Title of Paper: The Hospital Anxiety and Depression Scale: Factor Structure and Psychometric Properties in older adolescents and young adults with Autism Spectrum Disorder (ASD)

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Accepted Article

Abstract

Despite the high frequency of anxiety and depression symptoms in individuals with Autism Spectrum Disorder (ASD) and a significant impact of these comorbidities on both individuals with ASD and their families, research on the validity ~~and sensitivity~~ of anxiety and depression measures in the ASD population is currently lacking. The aim of this study was to explore the psychometric properties of the Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983) in a sample of older adolescents and young adults with ASD. One hundred and fifty one participants (UK Transition longitudinal study: $N=106$; 75 males, $Mean=16.04$ years, $SD=1.28$; Longitudinal Study of Australian Schools Leavers with ASD: $N=45$, 30 males; $Mean=18.35$ years, $SD=2.55$) completed the HADS and a range of mental health and well-being measures. Combination of the Principal Component Analysis and Parallel Analysis indicated two factors as an optimal solution in our sample, accounting for 43.77% of variance with factors being identical in terms of content with the structure found in the general population. Internal consistency was good for the HADS anxiety scale (HADS-A; .82-.84) and acceptable for the HADS depression scale (HADS-D; .60-.72). Convergent validity of both HADS-A and HADS-D scales was excellent and divergent validity was acceptable. Our study represents a significant contribution to the literature by providing an initial validation of the HADS in older adolescents and younger adults with ASD.

Lay Summary: Research on the validity of measurement of anxiety and depression in ASD is currently lacking. The aim of this study was to explore the properties of the Hospital Anxiety and Depression Scale (HADS) in a sample of 151 young people with ASD. Participants completed HADS and a range of mental health and well-being measures. Encouragingly, our findings suggest that HADS provides a reliable and valid assessment of anxiety and depression in ASD.

Comment [mu1]: Change made in response to Comment 2 raised by Review 1

Key words: Hospital Anxiety and Depression scale, HADS, anxiety, depression, autism, ASD.

Accepted Article

Introduction

Linked to Autism Spectrum Disorder (ASD) since the original descriptions by Leo Kanner (1943) and Hans Asperger (Wing, 1981), anxiety in autism has only become a focus of research in the past 20 years. During this time anxiety has been found to be more prevalent in ASD when compared to the general population (Kim, Szatmari, Bryson, Streiner, & Wilson, 2000; Bellini, 2004; Lopata et al., 2010), and a range of other clinical groups, including Down Syndrome (Evans, Canavera, Klinepeter, Taga, & Maccubbin, 2005), Conduct Disorder (Green, Gilchrist, & Cox, 2000), Specific Language Impairment (Gillott, Furniss, & Walter, 2001), Williams Syndrome (Rodgers, Riby, Janes, Connolly, & McConachie, 2012), and non-specific learning disabilities (Gadow et al., 2005; Gillot & Standen, 2007). Recent large scale studies and systematic reviews have suggested the most realistic figure for individuals who meet the criteria for clinically significant anxiety to be 40% among children and adolescents (van Steensel, Bogels, & Perrin, 2011) and up to 60% in adults (Buck et al., 2014; Croen et al., 2015; Hofvander et al., 2009; Joshi et al., 2013; Lever & Geurts, 2016; Ljungegard, Hallerback, & Gillberg, 2011).

Studies using parent report (Mayes, Calhoun, Murray, Ahuja, & Smith, 2011) and self-report (Hedley & Young, 2006) measures, as well as the clinician administered Autism Comorbidity Interview-Present and Lifetime Version (ACI-PL) and DSM-IV criteria (Leyfer et al., 2006), have suggested that between 25% and 54% of children and adolescents with ASD have depression symptoms. Although there is considerably less research on depression in adults with ASD, results suggest that it is one of the most prevalent co-morbid problems in this population (Ghaziuddin, Ghaziuddin, & Greden, 2002; Sterling, Dawson, Estes, & Greenon, 2007). For example, in a large sample of 374 individuals who had been diagnosed with Asperger's syndrome during adulthood, Cassidy et al. (2014) found that 31% self-reported depression, 66% self-reported suicidal ideation, and 35% self-reported suicidal

attempts or plans. A recent systematic review by Wigham, Barton, Parr and Rodgers (2017) showed rates of depression tend to be lower when depression-specific measures, rather than general measures with a depression subscale, are used, with rates of 29% in childhood and 35% in adulthood.

Anxiety and depression have a significant negative impact on the functioning of individuals with ASD and their families, often over and above the contribution of core-ASD traits and developmental level (Kerns et al., 2015). For example, high levels of anxiety in individuals with ASD have been found to be associated with increased levels of repetitive behaviours (Lidstone, Uljarević, et al., 2014; Uljarević & Evans, 2016), externalizing problems, including aggression and self-injury (Mattila et al., 2010), loneliness (White & Roberson-Nay, 2009), insomnia symptoms (Richdale, Baker, Short, & Gradisar, 2014), higher need for support and professional help (Leyfer et al., 2006), lower levels of employment (Hedley, Uljarević, et al., 2016), as well as with parental concerns for their child's future (Kim et al., 2000) and parents' own levels of stress and anxiety (Kerns et al., 2015).

Despite the high frequency and significant impact of these comorbidities, research on the validity and sensitivity of standardised anxiety and depression measures in the ASD population has emerged only relatively recently (Davis III, White, & Ollendick, 2014) and focussed exclusively on children and younger adolescents (hereinafter defined as 'youth'). A review by Lecavalier et al. (2014) appraised evidence for the suitability of 10 measures for assessing anxiety in youth with ASD, concluding that although none of the instruments possessed evidence for good or excellent reliability and validity in ASD across all relevant indices, several could be considered as 'appropriate with conditions'. A systematic review by Wigham and McConachie (2014) identified the Spence Children's Anxiety Scale (SCAS; Spence, 1998), the Revised Children's Anxiety and Depression Scale (Chorpita, Yim, Moffitt,

Umemoto, & Francis, 2000), and the Screen for Child Anxiety Related Emotional Disorder (SCARED; Birmaher et al., 1999) as robust outcome measures for Cognitive Behavioural Therapy trials (although see Rodgers et al., 2016 [for a discussion on the importance of supplementing standard anxiety measures to accommodate for atypical expression of anxiety symptoms](#)).

Comment [mu2]: Addition made in response to Comment 2 raised by Reviewer 2

However, there is considerable overlap between the behavioural symptoms of ASD and those attributed to affective disorders and in particular anxiety, despite the distinction in their function in the internationally recognised diagnostic classification of disorders (DSM 5, 2013; ICD-10, 1994). For example, social avoidance and withdrawal can be considered as a symptom of anxiety, and also as a potential manifestation of the social communication impairment that characterises ASD. Similarly, obsessive and compulsive behaviours are a recognised manifestation of particular types of anxiety, but might also be an expression of certain types of the core restricted and repetitive behavioural characteristics required for a diagnosis of ASD. Thus, an anxiety disorder that manifests with social avoidance and ritualistic behaviours, while easily identifiable in a child without ASD, might not be recognised as part of the behavioural presentation of a co-occurring mental health disorder and so go unnoticed in a child with ASD (Hellerschou & Martinsen, 2011; Kerns et al., 2015; Uljarević, Nuske, & Vivanti, 2016). Further, individuals with ASD might present with idiosyncratic symptoms including unusual specific phobias (e.g., vacuum cleaners, toilets) and fears of change or novelty (Kerns & Kendall, 2012; Kerns et al., 2016; Mayes et al., 2013; Renno & Wood, 2013; Rodgers et al., 2016). Therefore careful consideration about how best to consider the differential diagnoses in individuals with neurodevelopmental disorders including ASD is needed (Uljarević et al., 2016). This includes making judgements about the appropriate use of standardised tools such as anxiety instruments, originally developed for the general population, with individuals with ASD (Lecavalier et al., 2014;

Wigham and McConachie, 2014; Wood & Gadow, 2010). Similar concerns have been raised with regards to the assessment and diagnosis of depression as, on the one hand, ASD related behaviours can be mistakenly interpreted as signs of a co-occurring depression, and on the other hand, depressive symptoms can be expressed in atypical ways in individuals with ASD, and either missed or ascribed to the underlying ASD (Gotham, Unruh, & Lord, 2015; Magnuson & Constantino, 2011; Stewart, Bernard, Pearson, Hasan, & O'Brien, 2006).

To address these issues, several recent studies have investigated the relevance of existing measures for the assessment of anxiety symptoms in ASD youth. Rodgers et al. (2016) created the Anxiety Scale for Children – ASD (ASC-ASD) by modifying the Revised Children's Anxiety and Depression Scale (RCADS; Chorpita et al., 2000) to incorporate items related to intolerance of uncertainty, sensory over-sensitivity and phobias. They reported that the newly developed scale had good internal consistency, validity, and 1-month test-retest reliability. Kerns et al. (2014; 2015; 2016) have also shown that the Autism Spectrum Addendum (ASA) to the Anxiety Disorders Interview Schedule (ADIS; Silverman & Albano, 1996), had satisfactory psychometric properties, and convergent and discriminant validity in both low-anxiety (Kerns et al., 2014) and treatment seeking (Kerns, Renno, Kendall, Wood, & Storch, 2016) samples of children with ASD. Further, Kerns et al (2014) reported that the ASA was designed to enable assessment of ambiguous anxiety-like symptoms across the following five categories: fears of change, negative reactions to change, social fear, unusual phobias, and special interest fears.

Despite the suggestions that measures originally developed for the assessment of anxiety and depression might not be appropriate for use in the ASD population, the use of the measures that assess these aspects of mental health disorders in ASD can facilitate the investigation of potential commonalities and differences between anxiety and depression in ASD and other populations. Indeed, it has been argued that, rather than developing novel

measures specific for use in individuals with ASD, it might be more useful as a first step, to investigate the psychometric properties of standardised measures with well validated population norms in the ASD population (Rodgers et al., 2016; Uljarević, 2013). To our knowledge, no studies to date have explored in detail the properties of anxiety and depression measures in a population of older adolescents or adults with ASD. Thus, this study explores the psychometric properties of one such measure - the Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983) in a sample of older adolescents and young adults with ASD.

The HADS is a brief, self-report questionnaire originally created to assess symptoms of anxiety and depression. The HADS was chosen as a potentially useful measure for individuals with ASD for several reasons. It provides a quick assessment of both anxiety and depression symptoms, has been shown to demonstrate good to excellent psychometric properties across general and clinical populations (Bjelland, Dahl, Haug, & Neckelmann, 2002; Brennan, Worral-Davies, McMillan, Gilbody, & House, 2010), and provides an optimal balance between sensitivity and specificity to both clinical conditions. A review by Brennan et al. (2010) showed that across 41 studies conducted with general, inpatient and outpatient samples, the HADS demonstrated good sensitivity (Major Depressive Disorder [MDD]: mean = .82, range: .73–.89; Generalized Anxiety Disorder [GAD]: mean = .72, range: .62–.80) and specificity (MDD: mean = .74, range: .60–.84; GAD: mean = .86, range: .79–.90). The HADS was designed as a screen for anxiety and depressive symptoms in community and non-psychiatric populations and does not include symptoms such as dizziness, headache, weight loss, fatigue and anergia, and insomnia) making it more ~~sensitive to~~ appropriate for assessing subtler symptom expression and less prone to sampling symptoms that can be reflective of physical symptoms or conditions other than anxiety and depression. Indeed, HADS has been shown to ~~be sensitive effectively sample to~~ subtler anxiety and depression

Comment [mu3]: Changes made in response to Comment 2 raised by Review 1

symptom expression (Brennan et al., 2010). Finally the HADS is freely available, translated and validated in more than 20 languages, and accessible for use across a range of low-income settings.

The main goals of this study were to evaluate the factor structure of HADS in a sample of older adolescents and young adults with ASD, establish its psychometric properties, report convergent and divergent validity, and to examine associations between depression and anxiety symptoms, age and ASD severity.

Methods

Participants

One hundred and fifty-one adolescents and young adults with ASD took part in the study. One hundred and six were recruited through child mental health services as a part of the UK Transition longitudinal study (31 females, 75 males; $M_{\text{age}} = 16.04$ years, $SD = 1.28$ [Merrick et al., 2015]). All participants had a clinical diagnosis of ASD and additional mental health difficulties (37.4% Attention Deficit Hyperactivity Disorder [ADHD; 30.8 ADHD alone and 6.6% ADHD + additional condition], 25.3% Anxiety [9.9% Anxiety alone, 6.6% dual diagnosis of anxiety and depression/low mood, and further 8.8% anxiety plus another condition], 14.3% Depression/Low mood, 8.8% Challenging behaviours and Obsessive Compulsive Disorder [OCD] each, and 5.5% “other” [e. g., sleep difficulties, conversion disorder, hallucinations]).

Forty-five participants were recruited from the nation-wide Longitudinal Study of Australian Schools Leavers with ASD and their families within the Cooperative Research Centre for Living with Autism (Autism CRC); 15 females, 30 males; $M_{\text{age}} = 18.35$ years, $SD = 2.55$). The participants were recruited via various channels including state based ASD organizations, parent support groups, secondary and tertiary education organizations,

participant data bases and clinicians. All participants reported receiving a clinical diagnosis of ASD (Asperger Syndrome: 46.7%; ASD: 37.8%; High Functioning Autism: 11.1%; Autistic Disorder: 2.2%; PDD-NOS: 2.2%). Eighty percent of the Australian sample reported that in addition to ASD, they had received a range of additional diagnoses (17.8% anxiety, 8.9% SLI, 6.7% ADHD, 2.2% depression, and 44% anxiety combined with other diagnoses [17.8% anxiety + depression, 13.3% anxiety + depression + ADHD, 8.9% anxiety + ADHD, 4.4 anxiety + OCD]). Eighty-six percent of individuals who reported receiving a diagnosis of anxiety or depression also reported receiving treatment for this diagnosis. The Social Responsiveness Scale Second Edition UK sample), and the abridged version of the Autism Spectrum Quotient (Australian sample) were used to measure the participants’ autism characteristics, with all participants exceeding suggested cut off scores. Descriptive statistics are presented in Table 1.

Insert Table 1 here

Procedures

The UK Transition study received a favourable ethical opinion from Newcastle and North Tyneside 1 Research Ethics Committee (12/NE/0059). The Australian Autism CRC study was approved by the La Trobe University Human Ethics Committee (14-095), and other institutional or organisational ethics committees as appropriate. All individuals read a participant information statement about their respective longitudinal study and provided informed consent in writing. Parental consent was obtained for individuals younger than 18 years. UK participants were visited at home to complete questionnaires. Australian participants were sent a link to an online survey.

Measures

Baseline characterisation measures:

Comment [mu4]: Correction made in response to Comment 3 raised by Reviewer 2

*Autism CRC sample**Abridged version of the Autism-Spectrum Quotient (AQ-Short; Hoekstra et al., 2011)*

is an abbreviated, 28-item version of the 50-item self-report measure of autistic traits (Baron-Cohen et al., 2001). Each item is rated on a 4-point Likert scale, from “1 = definitely agree” to “4 = definitely disagree”. Unlike the original AQ, where items are coded categorically, the full range is endorsed in the AQ-Short. A score of > 65 has a sensitivity of .97 and a specificity of .82 for ASD.

DSM-5 Dimensional Anxiety Scales (DSM-5 DAS; Knappe et al., 2013; Lebeau et al., 2012; Beesdo-Baum et al., 2012) is a self-report, norm referenced questionnaire designed to screen for the presence of anxiety symptoms, with a total score > 14 indicating significant anxiety (Beesdo-Baum et al., 2012).

Patient Health Questionnaire-9 (PHQ-9; Kroenke et al., 2001) is a 9-item, self-report, norm referenced, questionnaire designed to screen for the presence of depression across general and clinical populations. The PHQ-9 provides two types of cut-off scores (1) normal/minimal (0-9), moderate (10-14), moderately severe (15-19), severe (20+), and also a cut-off > 10 as indicative of major depression (sensitivity of .88 and a specificity of .88).

UK sample

Social Responsiveness Scale (SRS; Constantino & Gruber, 2005) is a 65 items, self-reported measure designed to index autism trait severity. It provides total score and subscale scores for social awareness, cognition, communication, motivation, and repetitive behaviour. The SRS-2 has good internal consistency (α .72–.93), and excellent sensitivity and specificity ($\geq .92$; Constantino & Gruber, 2005).

The Strengths and Difficulties Questionnaire (SDQ; Goodman, Meltzer, & Bailey, 1998) is a measure of psychological well-being assessing emotional, conduct, hyperactivity,

and peer problems, as well as prosocial behaviours. It consists of 25 items with each item rated on a 3-point Likert scale ranging from “not true” to “certainly true.” In this study we focused on the emotional problems subscale (scores ≤ 5 indicate no problems, 6 borderline and 7-10 abnormal).

Measures of Anxiety, Depression and Well-being:

Both Samples

The Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983) is a norm referenced questionnaire used to assess anxiety and depression. It contains 14 self-report items, with seven items forming the Anxiety subscale (HADS-A) and seven items forming the Depression subscale (HADS-D). Cut-off score of ≥ 8 has been found to offer the best balance between sensitivity and specificity for both HADS-A and HADS-D scales (Brennan et al., 2010).

The Warwick-Edinburgh Mental Well-being Scale (WEMWBS; Clarke et al., 2011) is a 14-item scale of mental well-being covering subjective well-being and psychological functioning, in which all items are worded positively and address aspects of positive mental health. The scale is scored by summing responses to each item answered on a 1- to 5-point Likert scale, with higher scores indicating higher levels of positive mental well-being.

Analysis Plan

Prior to running analyses, all questionnaires were screened for missing data. Pairwise deletion was used to handle missing data. Where missing data were detected, analyses were run specifying excluded cases pairwise option. The HADS was examined for latent components using the Principal Component Analysis (PCA)¹ with direct oblimin rotation. The initial PCA was run in order to establish the number of components with eigenvalues

¹ Principal Axis Factoring Exploratory Factor Analysis was also run in order to check the pattern of results

Comment [mu5]: Change made in response to Comment 3 raised by Reviewer 1

over Kaiser's criterion of 1. The Parallel analysis (PA; Horn, 1965; O'Connor, 2000) via the SAS-based code developed by O'Connor (2000), was used to determine the number of factors that should be retained in the final analysis. It has been reported that decisions based on this method are more robust and reproducible when compared to Scree Test and relying on Eigen values (O'Connor, 2000). The PCA was then rerun specifying the number of factors yielded through PA.

The reliability of extracted HADS factors was determined by using Cronbach's alpha. Convergent validity was examined by exploring the relationship between HADS factors with the SDQ subscales, WEMWBS total score, and discriminant validity by exploring the relationship with PHQ-9 and DSM-5 DAS scores.

Results

Preliminary analyses and descriptive statistics

Table 1 shows descriptive statistics for the key variables. Since a number of variables were not normally distributed, analyses were performed through bootstrapping using 5,000 resamples to provide more robust statistics (Efron & Tibshirani, 1993; Tabachnick & Fidell, 2014). Where multiple correlations were run, the significance level was set at .01.

Factor Analysis

No more than 0.6% of HADS data were missing for any questionnaire item, and there were no systematic differences in missing items. Before factor analysis was run the UK and Australian samples were compared in terms of HADS total, HADS-A (Anxiety) and HADS-D (Depression) scores. The Kruskal-Wallis H test showed that there was no statistically significant differences on HADS totals between the participant groups (HADS total: $\chi^2 = .05$, $p = .83$; HADS-A: $\chi^2 = .002$, $p = .96$; HADS-D: $\chi^2 = .73$, $p = .39$, respectively). In addition, samples did not differ on any of the individual HADS items (please refer to Table A. 1.).

Appendix A for the full descriptives and comparison statistics). Assumptions of non-multicollinearity, sampling adequacy, and factorability were all met. The Kaiser-Meyer-Olkin (KMO) measure verified the sampling adequacy for the analysis: KMO = .82. Bartlett’s test of sphericity indicated that correlations were sufficiently large for PCA ($\chi^2 = 567.71, p < .001$).

Comment [mu6]: Addition made in response to Comment 1 raised by Reviewer 1.

The initial PCA indicated that four components had eigenvalues over Kaiser’s criterion of 1, accounting for 59.53% of total variance. Parallel analysis showed that factors 3 onwards had Eigen values less than that of those from simulations and a two-factor solution should be retained in the final analysis. Thus the PCA was rerun specifying a two-factor solution. Two factors were interpretable as Anxiety (HADS-A) and Depression (HADS-D) accounting for 43.77% of variance (Anxiety: 30.07%; Depression: 13.70%). Individual factor loadings are presented in Table 2². All of the items loaded in the same way as originally designed by Zigmond and Snaith, and replicated in subsequent studies across the life span (Bjelland, Dahl, Haug, & Neckelmann, 2002; Brennan, Worral-Davies, McMillan, Gilbody, & House, 2010) although as noted (see Table 2), item “I feel tense or wound up” loaded onto both HADS-A (.54) and HADS-D (.40) subscales.

Comment [mu7]: Footnote added in response to Comment 1 raised by Reviewer 1

Insert Table 2 Here

The mean correlation of the anxiety item total score and the HADS-A factor was .71 ($SD = .07$), and of mean anxiety items and HADS-D factor .24 ($SD = .13$). The mean depression items-HADS-D factor correlation was .56 ($SD = .10$), and the mean depression items-HADS-A factor correlation was .20 ($SD = .11$). Item-subscale correlations are presented

² Principal Axis Factoring Exploratory Factor Analysis that was also run resulted in the identical factor structure and item order.

³ PCA was re-run separately in the UK and Australian samples. For both samples, the Kaiser-Meyer-Olkin (KMO) measure verified the sampling adequacy for the analysis: KMO = .78 for UK and .74 for Australian sample. Bartlett’s test of sphericity indicated that correlations were sufficiently large for PCA (UK: $\chi^2 = 475.01, p < .001$; Australian sample: $\chi^2 = 246.52, p < .001$). PCA indicated 2 factors as optimal solution in both samples, and items loaded in identical way in UK and Australian samples, consistent with HADS factor structure in non-ASD populations. Anxiety factor accounted for 30.46% of variance in UK and 32.79% in Australian sample, and Depression factor accounted for 13.14% of variance in UK and 14.84% in Australian sample.

in Table 2. Comparison between the strength of item-subscale correlations for UK and Australian samples is presented in Table A. 1., Appendix A. As can be seen, with the exception of the item “I look forward with enjoyment to things” that correlated more strongly with HADS-D subscale in Australian when compared to UK sample, the strengths of item-subscale correlations were not statistically different across two samples.

Comment [mu8]: Addition made in response to Comment 1 raised by Reviewer 1.

Reliability

For the whole sample internal consistency (Cronbach's α) was good $\alpha = .83$ (UK: $\alpha = .84$; Australian: $\alpha = .82$) for the HADS-A scale and acceptable $\alpha = .65$ (UK: $\alpha = .60$; Australian: $\alpha = .73$) for HADS-D scale.

Validity

Convergent validity was demonstrated by:

- a. Whole sample: significant relationships between HADS-A and HADS-D scales and WEMWBS for the whole sample ($r = -.45, p < .001$, BCa 95% CI $[-.59; -.28]$; $r = -.60, p < .001$, BCa 95% CI $[-.69; -.49]$; respectively)
- b. UK sample: significant relationships between HADS-A and HADS-D with the SDQ emotional scale ($r = .80, p < .001$, BCa 95% CI $[.72; .86]$; $r = .29, p = .002$, BCa 95% CI $[.003; .08]$; respectively);
- c. Australian sample: significant relationship between HADS-A and DSM-5 DAS anxiety scale ($r = .71, p < .001$, BCa 95% CI $[.48; .86]$) and between HADS-D and PHQ-9 depression scale ($r = .56, p < .001$, BCa 95% CI $[.25; .77]$).

Divergent validity: The HADS-A and HADS-D scales were significantly related ($r = .34, p < .001$; BCa 95% CI $[.18; .49]$). The HADS-A scale was associated with the PHQ-9 ($r = .72, p < .001$, BCa 95% CI $[.55; .85]$), and the HADS-D scale was significantly related to the DSM-5 DAS scale level ($r = .53, p < .001$, BCa 95% CI $[.25; .70]$). The DSM-5 DAS and

PHQ-9 scales were also significantly inter-related ($r = .71, p < .001$, BCa 95% CI [.51; .85]). The association of the HADS-A and HADS-D with chronological age was not significant ($r = .04, p = .71$, BCa 95% CI [-.15; .22]; $r = -.003, p = .98$, BCa 95% CI [-.19; .20]; respectively), nor was the relationship between the HADS-A and HADS-D scores and ASD severity scores (Australian sample: relationship with AQ-28 total: $r = .24, p = .23$, BCa 95% CI [-.04; .53]; $r = .28, p = .07$, BCa 95% CI [-.01; .53]; respectively; UK sample: relationship with SRS-2 total: $r = .16, p = .10$, BCa 95% CI [-.04; .35]; $r = .09, p = .38$, BCa 95% CI [-.14; .30]; respectively).

Frequency of Anxiety and Depression

A comparison between UK and Australian samples showed that HADS-A and HADS-D scores were similar (HADS-A: $t = .12, p = .91$; BCa 95% CI [-1.43; 1.73], Cohen's $d = .02$; HADS-D: $t = .88, p = .38$, BCa 95% CI [-.82; 2.08], Cohen's $d = .15$). Sixty percent of the total sample scored above the cut off criteria for elevated anxiety and 26.8% above the cut off for depression; 75% of individuals who met the cut off criteria for depression also met the cut off criteria for elevated anxiety. For separate rates for the UK and Australian samples, please see Table 3. Endorsement rates for individual HADS items are presented in Table 2.

Insert Table 3 Here

Discussion

The aim of this study was to explore the properties of the HADS (Zigmond & Snaith, 1983) measure in a sample of older adolescents and young adults with ASD. We firstly focussed on whether the HADS showed the same factor structure as that already established in non-ASD populations. The two identified factors were identical in terms of content with

the original structure proposed by Zigmond and Snaith (1983) and subsequently replicated across different studies (Bjelland et al., 2002; Brennan et al., 2010). For both the whole sample, and for each sub-sample (UK and Australian) when tested separately, internal consistency was good for the HADS anxiety scale (HADS-A; .82-.84) and acceptable for the HADS depression scale (HADS-D; .60-.73).

Although no studies to date have compared the factor structure of the HADS in individuals with and without ASD, several studies have explored the factor structure of various other anxiety measures designed originally for use in typically developing youth, when used in youth with ASD. For example, White et al. (2015) failed to show factor equivalence of the Multidimensional Anxiety Scale for Children (March et al., 1997) in a sample of 109 youth with ASD. White et al. (2015) reported that in the youth with ASD there were similar factor loadings for separation/panic and physical symptoms factors to those found in typically developing youth, but none of the items loaded onto the factor resembling harm avoidance. Furthermore, the authors identified two factors broadly consistent with social anxiety (one corresponding to fears about rejection and humiliation, and the second one representing fears consistent with performance anxiety), but different in structure from the single social anxiety factor reported in the typically developing samples (March et al., 1997). In addition, three recent studies failed to provide full support for the original factor structure of the SCAS-Parent Report (Spence 1998) when used in a sample of children and younger adolescents with ASD (Glod et al., 2017; Jitlina et al, 2017; Magiati et al., 2017).

However, unlike HADS, which assesses only overall levels of anxiety, SCAS-P, in addition to providing measure of overall anxiety, also provides scores for the following 6 anxiety subtypes: panic attacks and agoraphobia, separation anxiety, physical injury fears, social phobia, obsessive-compulsive, and generalized anxiety disorder.

Comment [mu9]: Addition made in response to Comment 1 raised by Reviewer 2.

In contrast to previous findings, this study has reported an identical HADS factor structure in this large sample of older adolescents and young adults with ASD to the one commonly reported in both general and non-ASD clinical samples across a wide age range (Bjelland et al., 2002; Brennan et al., 2010). Unlike the above reviewed studies in youth with ASD that encompassed participants with a wide age range where developmental factors strongly influence expression of anxiety (van Steensel et al., 2011), our study had a relatively narrow age range and captured a period when expression of anxiety tends to be more stable (Lenze & Wetherell, 2011) – thus the HADS might be best used in studies with homogenous age groups. Finally, the HADS measures overall or general anxiety rather than specific DSM-IV or DSM-5 anxiety subtypes. This latter point may explain why all but one item ('I feel tense or wound up') load into distinct anxiety and depression factors. In the future it will be important to evaluate the factor structure of anxiety measures that specifically assess individual anxiety subtypes.

Correlational analyses indicated medium to large negative associations between HADS-A and HADS-D scales with positive aspects of well-being (measured by the Warwick-Edinburgh Mental Well-being Scale) in the whole sample, a large positive correlation between the HADS-A and the DSM-5 Dimensional Anxiety scale (DSM-5 DAS), a medium correlation between the HADS-D and the Patient Health Questionnaire-9 (PHQ-9; Australian sample), and a medium to large positive correlations between the HADS-A and HADS-D scales and the emotional scale of the Strength and Difficulties Questionnaire (SDQ; UK sample). These results indicate excellent convergent validity of both HADS-A and HADS-D scales.

It is important to note that while the Australian sample was a sample of opportunity, and all families and participating individuals understood that the primary focus of the study was to explore educational, vocation and well-being outcomes. In the period around transition

from secondary school. In contrast, the UK sample recruited individuals who had a clinical diagnosis of ASD and additional mental health difficulties. In light of these different recruitment foci, it is noteworthy that the two samples did not differ in terms of HADS-A and HADS-D scores. However, although all participants in the UK study had additional mental health difficulties, this study did not specifically recruit individuals with anxiety and depression. Indeed individuals had a wide range of mental health related diagnoses, including ADHD, OCD, anger, Tourette's, sleep difficulties, Conversion disorder, and hallucinations. Furthermore, the majority of the Australian sample reported that they had received co-morbid diagnoses of anxiety and/or depression as well as other diagnoses including ADHD. Considering this, it is probably not surprising that individuals from both sample reported similar levels of anxiety and depression.

Divergent validity of both the HADS-A and HADS-D scales was acceptable as shown by non-significant correlations with chronological age and ASD severity, and between the HADS-D and DSM-5 DAS. The finding that neither HADS-A or HADS-D scores were associated with chronological age was most likely due to the fact that there is a greater stability in anxiety and depression in the age range for our study. Sixty percent of our sample met the cut off criteria for clinically significant anxiety replicating findings on anxiety frequency across adolescence and adulthood in ASD (Buck et al., 2014; Croen et al., 2015; Hofvander et al., 2009; Joshi et al., 2013; Lever & Geurts, 2016; Lugnegard, Hallerback, & Gillberg, 2011), which is significantly higher than reported frequency in non-ASD populations (Lenze & Wetherell, 2011). Frequency of clinical levels of depression (24.7%) was somewhat lower than rates of depression reported in previous studies with adults with ASD (Cassidy et al., 2014; Hofvander et al., 2009; Lever et al, 2016); however, this finding was most likely due to the younger age of participants in our study and due to the fact that our study used dedicated measure of depression (Wigham et al., 2017).

The HADS-A and HADS-D scales were significantly inter-related, showing a medium strength relationship, while the HADS-A and PHQ-9 scales (as a measure of depression) showed a large positive relationship. These findings are in line with research in both the general, and a range of clinical populations showing medium to strong inter-relationships (r ranging from .45 to .75) between measures of anxiety and depression (Bjelland et al., 2002; Cosco et al., 2012; Watson, 2009). Although it has been suggested that anxiety and depression are distinguishable at the phenomenological level (Watson, 2009) and that high correlations are a hallmark of poor discriminant validity (Clarke & Watson, 1991), Burns and Eidelson (1998) have argued that this is to be expected, not because of symptom overlap and poor content validity, but because anxiety and depression share underlying mechanisms. Indeed, findings from the general population suggest that anxiety and depression frequently co-occur, with anxiety commonly predating the occurrence of depression (Wetzler & Katz, 1989; Watson, Gamez, & Simms, 2005), and this has been mirrored by our results where 75% of individuals who met the cut off criteria for depression also met the cut off criteria for elevated anxiety.

Anxiety and depression frequently occur in people with ASD across the life span (Lever & Geurts, 2016; Uljarević et al., 2016; van Steensel, Bogels, & Perrin, 2011; Wigham et al., 2017) and have a significant negative impact on both individuals with ASD and their families. Although significant progress has been made regarding the assessment of anxiety and depression in youth with ASD (Rodgers et al., 2017; Uljarević et al., 2016), as well as in terms of understanding underlying mechanisms and developing treatment options for anxiety and depression in this population (Davis III, White, & Ollendick, 2014), the ability to effectively screen for the presence of anxiety and depression beyond early adolescence is currently limited due to the lack of validated ~~and sensitive~~ measures for this population.

Comment [mu10]: Change made in response to Comment 2 raised by Review 1

Several limitations need to be taken into account when interpreting our findings. First, as the sample consisted only of participants who were most likely in the normal range of intellectual functioning, it is not possible to generalize our finding to individuals with intellectual disability. Second, despite all participants meeting suggested cut-off scores for ASD on self-report measures of ASD severity (AQ-Short and SRS-2) and reported receiving clinical diagnosis of ASD, it was not possible to independently confirm diagnosis of ASD for the Australian sample. Finally, our study did not include clinical interview measures of anxiety. This will be important to include in the future studies in order to examine the sensitivity and specificity of the current HADS cut-off scores for the ASD population and provide revisions if necessary. Future studies should replicate our findings and further extend them by examining the applicability of HADS across adulthood and in individuals with lower cognitive ability, as well as investigating the levels of agreement with subject and informant versions of semi-structured and structured clinical interviews (e.g., ADIS).

Despite the above noted limitations, our study provides a significant contribution to the existing literature by presenting the first validation of any measure of anxiety and depression in a population of older adolescents and adults with ASD. The stable factor structure, good internal consistency, and solid validity suggest that HADS is a viable measure for assessing general levels of anxiety and depression in individuals with ASD.

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Accepted Article

Table 1. Descriptive Statistics

	Mean (SD)	Shapiro-Wilk Test
Australian sample		
CA	18.35 (2.55)	.93*
HADS-A	9.23 (3.99)	.97
HADS-D	5.91 (3.68)	.94*
WEMWBS	41.27 (9.64)	.93*
AQ-28	80.18 (9.47)	.95
DSM-5 DAS	13.74 (8.08)	.94*
PHQ-9	9.11 (6.84)	.93*
UK sample		
CA	16.04 (1.28)	.96**
HADS-A	9.23 (4.85)	.97*
HADS-D	5.33 (3.23)	.96**
WEMWBS	45.76 (8.17)	.99
SRS Total	121.84 (23.32)	.98
SDQ emotional symptoms	4.8 (2.51)	.97*
Whole sample		
HADS-A	9.23 (4.6)	.98*
HADS-D	5.50 (3.43)	.95**
WEMWBS	44.42 (8.84)	.98*

Note: * $p < .05$; ** $p < .01$

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Table 2. Factors Analysis, item-subscale correlations and item endorsement for Hospital Anxiety and Depression Scale

	Item	Item-subscale Correlations			Frequency ²			
	Factor	HADS-A	HADS-D	Fisher r-to-z	0 (%)	1 (%)	2 (%)	3 (%)
	Loading	r	r	Z				
Factor 1: Anxiety (30.07% of variance)								
I get sudden feelings of panic	.82	.78**	.20	7.25**	27.3	36.7	24	12
I get a sort of frightened feeling as if something awful is about to happen	.81	.73**	.08	7.3**	23.2	20.5	35.8	20.5
I get a sort of frightened feeling like 'butterflies' in the stomach	.79	.74**	.18	6.61**	31.8	47.7	14.6	6
Worrying thoughts go through my head	.70	.77**	.37**	5.44**	17.9	37.1	21.2	23.8
I can sit at ease and feel relaxed	.56	.68**	.34**	4.09**	17.9	42.4	31.8	7.9
I feel tense or 'wound up' ¹	.54	.68**	.43**	3.18**	9.3	58.3	21.2	11.3
I feel restless as I have to be on the move	.52	.56**	.12	4.41**	15.9	39.1	31.8	13.2
Factor 2: Depression (13.70% of variance)								
I look forward with enjoyment to things	.73	.24*	.70**	5.36**	53.0	29.8	13.2	4.0
I feel cheerful	.66	.37**	.65**	3.33**	31.1	49.7	12.6	6.6
I still enjoy the things I used to enjoy	.61	.20	.61**	4.35**	50.3	29.8	15.2	4.6

I can laugh and see the funny side of things	.50	.16	.47**	3.0**	68.7	24.7	4.7	2.0
I have lost interest in my appearance	.47	.14	.54**	3.98**	41.1	25.2	25.2	8.6
I can enjoy a good book or radio or TV program	.44	-.03	.40**	3.39***	61.6	28.5	4.6	5.3
I feel as if I am slowed down	.43	.27*	.58**	3.32***	26	49.3	11.3	13.3

Note: ¹this item also loads onto the Depression factor at .40; ²higher score implies higher frequency/severity; * p < .01; ** p < .001.

Table 3. Categorization of anxiety and depression across UK and Australian samples

		UK Sample (%)	Australian Sample (%)
HADS-A ¹	Below cut-off	41.5	36.4
	Above Cut-off	58.5	63.6
HADS-D ¹	Below cut-off	73.6	72.1
	Above Cut-off	26.4	27.9
SDQ-emotional symptoms ²	Normal	60	NA
	Borderline	12.4	
	Abnormal	27.6	
DSM-5Anxiety Scale ³	Below cut-off	NA	54.5
	Above cut-off		45.5
	Normal		55.6
	Moderate	NA	24.4
	Moderately severe		11.1
	Severe		8.9
PHQ-9 ⁴	Below cut-off		60
	Above Cut-off		40

Note: ¹ For both HADS-A and HADS-D a cut-off score of ≥ 8 been suggested (Brennan et al., 2010); ² For SDQ-emotional symptoms scores ≤ 5 indicate no problems, 6 borderline and 7-10 abnormal; ³ For DSM-5 Anxiety Scale cut-off score of > 14 indicates significant anxiety (Beesdo-Baum et al., 2012); ⁴ PHQ-9 provides two types of cut-off scores (1) normal/minimal (0-9), moderate (10-14), moderately severe (15-19), severe (20+), and also a cut-off >10 as indicative of major depression (Kroenke et al., 2001).

Table A. 1. Item-subscale correlations and item comparison between UK and Australian Samples

	Item-subscale Correlations								
	UK Sample	Australian Sample	Fisher r-to-z Z	UK Sample	Australian Sample	Fisher r-to-z Z	UK Sample	Australian Sample	Comparison
	HADS-A r	HADS-A r		HADS-D r	HADS-D r		Mean (SD)	Mean (SD)	χ^2, p
Factor 1: Anxiety									
I get sudden feelings of panic	.77**	.87**	1.79	.26**	.15	.66	1.18 (1.05)	1.22 (.89)	$\chi^2 = .07, p = .786$
I get a sort of frightened feeling as if something awful is about to happen	.76**	.68**	.96	.07	.20	.76	1.47 (1.09)	1.62 (.90)	$\chi^2 = .73, p = .393$
I get a sort of frightened feeling like 'butterflies' in the stomach	.76**	.59**	1.82	.24**	.09	.88	.96 (.89)	.88 (.66)	$\chi^2 = .30, p = .583$
Worrying thoughts go through my head	.79**	.73**	.82	.35**	.43**	.54	1.46 (1.05)	1.56 (1.01)	$\chi^2 = .32, p = .575$
I can sit at ease and feel relaxed	.67**	.65**	.20	.35**	.42**	.47	1.25 (.92)	1.28 (.64)	$\chi^2 = .05, p = .822$
I feel tense or 'wound up'	.66**	.76**	1.16	.48**	.38**	.70	1.36 (.81)	1.30 (.73)	$\chi^2 = .19, p = .66$
I feel restless as I have to be on the move	.56**	.56**	0.00	.16	.15	.06	1.49 (.93)	1.24 (.79)	$\chi^2 = 2.67, p = .104$
Factor 2: Depression									
I look forward with enjoyment to things	.23*	.38**	.95	.66**	.84**	2.45*	.71 (.85)	.62 (.85)	$\chi^2 = .38, p = .536$
I feel cheerful	.40**	.36*	.27	.64**	.73**	.98	.91 (.86)	.92 (.80)	$\chi^2 = .001, p = .969$
I still enjoy the things I used to enjoy	.18	.29*	.67	.60**	.61**	.09	.74 (.89)	.74 (.78)	$\chi^2 = .001, p = .980$

I can laugh and see the funny side of things	.16	.22	.36	.43**	.61**	1.43	.36 (.65)	.45 (.68)	$\chi^2 = .65, p = .423$
I have lost interest in my appearance	.17	.19	.12	.59**	.49**	.81	1.00 (1.05)	.98 (.87)	$\chi^2 = .014, p = .906$
I can enjoy a good book or radio or TV program	.001	-.15	.87	.40**	.38**	.14	.48 (.82)	.70 (.76)	$\chi^2 = 2.68, p = .104$
I feel as if I am slowed down	.29**	.27	.12	.55**	.59**	.34	1.05 (.90)	1.24 (1.01)	$\chi^2 = 1.49, p = .224$

Note: * $p < .01$; ** $p < .001$.

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