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Matrix Reasoning and Anhedonic Depression in Male Adolescents with Autism

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Abstract

Background: Almost half of samples of young people with Autism Spectrum Disorder (ASD) experience depression but little is known about the role of overall and specific cognitive function in that depression. Investigation of this link could help explain the pathway between cognitive function and depression.

Methodology: Fifty-one male adolescents with ASD, plus 18 male adolescents without ASD, completed the Wechsler Abbreviated Intelligence Scale (2nd ed.) (WASI-II) plus the Child and Adolescent Symptom Inventory-Depression (CASI-MDD) subscale. Data were analysed at the global (total IQ, depression) and subtest (IQ) and symptom (depression) levels.

Results: Although there were no significant differences in overall IQ or any of the WASI-II subtests between the ASD and non-ASD samples, the ASD sample had significantly higher CASI-MDD scores. There was a significant correlation between global IQ and Matrix Reasoning with CASI-MDD total and anhedonia scores for the ASD sample, but no significant correlations between these variables for the non-ASD sample.

Conclusions: Matrix Reasoning appears to be implicated in the development of anhedonic depression in adolescents with ASD.

Keywords: Autism; Matrix Reasoning; Depression; Anhedonia

Introduction

Autism Spectrum Disorder (ASD) includes a range of neurodevelopmental conditions characterised by difficulties in understanding social interaction and social communication, plus the presence of restricted and repetitive behaviours [1]. Comorbidity of other psychological disorders in young people with ASD is relatively high at over 90% [2], and the prevalence of Major Depressive Disorder (MDD) is one of those comorbid disorders that is significantly elevated in young people with ASD compared to their Non-ASD (NASD) counterparts [2]. For example, one recent study of 70 young males with ASD and 50 NASD peers (all aged between 6 yr and 18 yr) found that the prevalence for MDD among the ASD males was 47.1% compared to just 3.9% for the NASD males [3].

Depression has major aversive effects on overall functioning. For example, in the general community, depression adversely affects physical health, relationships and cognitive performance, produces the greatest decrement in personal health, is among the highest cost of care for chronic diseases [4] and has been described as the major contributor to total disease burden [5]. A similar picture has been found for individuals with ASD, where higher levels of depression have been associated with poorer global functioning in children and adolescents [6]. However, initial treatments for MDD succeed as infrequently as one-third of the time, often with significant inter-patient variability in outcomes [7]. It has been suggested that at least some of this variability in treatment outcomes may be the result of differences between patients' correlates of depression [8] and their particular symptom profiles [9]. Assessment of predictors of MDD and the symptom profiles of patients has been suggested as a possible method for increasing the efficacy of treatments by individualizing treatment to symptom profiles [10].

In the search for possible correlates of elevated depression in ASD, cognitive ability has been directly and significantly associated with depression in adults with ASD [11] but no data have been reported for

this association in younger people with ASD. In addition, although IQ is often used to represent global cognitive ability, the standard models of IQ refer to a number of components of overall intelligence, including such factors as fluid intelligence, crystallized intelligence, verbal and perceptual aspects of intelligence, etc. [12], and these are differentially measured in IQ scales that produce specific subtest data. Initial examination of the symptom profiles of MDD in boys with ASD has recently suggested that it is more severely anhedonic than sad [3], but the association between overall and specific aspects of cognitive ability and symptom profiles of MDD was not examined at a detailed level in that study.

In order to focus on the role of IQ as a correlate of depression among young people with ASD at general and specific levels, we measured the association between global IQ and four of its major components and total and symptom scores for MDD. To enable comparisons with non-ASD peers, we collected data from a sample of young people with ASD and also from a non-ASD sample matched for age and IQ. The current prevalence of ASD has an average ratio of 4:1 across boys and girls [1], and so a male-only sample was chosen to maximise generalisability. Similarly, due to the increase in MDD during adolescence [1], young males aged between 13 and 17 were recruited for this study. The overwhelming body of research on treatment efficacy for depression has been conducted on the non-ASD population, with a normal IQ

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distribution. Therefore, in order to maximise the possibility of using the findings for the purposes of recommending possible treatments for depression among adolescents with ASD, the sample was restricted to those who were described as 'high-functioning' by their parents, and who had an IQ score of at least 70. Finally, the previous work with adults with ASD reported above [11] used data for the Full Scale IQ, Performance and Verbal IQ Composite Scores from the Wechsler Adult Intelligence Scale - Third Edition (WAIS-III). These are summary scores, compiled from several individual subtests such as Vocabulary, Similarities, Block Design, and Matrix Reasoning. The measurement of the association between MDD and these specific subtests of cognitive ability has not previously been reported for adolescents. Moreover, use of those subtests that each tap a particular aspect of overall IQ allows for some initial hypothetical allocation of the results to particular brain regions, depending upon the cognitive ability that is measured by those subtests. Therefore, based on the previous work on overall cognitive ability and depression in ASD adults reported above [11], it was hypothesised that higher overall and subtest IQ scores would be significantly and directly associated with higher rates of MDD.

Materials and Methods

Participants

ASD sample: The ASD sample consisted of 51 male adolescents aged between 13 yr and 18 yr (M age=14.6 yr, SD=1.5 yr) plus one of their parents (3 fathers, 48 mothers) for consent purposes. All these adolescents had received a diagnosis of ASD *via* the Autism Diagnostic Observation Schedule (ADOS) [13] by a research-reliable assistant during recruitment; they all also had a Full Scale IQ above 70 on the Wechsler Abbreviated Scale of Intelligence (2nd ed.) (WASI-II) [14] measured as part of the recruitment process. They had adequate reading skills to comprehend the self-assessment process using the CASI described below, and were able to undertake sufficient self-care and attend a mainstream school, so that their parents described them as 'high-functioning'. These participants were recruited from parent support groups and other service organisations in Queensland, Australia. Their parents reported that 14 of their sons also had a diagnosis of ADHD (n=10), OCD (2), or a combination of these disorders (2).

Non-ASD (NASD) sample: The NASD sample consisted of 18 males (M age=14.7 yr, SD=1.6 yr, range=13 yr to 18 yr) plus their mothers for consent purposes. These participants were recruited from local schools *via* a newsletter to parents. All parents gave written informed consent for their sons to participate and their sons gave verbal or written assent to participate, depending upon their age. None of the boys had any reported indications of ASD or other disorders.

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Materials

IQ: The WASI-II [14] is a screening test of intelligence that possesses strong validity with the WISC-IV when used with high-functioning people with ASD. It contains four subtests (Vocabulary, Similarities, Block Design, Matrix Reasoning) with average reliability coefficients of between 0.92 and 0.96, which are computed to two composite scores (Verbal Comprehension, Perceptual Reasoning) and a Full Scale IQ score. The Full Scale score, plus all four subtests were measured in this study. For the four subtests, the T-Scores were used to avoid any confounds due to age-related differences in raw scores.

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Depression: MDD was measured *via* the fourth edition of the Child and Adolescent Symptom Inventory (CASI-4), which consists of 148 items drawn from DSM-IV diagnostic criteria for a range of psychiatric disorders. Responses indicate the frequency of symptoms, rated on a four-point Likert scale ranging from 0 (never) to 3 (very often). The CASI-4 has satisfactory internal consistency (r=0.74). Prior research has supported the use of the CASI-4 with ASD children and the CASI-4 test manual provides normative data for ASD children [15,16].

The CASI-4 consists of several subscales. The subscale relating to MDD (called the CASI-MDD here) consists of 10 items and includes the nine diagnostic criteria for MDD in the DSM-5 [1] plus the 'irritability' symptom that may be present in children as an additional or replacement symptom for depressed mood. Six of the CASI-MDD items measure the symptoms of irritability, feeling depressed, anhedonia, and suicidal ideation, feelings of worthlessness or guilt, and fatigue via responses of "Never", "Sometimes", "Often" or "Very often", which correspond to values of 0 through to 3. Four other items measure change in appetite or weight, sleeping habits, activity level, and ability to concentrate or make decisions; responses for these items are "Yes" or "No", scored as 1 or 0 respectively. Thus, the possible range of scores for the CASI-MDD is from 0 to 22. The CASI-MDD has been used in studies of children with an ASD [16] and has sensitivity of 0.81 and specificity of 0.73 with clinical diagnoses [15]. Construct validity is high because of the inclusion of the diagnostic criteria for MDD set out in the DSM-5 [1] and discriminant validity against clinical diagnosis (p<0.001) [17]. Normative data for the CASI-MDD are described in the CASI-4 Test Manual and elsewhere [15] and psychometric data indicate satisfactory (p<0.001) test-retest reliability over a six-week period and internal consistency (Cronbach's alpha) of 0.74 [15].

Procedure

Data-collection was conducted in the adolescents' homes to reduce the likelihood of stress or anxiety that might accompany transfer to a different location for assessment. All the adolescents were given written instructions for completion of the CASI-MDD at the same time (approximately 30 min after waking in the morning) so as to reduce the confounding effects of daily events. WASI-II assessments were conducted within two weeks before these procedures. The study protocol was approved by the Bond University Research in Human Ethics Committee, according to the standards set out in the 1964 Helsinki declaration and its later amendments.

Statistical analysis

Data were analysed via IBM SPSS 24. Descriptives was used to obtain mean, SD, 5% trimmed mean, ranges, and normality was assessed by the Kolmogorov-Smirnov statistic. Internal consistency was evaluated for the CASI-MDD subscale. MANOVA was used to determine the presence of any significant differences between the WASI-II Full Scale and subtest scores, and for the CASI-MDD subtest, for the ASD and NASD samples, with age as a covariate. Pillai's Trace and the Type II Sum of Squares model were used to determine the MANOVA main and univariate effects because of the difference in sample sizes, and appropriate Bonferroni corrections were applied to the alpha level when testing univariate effects for the four WASI-II subtests because of their relatedness. The associations between WASI-II scores and CASI-MDD were examined with Pearson correlations and Spearman correlations, as appropriate. Because of the disparity in sample sizes across the ASD and NASD groups, results from those correlational analyses were evaluated by reference to the overall strength of the relationships as well as the statistical significance of outcomes.

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Results

Data

All raw data met the requirements for normality and no transformations were required. Table 1 shows the age, WASI-II and CASI-MDD data for the two samples. There was a significant MANOVA main effect F (7,61)=4.737 (Pillai's Trace), p<0.001, μ 2=3.52, and the univariate tests for differences between the ASD and NASD participants are presented in Table 1. There was no significant inter-group difference in the ages or the WASI-II Fullscale score or any of the four subtests (at the corrected p value of 0.05/4=0.0125 to account for family-wise error rate in the four related subtests of IQ), but the ASD sample had a significantly higher CASI-MDD score than the NASD sample, as is expected from the previous literature regarding the elevated depression status of young males with ASD. There was no significant correlation between age and CASI-MDD scores for either the ASD sample r=0.119, p=0.404, or the NASD sample r=0.291, p=0.242, nor between the ages of these two subsamples any of their WASI-II scores (all r<0.291, p>0.094).

IQ and MDD

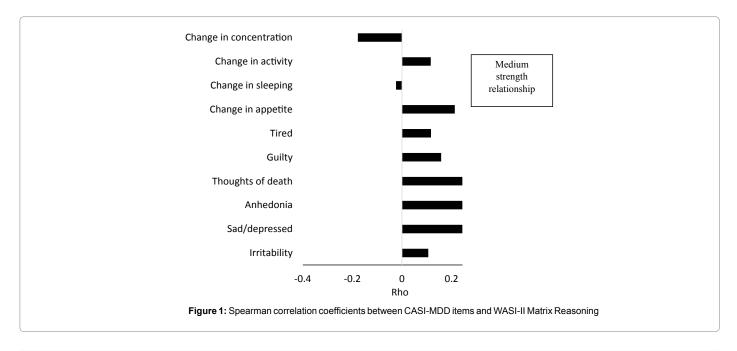
Because of the significant difference between the CASI-MDD scores of the two samples, testing for presence of a significant correlation between IQ and MDD was undertaken within each sample separately. For the ASD participants, there was a significant Pearson correlation between WASI-II Fullscale score and CASI-MDD total score (r=0.325, p=0.020) but the same association was not statistically significant for the NASD participants (r=0.290, p=0.244). When examined at the level of the four WASI-II subtests, there was only one significant correlation, and that was between WASI-II Matrix Reasoning and CASI-MDD total score for the ASD participants r=0.305, p=0.030. This association was further explored at the MDD symptom level.

Matrix Reasoning and MDD symptoms in ASD

To explore the precise ways in which Matrix Reasoning was associated with the various discrete symptoms of MDD in the ASD participants, Spearman correlation coefficients (because of the four-point categorical scale for each CASI-MDD item responses) were calculated for each of the 10 CASI-MDD symptoms and total Matrix Reasoning score. The correlation coefficients for each CASI-MDD item and Matrix Reasoning are shown in Figure 1, and indicate that only one of the coefficients between Matrix Reasoning and CASI-MDD items reached the Bonferroni-adjusted level of significance of 0.005 or the medium strength relationship (0.29-0.49) defined by Cohen [18] and depicted by the vertical dashed line. That association was for the CASI-MDD item "I am not interested in or enjoy nice or fun activities" (r=0.417, p=0.002), accounting for 17.4% of the variance between Matrix Reasoning and this index of anhedonia. This was also the only CASI-MDD item to show an association with Matrix Reasoning that was above the 'small' level [18]. When examined at the WASI-II Full Scale IQ level, the same isolated significant correlation at the corrected p value was found with this CASI-MDD anhedonia item (r=0.400, p=0.004).

Variable		ASD M (SD)	NASD M (SD)	F	р	Partial eta square
Age		14.6 (1.5)	14.7 (1.6)	0.101	0.752	0.022
WASI-II	Full Scale	94.9 (10.9)	100.2 (10.5)	3.236	0.077	0.046
	Vocabulary T score	44.1 (7.5)	47.2 (6.3)	2.391	0.1271	0.034
	Similarities T score	43.1 (8.2)	48.1 (6.9)	5.231	0.0251	0.072
	Block Design T score	50.1 (9.1)	51.1 (8.9)	0.174	0.6781	0.003
	Matrix Reasoning T score	51.9 (7.6)	54.3 (7.5)	1.367	0.2461	0.02
CASI-MDD		5.6 (3.7)	1.7 (1.6)	19.462	< 0.001	0.225

Table 1: Mean (SD) data for age, WASI-II and CASI-MDD scores for ASD and NASD participants, plus univariate F results



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Discussion

Four major findings emerged from this study. First, the significant direct association between total IQ and MDD for the ASD adolescents extends the previous report of the same association for adults [11] to a younger age group. Second, that previous finding was found for just one of the underlying four WASI-II subtests that are used to calculate the Full Scale IQ. Third, the associations between Full Scale IQ and MDD, and between Matrix Reasoning and MDD, were both direct, with higher IQ scores being significantly associated with higher MDD scores. Fourth, when examined at the MDD symptom level, the significant associations between MDD and Full Scale IQ and Matrix Reasoning was for the single CASI-MDD item used to measure anhedonia, also as direct correlations.

As such, these findings provide some support for suggestions made some time ago that awareness of their 'failure' in social interaction and communication is significantly associated with depression for adolescents with ASD [19,20]. Thus, greater awareness (as a product of higher WASI-II Full Scale IQ) of that shortcoming in social interaction and communication was associated with more severe depression in his study, as it has been in previous studies of ASD adults [11]. The additional finding that it was Matrix Reasoning alone of the four WASI-II subtests that was significantly associated with elevated CASI-MDD scores (and specifically anhedonia), suggest a more specific association between overall cognitive ability and these adolescents' self-rated higher depression scores.

It is relevant to describe how Matrix Reasoning is measured so as to better understand how the cognitive skills inherent in it might relate to depression in adolescents with ASD. Respondents are shown a series of coloured matrices or pictures, in which the last picture/matrix has one component missing. A set of possible options for the missing section is offered, and test-takers choose which option they think is correct. That choice is based upon an understanding of the relationships between the previous matrices or pictures in the series and then predicting what the next (missing) matrix/picture should look like. As such, Matrix Reasoning tests measure "visual-perceptual analogic reasoning ability without a speed component" [21, p.340], particularly the cognitive skills of nonverbal fluid reasoning, induction, reasoning ability, and ability to form analogies. Many of these cognitive skills are involved in understanding complex social situations and deciding how to interact in them. There is evidence that young people with ASD desire to socially interact with their peers [22], and that learning how to do so successfully is associated with reduced depression [23]. As such, being able to better understand the need to socially interact appropriately (outcomes of high Matrix Reasoning scores) but also being unable to do so (because of their ASD), may be understandably associated with frustration and depression.

Although any such explanation must be tentative because of its reliance on mental testing rather than direct measurement of brain function, it may be that a specific area of the brain could be involved in the association between Matrix Reasoning and depression. For example, Matrix Reasoning processes are thought to occur in the Pre-Frontal Cortex (PFC) [24], particularly the most anterior region of the PFC known as the rostral prefrontal cortex (rPFC) [25]. This region is implicated in the ability to combine remote information in a meaningful manner to form 'gestalts' rather than focussing upon peripheral items of information [26]. The current findings therefore raised the possibility that this brain region may be implicated in the association between reduced ability to socially interact and depression among adolescent males with ASD. This possibility requires a great deal

of further investigation before it could be considered as likely, but may present a valuable focus for future research using information collected directly regarding brain function (e.g., from EEG or fMRI studies) for confirmation.

The significant association between Matrix Reasoning and anhedonia is congruent with information about the profile of depressive symptomatology in boys with an ASD, which has recently been shown to be more severely anhedonic [3] rather than exhibiting sadness (the second major identifier of MDD). Parents' ratings of their adolescent sons' tension in social situations has also been significantly correlated with the anhedonia experienced by these young males with ASD [27]. As defined in the DSM-5 [1], anhedonia is usually felt towards previously-valued rewards rather than new rewards. If this model of anhedonia were applied to the current data, then it may function in the following steps: (a) as proficiency increased in cognitive tasks that involved fluid intelligence or an ability to comprehend the 'gestalt' of social events and stimuli, so did (b) awareness of the value of social interaction as rewarding, but (c) an also increasing awareness of an ASD-related reduced ability to undertake those social interactions tasks successfully, leading (d) to frustration, general depression and specific anhedonia regarding those (unavailable) social interaction rewards. This hypothetical model is untested as yet and requires further investigation before it can be considered as explaining the reason why depression in young people with ASD is often anhedonic.

These findings have two major clinical implications. First, in terms of assessment protocol to understand ASD-related depression in young males with ASD, it may be valuable to also investigate whether (a) overall depression is actually anhedonic, (b) Full Scale IQ and Matrix Reasoning are elevated, (c) the person with ASD also experiences greater difficulty in social interactions, and (d) they appear to have withdrawn from such interactions. Second, direct clinical treatment of anhedonia is difficult because it is likely to be resistant to rapport-building strategies from psychotherapists, or suggestions to undertake the kinds of cognitive-behavioural 'homework' activities that are designed to help persons suffering from anhedonia to build more satisfying lifestyles and which may be used with patients who exhibit depressed mood without anhedonia [28]. Medication might be considered, at least as an adjunctive therapy in some cases. Alternately, the process of teaching young people with ASD to undertake successful social interactions has been shown to lead to reduced depression [23], and it may that this psychoeducational treatment model might be beneficial.

As in all research, there are several limitations upon the generalisability of the present data. The sample was recruited in a specific geographical and cultural region, and consisted of males or a selected age only; extension to other settings and to females would be valuable. Recruitment of younger and older participants would enable testing of the generalisability of these findings across age groups. Similarly, recruitment in this study was via parent referral, and it may be that those parents who responded to the call for participants are atypical in some way (e.g., take more interest in their child's welfare). The CASI-MDD data were collected from the adolescents' self-reports, as is common and accepted, but diagnoses of MDD from parents or a clinician would provide greater validity. The limitations of the current study's design as a 'snapshot' study would be reduced by collection of prospective data over a period of time. Finally, although the specific focus of this study was high-functioning adolescents with ASD, the restriction of IQ to >70 also restrict the generalizability of the results to young people with ASD who have lower IQ scores. However, as mentioned in the Introduction, possible therapy for depression may be

easier to apply to high-functioning patients, and so this limitation has some basis. Strengths of this study were the use of sound measures of Matrix Reasoning and MDD, that data were collected under controlled conditions, and that the samples of ASD and NASD boys were matched on age and IQ.

Not withstanding these limitations, the current data extend the field by reporting on the association between IQ and depression in an adolescent sample, by drilling down into the component subtests of IQ that comprise the WASI-II Full Scale score, and by examining MDD at its symptom level. These findings provide some greater understanding of how relatively high-functioning adolescent males with ASD cope (or fail to cope) with their feelings of frustration about their relative inability to interaction socially, and which aspects of their cognitive function are most closely related to those feelings of anhedonia that result from their ASD-related difficulties in undertaking effective social communication.

Compliance with ethical standards

Conflict of interest

The authors declare that they have no conflict of interest.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/ or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent

Informed consent was obtained from all individual participants included in the study.

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