the time the diagnosis was made.

Participants in both groups were excluded from the study if they had a full scale IQ score below 75. At the US site IQ was assessed with the Wechsler Abbreviated Intelligence Scale, 2nd Edition (WAIS-II; Wechsler, 2011), and at the UK site with the Wechsler Adult Intelligence Scale, 3rd Edition (WAIS-III; Wechsler, 1999) or the Wechsler Adult Intelligence Scale-Revised (WAIS-R; Wechsler, 1981). Three ASD participants were excluded due to low IQ, as there were concerns that they would have difficulty completing the questionnaires accurately. In addition to an IQ below 75, potential participants from the control group were excluded if they self-reported any psychiatric and/or neurological illness or if they scored above the cut-off (i.e. 32) on an autism screening measure called the Autism Spectrum Quotient (AQ; Baron-Cohen, Wheelwright, Skinner, Martin, & Clubley, 2001). One neurotypical participant scored at the cutoff of 32 on the AQ. This participant was not excluded, as the AQ was not designed to be diagnostic but rather a dimensional measure of ASD traits.

Measures

All of the measures below have been shown to have good- to excellent psychometric properties including reliability and validity.

<u>AQ</u>: The Autism Spectrum Quotient (Baron-Cohen et al., 2001) is a 50–item questionnaire that asks participants to indicate the extent to which they can identify with statements describing behaviors and attitudes that reflect core facets of the ASD phenotype. It has been used as a dimensional measure of ASD-symptoms in clinical populations and in the general public, and is demonstrated to be sensitive to subclinical ASD symptoms (Bishop et al., 2004).

<u>IUS-12</u>: The Intolerance of Uncertainty Scale-12 (Carleton, Norton, & Asmundson, 2007) is a 12-item measure and includes questions about the unknown regarding one's prospective anxiety (e.g. "Unforeseen events upset me greatly") and inhibitory anxiety (e.g. "Uncertainty keeps me from living a full life"). While these two subdomains can be scored separately, only the total score was used in the current study. The IUS-12 has been successfully used to show an association between intolerance of uncertainty and anxiety in children and adolescents diagnosed with ASD (Boulter et al., 2014; Chamberlain et al., 2013).

<u>TAS-20</u>: The Toronto Alexithymia Scale-20 includes three subscales: identifying feelings, difficulty describing feelings to others, and an externally oriented way of thinking (Bagby, Parker, & Taylor, 1994). While each scale has good internal consistency, our analyses focused on the first two sub-scales because of past research suggesting a weak relationship between externally oriented thinking and anxiety compared to a strong relationship between anxiety and difficulties identifying and describing feelings (Berthoz, Consoli, Perez-Diaz, & Jouvent, 1999; Liss, Mailloux, & Erchull, 2008). The TAS-20 has been used to show emotion recognition difficulties in samples with ASD (Berthoz, Lalanne, Crane, & Hill, 2013; Cook, Brewer, Shah, & Bird, 2013)

<u>FFMQ-Nonreactivity</u>: The Five Facet Mindfulness Questionnaire is widely used in the mindfulness literature to assess the empirically-derived and conceptually-distinct facets of mindfulness (Baer et al., 2008, 2006). As noted above, we have found largest deficits in ASD for the Nonreactivity factor. The developers of the scale described the Nonreactivity factor as measuring the ability of allowing inner experience to come and go without getting caught up or reacting to them and noted that this facet can help operationalize acceptance of internal experience (Baer et al., 2008, 2006). Moreover, the nonreactivity to inner experience facet has been shown to have convergent validity with a number of other acceptance-related measures (Fledderus, Oude Voshaar, Ten Klooster, & Bohlmeijer, 2012; Hoffmann, Halsboe, Eilenberg, Jensen, & Frostholm, 2014; Veehof, Klooster, Taal, Westerhof, & Bohlmeijer, 2011). Ongoing research in our lab suggests a moderate to moderately strong negative relationship between the FFMQ-nonreactivity facet and anxiety for people with ASD.

<u>STAI-T Form-Y:</u> The 20-item trait anxiety form of the State Trait Anxiety Inventory Form-Y (Spielberger, Gorusch, Lushene, Vagg, & Jacobs, 1983) focuses on how a person generally tend to feel everyday rather than at the present moment and is one of the most frequently used research measures of anxiety.

<u>PSWQ</u>: The Penn State Worry Questionnaire is a 16-item questionnaire that measures the severity of worry thoughts in both clinical and non-clinical populations (Meyer, Miller, Metzger, & Borkovec, 1990). It has been shown to have good discriminant validity and convergent validity, to be unrelated to other measures of depression (measured by the Beck Depression Inventory) and general anxiety (measured by the STAI), and to be sensitive to cognitive orientated treatment (Dear et al., 2011; Meyer et al., 1990).

<u>FNE-Brief</u>: The brief version of the Fear of Negative Evaluation Scale (FNE) contains 12 items intended to measure social anxiety regarding apprehension of being judged and evaluated undesirably by others (Leary, 1983).

SEM Analysis

Raw scores of measures were utilized for all analyses except for IQ scores, which were standardized. Prior to analyses, variables were examined for missing data. All variables were missing less than 10% of data except for the TAS-20, which was missing 11%. This is considered to be in the acceptable limits of missing data, not likely to bias the results (Bennett, 2001). Further, missingness was determined to be missing at random (MAR) by correlating missing data with all outcome measures. Moreover, both SEM and mediation analyses utilized a full information maximum likelihood approach which maximized effective sample size and power and is considered superior to other approaches to handling missing data (Dong & Peng, 2013; Enders & Bandalos, 2001).

Next, the normality of all variables was inspected. Three variables with non-normal distributions (STAI-T, TAS-Describe, and IUS-12) were log transformed (Tukey, 1977) and

multivariate normality was shown to be satisfactory across multiple tests (Doornik & Hansen, 2008; Henze & Zirkler, 1990; Mardia, 1970). Separate analyses using untransformed variables show similar results but the transformed variables are reported here.

Structural equation modeling is used to test theoretical models based on explicitly-stated concepts. As noted above, the structural equation model (SEM) combined ASD and CON groups together in the model because we wished to take into account the dimensional nature of ASD symptomology (Austin, 2005; Ingersoll & Wainer, 2014; Kamp-Becker et al., 2010). Anxiety was represented as a latent variable comprising scores from the STAI-T, FNE, and PSWQ surveys. Alexithymia was also represented as a latent variable including the TAS-Identify and TAS-Describe subscales. SEM and SEM-based mediation analyses (Shrout & Bolger, 2002) were carried out with STATA version 13 while the individual effects mediation analyses were conducted using Rmediation software (Tofighi & MacKinnon, 2011).

Results

Table 2 shows that the ASD group self-reported overall higher scores for all symptom measures. The UK site reported higher autism symptom scores and trait-anxiety scores than the US site. We next examined patterns of simple correlations between measures (see Table 3). As expected, there are moderate- to strong associations among dimensional autism symptoms, IU, alexithymia, and mindfulness. These patterns were consistent when broken down by test site as well as diagnostic groups.

Structural Equation Modeling

Figure 1 models the predictive roles that IU, alexithymia, and emotional acceptance play in anxiety for people with autism symptoms. Overall fit for this model was shown to be excellent χ^2 (13) = 13.89, *p* =.381; RMSEA = 0.021; CFI = .998, TLI = .997. This model provides evidence for the hypothesis that alexithymia, emotional acceptance, and IU all play a significant role in the relation between anxiety and scores on dimensional characteristics related to autism. First, all pathway loadings were in the expected directions. Autism core symptoms directly predicted less emotional acceptance ($\beta = -.39$, p < .001), more alexithymia ($\beta = .69$, p < .001), and more IU ($\beta = .45$, p < .001). Next, this model shows that autism core symptoms did not independently predict anxiety when controlling for emotional acceptance, alexithymia, and IU (B = .12, p > .05). However, both acceptance ($\beta = ..45$, p < .001) and alexithymia ($\beta = .32$, p < .01) were shown to be moderately strong predictors of anxiety when controlling for autism symptoms, and alexithymia was furthermore also a significant predictor of IU ($\beta = .31, p < .01$). Conceptually, if people have a difficult time gaining insight to their internal states, they will be prevented from accessing important information from their emotional states about the world around them, leading them to feel more uncertain about the future (Greenberg, 2002). The error terms of alexithymia and emotional acceptance were also correlated in this model, suggesting an additional factor, not included in this model, which drives unaccounted for variance between mindfulness and alexithymia.

Mediation Analyses

In accordance with Shrout & Bolger (2002), two mediation analyses were conducted through SEM. The first aimed to replicate previous findings from children diagnosed with ASD about how well IU by itself (without emotional acceptance or alexithymia contributing variation) mediated the relationship between autism core symptoms and anxiety (see Figure 2) (Boulter et al., 2014). The second, then examined the relative contributions of all three constructs.

First, when examining IU in a model excluding emotional acceptance and alexithymia, IU was a significant predictor of greater anxiety ($\beta = .33$, *p* <.01) and model fit remained

excellent, $\chi^2(3) = 2.60$, p = .46; RMSEA = 0.00; CFI = 1.00, TFI= 1.00. Mediation analysis showed that when the variance related to IU was constrained to 0, autism symptoms served as a very strong direct predictor of anxiety ($\beta = .62$, p < .001). However, when IU was included as a mediator for anxiety, autism core symptoms became a much weaker, though still significant, predictor of anxiety ($\beta = .40$, p < .001). These results support previous findings that IU is an important mechanism underlying anxiety in adults with ASD.

The second mediation analysis added emotional acceptance and alexithymia as mediators of the relationship between autism symptoms and anxiety (see Figure 3). In this model, autism symptoms no longer predicted a significant proportion of the variance in anxiety ($\beta = .12, p >$.05), showing that the relationship between autism symptoms and anxiety is mediated almost entirely by emotional acceptance, alexithymia, and IU. Moreover, whilst autism symptoms continued to predict IU in this mediation model, IU no longer predicted anxiety ($\beta = .15, p >$.05), suggesting that emotional acceptance and alexithymia on their own, account for much of the relationship between autism symptoms and anxiety.

To get a better understanding of how much variance each construct independently explained in the mediation model, we determined the ratio of indirect effect to direct effect for each construct separately (See Table 4). We calculated the direct effect by removing the variance from all three variables at the same time. Emotional acceptance independently explained 28% of the effect of autism core symptoms on anxiety, and alexithymia explained 36%. When emotional acceptance and alexithymia were included in the model, IU no longer served as a significant mediator for autism symptoms leading to anxiety.

Categorical versus Dimensional Data

There is a clear mandate in current mental health research to view data in dimensional terms wherever possible (Brown & Barlow, 2005; Kamp-Becker et al., 2010). Nonetheless this may overlook important extremes of behavior more associated with categorical diagnostic definitions. In our data, the combined sample was adequately normally distributed, but did show between-groups separation in that the ASD group scored higher on all dimensional measures of autism symptoms and anxiety. This creates the possibility of a Simpson's paradox-type problem in which variance is inflated or interpretations may be altered by the confluence of two distinct samples. This doesn't seem to be generally the case in this study but to explicitly address the possibilities we have included separate SEM analyses for each group in the supplemental data. Both groups showed overall similar pathway directions and values, supporting our position for a dimensional model. However, there were two notable differences between groups. First, for the ASD group, dimensional autism symptoms more strongly predicted less emotional acceptance. Second, for the control group, dimensional autism symptoms more strongly related to intolerance of uncertainty than for the ASD group. However, for both groups alexithymia and emotional acceptance directly predicted anxiety, while intolerance of uncertainty did not.

Discussion

Intolerance of Uncertainty

The first objective of this study was to replicate previous research showing that IU not only predicted greater anxiety in people with ASD, but that it also served as a mediator (Boulter et al., 2014). When IU was entered as the only explanatory variable in the model, both autism symptoms and IU directly predicted increased anxiety, and autism symptoms directly predicted IU. Moreover, IU partially mediated the relationship between autism symptoms and anxiety, explaining 36% of the total effect. This finding supports previous research and suggests that IU is an important factor in explaining the anxiety people with ASD often feel.

Importantly, however, the constructs of emotional acceptance and alexithymia took up much of the predictive power of IU while both autism symptoms and alexithymia predicted IU directly. Recent findings that impaired interoceptive awareness—the ability to track internal visceral and emotional states—underlies alexithymia in neurotypical samples (Ernst et al., 2014; Herbert, Herbert, & Pollatos, 2011) has been linked with interoceptive deficits in ASD (Brewer, Happé, Cook, & Bird, 2015; Quattrocki & Friston, 2014). It may be that, in autism, the inability to identify and communicate internal experiences increases the desirability for more external control, but atypical sensory processing (Rodgers, Glod, Connolly, & McConachie, 2012; Wigham, Rodgers, South, McConachie, & Freeston, 2015) and other difficulties integrating internal and external information increase feelings of uncertainty. This increase in IU may be manifested as insistence on sameness or restricted/repetitive behaviors (RRBs) to cope with their anxious distress.

Alexithymia

Results from the current study tie together important extant findings in the field of autism and alexithymia. It is clear from established research that people with autism have increased levels of anxiety (Bejerot et al., 2014; Lugnegård et al., 2011; White et al., 2009) and greater levels of alexithymia (Berthoz et al., 2013; Hill, Berthoz, & Frith, 2004). Our data suggests that when taking into account the core symptoms of autism (e.g., poor social skills & restricted behaviors), increased levels of alexithymia directly predict elevated anxiety. These data support Bird's suggestions (Bird & Cook, 2013; see also Mazefsky & White, 2014) that many socioemotional skills deficits in people with ASD are actually due to alexithymia, but not ASD itself. We extend that idea and propose a direct link from alexithymia to anxiety in ASD. One possible explanation for this is that when people have a difficult time clearly delineating or describing their internal experiences, their feelings may seem especially frightening and overwhelming. Not being able to clearly distinguish different emotions may lead people to become confused about what course of action to take in order to soothe their anxious arousal (Mennin & Fresco, 2009).

While our model assumes a causal relationship between ASD and alexithymia and provides evidence of statistical mediation, is it possible that alexithymia is, in fact, independent of ASD. Indeed, there are elevated rates of alexithymia across a multitude of psychiatric disorders including depression (Kim et al., 2008), eating disorders (Nowakowski, McFarlane, & Cassin, 2013), alcohol use disorder (Evren et al., 2008), as well as neurological disorders (Ricciardi, Demartini, Fotopoulou, & Edwards, 2015) and personality disorders (New et al., 2012).

While the exact causes of alexithymia are largely unknown, Karukivi and Saarijärvi (2014) reviewed the literature and found various potential contributors including neurobiological (e.g., amygdala, anterior cingulate cortex), environmental (e.g., socio-economic status, education level, social support, neglect), and developmental factors (e.g., delayed speech development). Similar neurobiological and developmental factors are also found in autism (see Eigsti, de Marchena, Schuh, & Kelley, 2011; Mundy, 2003; Schultz, 2005). Additional research is needed to better understand the actual contribution of the shared factors between ASD and alexithymia. Interestingly, alexithymia and emotional acceptance also share similar neurobiological correlates including the insula, anterior cingulate cortex, and amygdala (Paul, Stanton, Greeson, Smoski, & Wang, 2013; Taylor et al., 2011; Teper & Inzlicht, 2014; Teper, Segal, & Inzlicht, 2013; van der

Velde et al., 2013). This could be an explanation for the correlated error variance between alexithymia and emotional acceptance in our model. Future experimental studies concurrently investigating alexithymia and emotional acceptance may help to better understand possible shared etiological processes.

Emotional Acceptance

Results from the current study also provide support that the growing field of mindfulnessbased "third wave" cognitive behavioral therapies may be especially helpful for people with high-functioning ASD. While a few studies have shown that mindfulness-based techniques can be helpful for people with ASD (Kiep et al., 2014; Pahnke et al., 2014; Spek et al., 2013), this is the first study that has shown that one specific component of mindfulness, emotional acceptance of internal experience, can play a major role in the high levels of anxiety associated with ASD. This supports Mazefsky and White's (2014) assertion that acceptance-based approaches would likely enable people with ASD to learn emotion regulation skills and cope with their negative emotions in more adaptive ways.

Mindful acceptance-based approaches may be especially helpful for people with ASD given their tendency to have rigid and restricted thinking and behavior patterns. Instead of teaching them various ways to identify and change thinking errors like in traditional cognitive behavioral therapy (CBT), acceptance based approaches would simply have them watch their experience and allow their thoughts and feelings to be present without trying to change them. This is a more experiential approach than actively targeting and arguing with thoughts, and it may be easier for people with ASD to utilize (Mazefsky & White, 2014). In fact, mindfulness techniques are even being incorporated in new CBT protocols for people with ASD (McGillivray & Evert, 2014).

It is important to note that the current study does not provide direct evidence that a specific mindfulness-based intervention will assuage anxiety for people with high functioning ASD. This study does suggest that increasing one's ability to mindfully accept their internal experience may be one especially helpful avenue in treating anxiety, but given the cross-sectional design of the current study the authors can't comment on the efficacy of specific therapeutic techniques. While this study is a first step in that direction, future research examining distinct mindful- and acceptance-based interventions in samples with ASD will be able to examine this issue in more depth.

Limitations and Future Directions

One major limitation of this study has to do with generalizability of results to lowerfunctioning populations. Considering the average IQ of the ASD group in this study was 113 for the UK sample and 109 for the US sample, it is unknown if the proposed model would work for lower-functioning people with ASD. While this study needs to be replicated with a lowerfunctioning sample, there is reason to speculate that this model may still work. This is due to a bourgeoning body of research suggesting there may be benefits of emotional acceptance for people with intellectual disabilities (Harper, Webb, & Rayner, 2013; Idusohan-Moizer, Sawicka, Dendle, & Albany, 2015) which is a common co-occurring difficulty for people with a diagnosis of ASD (Buck et al., 2014).

Similarly, this study only included control participants who reported no comorbid diagnoses (including anxiety disorders), which restricts the range in this group but not in the ASD group. This was done because many of the control group participants were recruited from data-bases requiring this more strict criteria for studies, and the high prevalence of anxiety in

people with ASD prevents us from using it as exclusionary criteria. Future research needs to take into account controls who report similar levels of anxiety as the ASD group.

This study relied exclusively on self-report data, and may be limited in asking people with high rates of alexithymia to gauge the trouble they may have in accurately appraising their internalizing symptoms. Future research examining the roles of alexithymia and emotional acceptance on autism may benefit from observer and/or physiological ratings of anxiety and situation-based emotion recognition scenarios. Likewise, while the "non-reactivity to inner experience" facet of the FFMQ captures some aspects of emotional acceptance, it is a complex construct which is difficult to fully conceptualize using one questionnaire.

Another important consideration is the few significant differences between participants in the two study sites. Specifically, participants from the UK site tended to be older and have more elevated trait anxiety and core autism symptoms than the US site. However, both sites showed similar patterns of the relationship between autism symptoms and anxiety, and the age difference was helpful to get a broader range of data, helping with external validity. Moreover, other measures of anxiety were not different between sites (fear of negative evaluation and trait worry), and fit statistics provided evidence for the accuracy of our model including ostensible site differences. Finally, although there were missing data on all variables, it is likely that this missingness did not bias the results due to a small percentage on each variable, the data appear to be MAR, and the use of a full information maximum likelihood approach (Bennett, 2001; Enders & Bandalos, 2001).

A real strength of this model was the combination of dimensional measures of autism symptoms and anxiety that capture a large range of both constructs and diminish the need for overly-narrow diagnostic categories. Nonetheless there is still a large portion of predictive variance unaccounted for by the model. As noted above, imprecise measurements of key constructs is important, but our model also suggested other factors at work, including ways in which alexithymia and mindfulness are related. It is important to reiterate that the cross-sectional nature of these data preclude comments on causality. Future studies should examine the development and implements of interventions meant to increase emotional acceptance and to decrease alexithymia and IU using randomized controlled study designs.

Clinical implications

The current study posits that when treating comorbid anxiety in people diagnosed with high-functioning ASD it may be useful for clinicians to assess for and target their client's levels of emotional acceptance, alexithymia, and IU. While these results converge with extant anxiety research in neurotypical populations (see Cameron et al., 2014; Carleton, 2012; Kohl et al., 2012), they are especially pertinent to people with ASD for two primary reasons reasons: a) anxiety in adults with ASD has largely unexamined in the literature, especially in the area of anxiety interventions (Binnie & Blainey, 2013; Spain et al., 2015) and b) adults with ASD have elevated anxiety, alexithymia, and IU compared to neurotypical people, and they are more salient factors affecting their day-to-day functioning (Bird & Cook, 2013; Boulter et al., 2014; Buck et al., 2014; Wigham et al., 2015).

Interestingly, mindfulness-based interventions may be helpful in the treatment of poor emotional acceptance, alexithymia, and IU. While no current gold-standard treatment modalities exist for alexithymia, Cameron et al. (2014) emphasizes the utility of skills training to increase emotional awareness and physiological sensations. Mindfulness seems like an especially helpful treatment in this area, as many of the practices help clients focus their attention directly onto their feelings and sensations (Harris, 2009; Kabat-Zinn, 1990). Such exercises will also likely help increase their acceptance of distressing emotions. Nearly all mindfulness exercises contain a component of acceptance, where instructions often include phrases in the vein of "allow your experience to come and go" or "make room for whatever is present and re-focus your attention on your breath."

Some meditation practices may be especially helpful in increasing acceptance of anxiety by having people think of anxiety provoking situations and using mindfulness to make room for the anxiety (Eifert & Forsyth, 2005). Finally, considering the "present moment" focus of mindfulness skills, mindfulness may be a useful tool in helping people with autism cope with IU and related insistence on sameness and repetitive behaviors (Rodgers et al., 2012; Wigham et al., 2015). Mindfulness and acceptance skills have been shown to successfully reduce self-reported measures of intolerance of uncertainty in people diagnosed with generalized anxiety disorder (Treanor, Erisman, Salters-Pedneault, Roemer, & Orsillo, 2011) and with multiple sclerosis (Hankin, 2009). As previously noted, the cross-sectional nature of the current study prevents us from directly commenting on the efficacy of these or other mindfulness-based skills or interventions. However, they may be particularly helpful approaches in order to increase emotional acceptance and reduce alexithymia, both constructs which seem to play major roles in the anxiety of high functioning adults with ASD.

It is important to note that our data emphasize the importance of interventions focused on an increasing of emotional acceptance skills and decreasing of alexithymia. Anxiety reduction in ASD may not necessarily depend on IU reduction in the sense of re-appraisal of uncertainty but rather a general broadening of emotional acceptance abilities and a reduction in alexithymia which would also ameliorate what may be the felt sense that underpins IU.

21

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	UK (n=	=77)	US (<i>n</i> =74)		
	ASD (n=40)	CON (<i>n</i> =37)	ASD (<i>n</i> =36)	CON (<i>n</i> =38)	
IQ	113.14 (16.51)	111.57 (15.57)	108.70 (12.94)	113.50 (8.49)	
Range	80 - 138	77 - 140	82 - 136	94 - 137	
Age	44.7 (12.76)	45.89 (14.32)	21.74 (4.56)	19.95 (5.00)	
Range	26 - 70	22 - 67	17 - 36	17 - 24	
Gender					
Male	30	26	29	32	
Female	10	11	7	6	
Ethnicity*					
African Descent	0	4	1	0	
Asian	2	5	0	3	
Caucasian	38	28	32	28	
Hispanic	0	0	1	0	

Table 1 Demographic information

Note: Demographic data for participants separated by site and group (N=151). ASD = Autism Spectrum Disorder;CON = typical control. There were no significant differences in IQ between diagnostic groups or study sites. There were no significant within-site differences for age but the UK sample was significantly older than the US sample. There was no significant differences for gender between diagnostic groups or study sites.

*Ethnicity was not reported for 2 ASD participants and 7 CON participants.

Table 2. Anxiety measures and Autism symptoms compared by groups and sites, with means and standard deviations.

	ASD	CON	UK	US
AQ	31.26 (8.55)	15.65 (6.77) ***	25.14 (12.16)	21.34 (9.40)*
Range	9 - 48	1 - 32	1 - 47	2 - 48
Emotional	19.88 (5.14)	22.49 (4.64) **	20.27 (5.29)	22.24 (4.59)*
Acceptance				
Range	7 - 34	8-32	7 - 32	12 - 34
TAS-Identify	17.63 (5.01)	12.52 (4.13) ***	13.94 (4.92)	15.83 (5.25)*
Range	5 - 28	5 - 24	5 - 24	7 - 28
TAS-Describe	18.41 (6.96)	12.69 (4.92)***	17.12 (7.89)	13.80 (4.66) *
Range	7 – 33	5 - 27	7 – 33	5 - 22
FNE	35.81 (9.22)	32.80 (9.00)*	34.60 (9.35)	33.94 (9.06)
Range	14 - 56	14 - 57	14 - 56	14 - 57
PSWQ	52.37 (14.26)	42.24 (14.61) ***	47.80 (16.44)	46.63 (13.95)
Range	21 - 80	16 – 73	19 - 80	16 – 77
STAI-Trait	47.43 (11.81)	38.72 (10.46) ***	45.42 (12.69)	40.44 (10.59)*
Range	25 - 71	20 - 63	20 - 71	21 - 63
IUS-12	36.16 (10.07)	25.17 (7.41) ***	29.65 (10.38)	32.80 (10.38)
Range	15 - 60	12 - 42	13-60	12 – 56

Note: *t*-tests were used to examine significant differences. N= 151. $p^* < .05$, $p^{**} < .01$, $p^{***} < .0001$.

Welch's approximation was used for t-tests for the following comparisons: AQ between groups, TAS-describe

between groups and sites, and IUS-12 between groups.

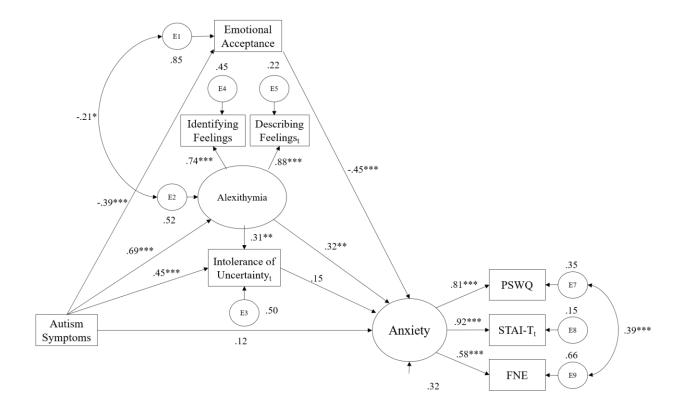
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Measures	1	2	3	4	5	6	7
1. AQ							
2. Emotional	41**						
Acceptance							
3. TAS Identify	.54**	28*					
4. TAS Describe	.61**	39**	.65**				
5. FNE	.40**	35**	.34**	.36**			
6. PSWQ	.51**	55**	.33**	.45**	.66**		
7. STAI-T	.58**	62**	.41**	.59**	.53**	.74**	
8. IUS-12	.67**	32**	.51**	.51**	.42**	.49**	.52**

Table 3. Correlations of study variables, N = 151.

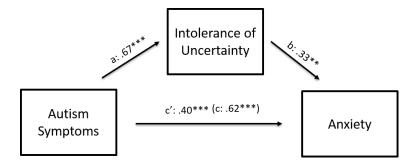
Note: AQ is the Autism Spectrum Quotient, TAS Identify and TAS Describe are subscales from the Toronto Alexithymia Scale-20, Emotional acceptance is the mindfulness facet of nonreactivity to inner experience, FNE is the Fear of Negative Evaluation scale, PSWQ is the Penn State Worry Questionnaire, STAI-T is the State Trait Anxiety Inventory-Trait form, and IUS-12 is the Intolerance of Uncertainty Scale-12; **p*<.001, ***p*<.0001

Figure 1



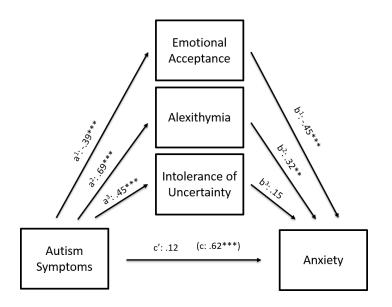
Note: Structural equation model showing the relationship between alexithymia, emotional acceptance, and IU in predicting anxiety for people with autism symptoms. Rectangles are observed variables while ovals are latent variables. Small circles represent error terms for a given variable. Single-headed arrows represent directional pathways, while double-headed arrows show correlations between error terms. All coefficients are standardized, and asterisks represent significance (*p<.05, **p<.01, ***p<.001). Small "t" represents log-transformed variables.

Figure 2: Mediation analysis examining the role of IU in the relationship between autism symptoms and anxiety.



Note: Mediation showed that when IU is constrained to 0, more autism symptoms served as a very strong predictor of greater anxiety ($\beta = .62, p < .001$). However, when IU was included as a mediator for anxiety, autism symptoms became a weaker predictor of greater anxiety ($\beta = .40, p < .001$). This shows that IU by itself serves as a mediator for autism core symptoms, because autism symptoms must operate through that mechanism to affect anxiety.

Figure 3: Mediation analysis examining the role of mindful acceptance, alexithymia and IU in the relationship between autism symptoms and anxiety.



Note: Mediation showed that when emotional acceptance, alexithymia, and IU were constrained to 0, more autism symptoms served as a very strong predictor of greater anxiety ($\beta = .62$, p < .001). However, when these variables were all included as mediators for anxiety, autism symptoms lost all of its power to predict anxiety significantly ($\beta = .12$, p < .05). This shows that emotional acceptance and alexithymia do serve as mediators for autism core symptoms, because autism symptoms must operate through those mechanisms to affect anxiety. IU was not shown to be a significant mediator.

	Alexithymia	Emotional Acceptance	Intolerance of Uncertainty
a	.69	39	.45
b	.32	45	.15
С	.62	.62	.62
с'	.12	.12	.12
indirect effect/total effect	.36	.28	Non-significant

Table 4: Test of mediation utilizing all variables

Note: *a* represents the pathway from dimensional autism symptoms to specified construct, whilst *b* represents the pathway from the specified construct to anxiety symptoms. *c* represents the direct pathway without the variance from the mediators included in the analysis, and *c*' represents the indirect pathway where the variance from the mediators is included in the analysis. The *indirect effect/total effect* shows the percentage of variance explained by that mediator.