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Psychopathology in Williams syndrome: the effect of individual differences across the lifespan

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Psychopathology in Williams syndrome: the effect of individual differences across the lifespan

Abstract

The present research aimed to comprehensively explore psychopathology in Williams syndrome (WS) across the lifespan and evaluate the relationship between psychopathology and age category (child or adult), gender and cognitive ability. The parents of 50 participants with WS, aged 6-50 years, were interviewed using the Schedule for Affective Disorders and Schizophrenia for School-Age Children (K-SADS-PL). The prevalence of a wide range of Axis I DSM-IV disorders was assessed. In addition to high rates of anxiety and Attention Deficit Hyperactivity Disorder (ADHD) (38% and 20% respectively), 14% of our sample met criteria for a depressive disorder and 42% of participants were not experiencing any significant psychopathological difficulties. There was some evidence for different patterns of psychopathology between children and adults with WS and between males and females. These relationships were largely in keeping with those found in the typically developing population, thus supporting the validity of applying theory and treatment approaches for psychopathology in the typically developing population to WS.

Psychopathology in Williams syndrome: Similarities and individual differences across the lifespan

Williams Syndrome (WS) is a genetic disorder characterised by a microdeletion of a sequence of genes on chromosome 7 including the gene for Elastin (ELN; Ewart et al., 1993). Cases occur sporadically and affect both genders equally. Prevalence is estimated to be around 1 in 20,000 (Martin, Snodgrass, & Cohen, 1984), however a higher rate of 1 in 7,500 has been reported (Stromme, Bjornstad, & Ramstad, 2002). Although there is some phenotypic heterogeneity (Mervis, Morris, Bertrand, & Robinson, 1999; Porter & Coltheart, 2005), the deletion typically results in dysmorphic facial features and short stature, medical problems such as supravalvular aortic stenosis, a mild to moderate intellectual delay and high levels of anxiety and attention problems.

Only a small body of work has explored psychopathology in large cohorts of WS individuals. The most consistently reported psychopathological findings support early descriptions of increased rates of hyperactivity, attention problems, anxiety and phobias in the WS population (Von Armin & Engel, 1964), when compared to intellectually impaired control groups (Dykens, 2003; Einfeld, Tonge, & Florio, 1997; Udwin, 1990). The present research aims to explore the prevalence of a wide range of psychopathology in children and adults with WS, using a diagnostic interview measure, and to explore the relationship between psychopathology and three individual difference variables in WS: age category (childhood vs adulthood), gender and cognitive ability.

The majority of research exploring psychopathology in WS has used behavioural questionnaires or checklists. These methods provide an efficient means of gathering data on large groups of subjects and have made a significant contribution to

understanding of emotional and behavioural difficulties in WS. The utility of these measures is, however, constrained by a number of limitations and more recent research has utilised interview measures validated against the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV; American Psychiatric Association, 1994).

These recent research findings have extended knowledge by demonstrating that individuals with WS not only experience high rates of anxiety and attention problems, but also increased rates of a number of clinical diagnoses. For example, Dykens (2003) conducted a detailed investigation of anxiety and fears in individuals with WS using the anxiety disorders section of the Diagnostic Interview for Children and Adolescents (DICA-R; Reich, 2000). The results indicated that 18% of the participants with WS presented with Generalised Anxiety Disorder (GAD) and 35% presented with Specific Phobia. Dykens (2003) further noted that 16% of WS participants met criteria for more than one anxiety disorder and highlighted the need for research assessing the comorbidity of anxiety and other psychiatric disorders.

The most thorough investigation of psychopathology in WS to date (Leyfer, Woodruff-Borden, Klein-Tasman, Fricke, & Mervis, 2006) utilised the Anxiety Disorders Interview Schedule (ADIS-IV; Silverman & Albano, 1996). Participants were aged between 4 and 16 years. The results supported previous findings of high rates of anxiety; 53.8% of the sample met criteria for a current diagnosis of Specific Phobia and 11.8% met criteria for a current diagnosis of GAD. Chavira, Stein, Bailey & Stein (2004) used the ADIS-IV to assess the prevalence of anxiety disorders in a large cohort of typically developing children and found that 3% met criteria for GAD and 10% met criteria for Specific Phobia. In comparing these prevalence rates to those

reported by Leyfer et al. (2006) it is apparent that individuals with WS may be at increased risk for these two anxiety disorders.

In addition to the high rates of anxiety disorders, Leyfer et al. (2006) also found that 64.7% of their sample met criteria for ADHD. Of those with ADHD, the majority met criteria for the Inattentive subtype. With regards to comorbidity, Leyfer et al. (2006) reported that half of their WS cohort met criteria for more than one diagnosis. In keeping with patterns of comorbidity found in the typically developing population, ADHD and Specific Phobia commonly co-occurred.

The research discussed has made an important contribution to the literature on psychopathology in WS by highlighting specific areas of risk. The findings further indicate that there is extensive heterogeneity within WS in terms of psychopathology; it is clear that not all individuals with WS meet diagnostic criteria for ADHD, GAD or Specific Phobia. Despite the progress made by recent research, there are a number of important limitations that need to be addressed: there has been no thorough examination of Axis I DSM-IV diagnoses in both children and adults with WS, as a result of this, research relating to diagnoses that are more common in adults such as psychosis and depression is severely lacking and descriptions of comorbidity are consequently limited. The present research aims to address these limitations whilst also exploring the relationship between psychopathology and three individual difference variables: age category (childhood vs adulthood), gender and cognitive ability.

Individual differences variables and psychopathology

There are a number of advantages to using diagnostic interviews validated against DSM-IV to assess psychopathology in WS. In particular, categorising symptoms according to DSM-IV diagnoses provides an opportunity to apply the

extensive knowledge that is associated with these diagnoses in typically developing individuals, to the WS population. However, Karmiloff-Smith (1998) highlights that although the behaviour of individuals with neurodevelopmental disorders may appear to be the same as that observed in typically developing individuals, it cannot be assumed that the underlying causes or processing mechanisms are also the same; similar end-states are possible via highly divergent developmental trajectories. Following this reasoning, before applying theory and treatment approaches based on work with typically-developing individuals to the WS population, we must first examine whether the causes and processes associated with the diagnoses are comparable in both populations. The present research aims to address this issue by examining associations between specific DSM-IV diagnoses and individual difference variables in WS and comparing these relationships with those reported for the typically-developing population. Further to this, examining these associations may also indicate possible sources of heterogeneity within the presentation of psychopathology in WS. The relationships between DSM-IV diagnoses and age category, gender and cognitive ability in the typically-developing population and in WS, will now be discussed.

Age category

In the typically developing population, ADHD and Specific Phobia generally have an early onset in childhood and depressive disorders and psychosis have a later onset in adolescence and adulthood (American Psychiatric Association, 1994; Lewinsohn, Clarke, Seeley & Rohde, 1994; Pineda et al., 1999). Onset of GAD typically occurs in later adolescence, although a subgroup of typically developing individuals develop GAD in mid-adulthood (Campbell, Brown, & Grisham, 2003). Very little research has explored age related changes in psychopathology in WS

across the lifespan (childhood to adulthood), although questionnaire-based research has indicated increased fears in older females with WS (Blomberg, Rosander, & Andersson, 2006; Dykens, 2003), and increased levels of withdrawal and depressive symptoms in adolescence and adulthood (Gosch & Pankau, 1997).

Several researchers have considered the effect of chronological age on psychopathology in children with WS, but findings are somewhat inconsistent. For example, Switaj (2000) examined differences between childhood, adolescence and late adolescence and found that as children aged, prevalence of anxiety increased. Leyfer et al. (2006) found a higher presence of GAD, but not Specific Phobia, with increasing age and found that ADHD was most prevalent in the 7-10 years age group, when compared with younger and older groups of children. These findings stand in contrast to those reported by Einfeld, Tonge, & Rees (2001) who conducted a longitudinal study of psychopathology in WS and reported that, with increasing age, children with WS showed slight reductions in levels of psychopathology.

Gender

In the typically developing population, externalising disorders such as ADHD tend to be more common in males and internalising disorders, such as depression and anxiety, tend to be more common in females, at least in adulthood (American Psychiatric Association, 1994; Gaub & Carlson, 1997; Parker & Hadzi-Pavlovic, 2004). Reports of the effect of gender on psychopathology in WS are scarce and findings are inconclusive. There is some evidence to suggest that fears/phobias are more common in females than in males with WS (Blomberg et al., 2006; Dykens, 2003). It has also been reported that adolescent and adult females with WS are less happy and more tearful than age equivalent males (Gosch & Pankau, 1997). Leyfer et al. (2006) reported no significant effect of gender on diagnostic status for ADHD,

Separation Anxiety, Specific Phobia and GAD, although a higher proportion of males met criteria for ADHD and a higher proportion of females met criteria for GAD.

Cognitive ability

There is evidence that both general and specific cognitive deficits co-occur with certain psychiatric diagnoses within the typically developing population. Whitaker and Read (2006) conducted a meta-analysis and reported that there is evidence for increased rates of psychiatric disorders in children, but not adults, with intellectual disabilities. However, there is little evidence for any relationship between intelligence and psychiatric disorders for adults or children whose cognitive ability falls within the normal range (Morasco, Gfeller & Chibnall, 2006; Rutter, 1964). With regards specific cognitive abilities, the following associations with psychopathology have been reported. In typically developing children, anxiety can cause specific impairments in verbal skills; word recognition, short-term verbal memory and verbal fluency, but not speed of processing or motor performance (For example, see Kusche, Cook, & Greenberg, 1993; Werry, Elkind, & Reeves, 1987). It contrast, recent research has reported that Specific Phobia and GAD do not affect neuropsychological functioning in adults (Airaksinen, Larsson, & Forsell, 2005). Depression in adults has been consistently associated with processing speed deficits (Tsourtos, Thompson, & Stough, 2002) and impairments in executive function and memory (Egeland et al., 2005). Deficits in executive function are also commonly reported in individuals with ADHD; these include response inhibition, working memory, and planning (Willcutt, E, Nigg, Faraone, & Pennington, 2005).

Extensive interest has been placed on cognitive functioning in WS, with reports of mild to moderate intellectual disability in the context of marked peaks and valleys in specific cognitive skills. Despite this interest in cognition in WS, there is a

dearth of research considering the relationship between cognitive and psychopathological aspects of the WS behavioural phenotype. There is evidence that the cognitive profile of WS is heterogenous (Porter & Coltheart, 2005; Stojanovik, Perkins & Howard, 2006). Consequently, in addition to examining whether any relationships between cognition and psychopathology in WS are consistent with those reported for the TD population, it will also be of interest to examine whether there is any relationship between cognitive heterogeneity and the heterogeneity that is apparent in the psychopathological profile of individuals with WS.

The few studies that have explored the relation between cognition and psychopathology in WS have utilised a general cognitive ability quotient (Dykens and Rosner, 1999; Leyfer et al., 2006). Such a quotient represents the individuals' average performance over numerous cognitive tasks that measure different abilities. Given the well-documented uneven cognitive profile reported in WS, these abilities are likely to be discrepant (Bellugi, Lichtenberger, Jones, Lai, & St, 2000). Consequently, a general cognitive ability quotient may not be particularly meaningful in WS. It is perhaps not surprising then, that studies exploring the relation between FSIQ and psychopathology in WS have failed to find significance. For individuals with WS, it is particularly important that specific cognitive skills are considered, rather than a general measure such as IQ, when exploring the relationship between cognition and psychopathology.

Aims and hypotheses

Given the findings discussed and the limitations of previous research exploring psychopathology in WS, the first aim of the present research was to extend previous findings using a comprehensive measure of psychopathology in children and adults with WS and to report prevalence rates and patterns of comorbidity. The

second aim of the current research was to examine the relationship between psychopathology and age category (childhood vs adulthood), gender and specific cognitive abilities in WS in order to explore whether the relationships are in keeping with those reported for the typically developing population and to identify potential sources of heterogeneity in psychopathology in WS.

In relation to the first aim, the predictions are that anxiety disorders (in particular Specific Phobia) and ADHD will represent the most prevalent diagnoses in our cohort of individuals with WS, and that there will be a high comorbidity between Specific Phobias and ADHD, as reported previously (Leyfer et al., 2006). In relation to the second aim, we will evaluate the hypothesis that relations between psychopathology and age category, gender and cognition observed in WS are consistent with the general population.

Method

Participants

Participants were 50 individuals (26 female, 24 male) with Williams syndrome (WS), aged between 6 and 50 years. Of these, 30 were aged 17 years and below and 20 were aged 18 years and above, these two sub-groups of participants will be referred to as the Child group and Adult group respectively. The age, gender and mental age of these two groups are shown in Table 1. Participants were recruited through the Williams syndrome associations of New South Wales, Victoria and South Australia and through an online WS forum. All participants were negative for the elastin gene when tested using the Fluorescent in situ hybridization (FISH) test. The mental age of participants was assessed using the Woodcock-Johnson Test of Cognitive Ability – Revised (WJ-COG-R; Woodcock & Johnson, 1989, 1990). The mean mental age of the entire sample was 6 years 3 months (range: 2.16 – 10.58

years); typical of the WS population. The mean mental ages of the Child and Adult groups are shown in Table 1.

[Insert Table 1]

Materials

Current diagnostic status, according to DSM-IV criteria, was obtained through an interview with the primary care-giver using the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL; Kaufman, Birmaher, Brent, Rao, & et al., 1997). As is standard procedure when assessing an intellectually impaired population, only caregivers were interviewed. The use of caregiver report for the diagnosis of psychopathology in adults with intellectual disabilities is discussed by Cooper, Melville and Einfeld (2003). These authors highlight that even adults with mild intellectual disabilities may have difficulty describing inner emotional experiences and accurately providing a full account of experiences. Consequently, assessors must rely on caregiver report even in adults with intellectual disabilities.

The K-SADS-PL is a semi-structured diagnostic interview that assesses 32 DSM-IV Axis I child psychiatric diagnoses. The interview assesses both current and past psychopathology. For a diagnosis to be considered 'past' the participant must have been symptom-free for 2 months. Given the difficulty inherent in asking parents of adult participants to accurately recall behaviour across the participant's life, only current prevalence rates will be reported.

A principal aim of the present research was to compare psychopathology in children and adults with WS. For ease of comparison, it was desirable to use a single instrument with both age groups. However, there is no diagnostic interview currently available that has been designed for use with both children and adults. Given the

developmental level of the participants, an instrument developed for use with children, that allowed caregiver report, was deemed most appropriate. The K-SADS-PL also has the advantage that it is semi-structured, which allows the interviewer to phrase questions such that they are appropriate for the participant's chronological age.

The K-SADS-PL has been used extensively for diagnosing Axis I disorders in typically developing children (Cortes et al., 2005; Hakko et al., 2006; Rucklidge, 2006) and has been used successfully with intellectually impaired populations (Antshel et al., 2006; Masi, Brovedani, Mucci, & Favilla, 2002). The K-SADS-PL also has excellent psychometric properties including an inter-rater reliability that is highly competitive with other diagnostic interviews, and has been validated against a number of other popular measures (Kaufman & Schweder, 2004).

The interviewer completed appropriate training provided by the authors of the K-SADS-PL. A registered Clinical Psychologist supervised the interviews and scoring.

The Woodcock-Johnson Test of Cognitive Ability – Revised (WJ-R COG; Woodcock & Johnson, 1989, 1990) was used to assess cognitive ability. Both the standard and supplemental battery were administered. The WJ-COG is a standardised test that provides age equivalent and standard scores for General Cognitive Ability (GCA) and cognitive cluster variables. Of these cluster variables, seven were used in the present study: Oral Language; Short-term Memory; Processing Speed; Auditory Processing; Visual Processing; Comprehension Knowledge; and Fluid Reasoning. The Oral Language cluster can be considered a measure of verbal ability: it incorporates both lower order and higher order abilities. The Short-term Memory cluster is analogous to working memory and measures a participants' ability to hold and recall verbal information. Processing Speed refers to the speed with which

participants can locate figures that are visually identical. The Auditory Processing cluster includes blending and recognition of sounds. The Visual Processing cluster includes spatial and visual recognition skills. The Comprehension Knowledge cluster includes vocabulary and analogical skills. The Fluid Reasoning cluster assesses problem-solving and concept formation. Importantly, the WJ-COG has norms for, and can be administered to, all ages from pre-school upwards so was suitable for use with all participants in the present study. Full details of the WJ-COG-R subtests are provided in Porter and Coltheart (2005).

Procedure

The WJ-COG was administered in two one-hour sessions, participants' individual level of motivation and concentration were considered and, where necessary, breaks were provided. The interview lasted, on average, one hour and was conducted on the same day as the cognitive assessment. The individual with WS was not present during the interview with their parent or caregiver unless they specifically requested to be present. All interviews were conducted in person and recorded, using a digital voice recorder, for subsequent transcription.

Results

Current prevalence rates (entire cohort)

Table 2 shows the number of participants who met criteria for an Axis I DSM-IV disorder, prevalence rates for the entire cohort and for the Child and Adult groups are reported. Only disorders for which one or more participant met criteria are included. As anticipated, anxiety disorders were the most prevalent diagnoses, with 38% meeting criteria for at least one anxiety disorder. As Table 2 indicates, rates of Attention Deficit Hyperactivity Disorder (ADHD) and Depressive Disorders were also high in this population. It is also noteworthy, that 42% of the cohort (37% of the

Child group and 50% of the Adult group) did not meet criteria for an Axis I diagnosis. In total, it was reported that clinical advice had been sought or intervention provided for 24% of participants. 58% of these had been prescribed medication.

[Insert Table 2]

Psychosis

No previous research has considered the prevalence of psychosis in WS; in addition to the one female participant who met criteria for schizophrenia, two other female participants were described by parents as having experienced definite psychotic symptoms. One of these participants had experienced delusions of persecution in the past, reporting that there was a stranger following and watching her. This participant did not meet criteria for any DSM-IV diagnoses at the time of assessment. The second participant experienced command hallucinations in the auditory modality and met criteria for Schizoaffective Disorder and GAD. The participant who met criteria for schizophrenia first exhibited symptoms during her mid-40s and had no previous history or family history of psychosis or other psychiatric concerns. For both of the participants who experienced psychotic symptoms, onset during late adolescence (16-18 years) was reported. All three participants had been assessed by a psychiatrist and prescribed medication. The medication was effective in the management of symptoms for two of these participants, including the participant who was diagnosed with schizophrenia, and had reduced symptoms in the third.

Age of onset

For depressive disorders, onset of threshold symptoms most often occurred between mid adolescence and early adulthood (15-25 years); only one participant was described as experiencing symptoms from early childhood. Onset of GAD was

typically mid to late adolescence, although some anxiety symptoms, particularly related to fears, were typically described as having been present since early childhood. Onset of ADHD symptoms and specific phobia were most commonly described as occurring in young childhood.

Individual difference variables and psychopathology

For the following analyses, a p-value of 0.05 was used to indicate statistical significance in order to minimise the possibility of Type II error (see Rothman, 1990).

Age category (Child vs Adult groups).

Table 2 indicates interesting differences between the Child and Adult groups in prevalence rates. Higher rates of depressive disorders were reported for the Adult group and higher rates of ADHD were reported for the Child group. Furthermore, GAD was only reported for the Adult group. To further explore these effects of age category, Fishers exact tests were conducted to examine differences between the Child and Adult groups in prevalence rates. Significantly higher prevalence rates of Depressive disorders (p=0.032) and GAD (p=0.007) were found for the Adult group and significantly higher prevalence rates for ADHD (p=0.003) were found for the Child group. No age group differences were found in relation to prevalence of Specific Phobia.

For all further analyses, participants were divided into groups based upon their current diagnostic status (present/absent) with regard to the disorders contained within Table 2. Due to the small sample size, schizophrenia and OCD were excluded, and the depressive disorders (see Table 2) were collapsed together. To summarise, two groups (diagnosis present/absent) were created for each of the following: Depressive Disorders; Specific Phobia, GAD, ADHD. These groups will be referred to as diagnostic groups. Table 3 shows the gender distribution and mean cognitive ability of

each diagnostic group. Due to the small sample size of diagnostic groups, effect size is also reported in Table 3.

To ensure that comparisons between the diagnosis present/absent groups were valid, it was important that the differences between the Child and Adult groups were taken into account. Given that all of the participants who met criteria for ADHD were in the Child group, the ADHD present/absent diagnostic groups comprised only participants from the Child group. Furthermore, as the majority of the participants who met criteria for GAD or for a Depressive Disorder were in the Adult group, the GAD present/absent diagnostic groups and the Depressive Disorder present/absent diagnostic groups only comprised participants from the Adult group. As no Child/Adult group differences were found for Specific Phobia, the Specific Phobia present/absent diagnostic groups comprised the entire cohort.

[Insert Table 3]

Gender.

Table 3 shows that Depressive disorders, Specific Phobia and GAD were more common in female participants whereas ADHD appeared more common in male participants. Gender differences between diagnostic groups were assessed using Fisher's exact tests, no gender difference reached statistical significance.

Cognitive ability.

To explore the relationship between DSM-IV Axis I diagnoses and cognitive ability, the diagnostic groups were compared on general cognitive ability (GCA) and the seven cognitive cluster variables from the WJ-COG-R: Oral Language; Short-term Memory; Processing Speed; Auditory Processing; Visual Processing; Comprehension Knowledge; and Fluid Reasoning. Age equivalent scores were used for the analyses

reported below. The analyses were also conducted using standard score data and an identical pattern of results was found.

Means and standard deviations for each diagnostic group on cognitive variables are also shown in Table 3. The data shows that, in general, between-group differences in general cognitive ability, or mental age, were minimal. In keeping with this, few of the cluster variables showed large group differences and between-group t-tests showed no significant differences between diagnostic groups on GCA or the cognitive cluster variables.

Discussion

Current prevalence rates

This research had two aims. The first aim was to extend earlier research by comprehensively examining psychopathology in WS, reporting prevalence rates of a wide range of diagnoses and patterns of comorbidity. As predicted, anxiety was the most prevalent type of psychopathology observed. Specific Phobia and ADHD were the most prevalent individual diagnoses and the predicted comorbidity between these two diagnoses was supported.

The prevalence rates of anxiety disorders and ADHD in our cohort of individuals with WS were largely in keeping with previous findings (Dykens, 2003; Einfeld et al., 1997). Rates for GAD and Specific Phobia showed consistency with those reported by Dykens (2003). The results also supported previous findings of a high rate of ADHD in WS, particularly the Inattentive subtype (Leyfer et al., 2006). However, the prevalence rate of Specific Phobia in our cohort (30%) was notably lower than the rate (53.8%) reported by Leyfer et al. (2006), as was the prevalence rate of ADHD (20% compared to 64.7%).

There are a number of possible reasons for the differences in prevalence rates between the present research and those reported by Leyfer et al. (2006). Firstly, these differences may be due to age differences between the samples; Leyfer et al. (2006) only assessed psychopathology in children with WS. However, even the prevalence rates for the Child group only (ADHD – 33%, Specific Phobia 37%) remain significantly lower than the rates reported previously. A second reason for the lower prevalence rates in our cohort may have been our stringent consideration of each individuals' level of intellectual ability and whether the symptoms reported were over and above what would be expected based upon the individuals particular developmental level. To give an example, a fear of ghosts or monsters may appear abnormal for a 15 year-old. However, if that 15 year-old has a mental age that is equivalent to a typically-developing 4 year-old, this fear may not be considered atypical. As the interviewer also conducted the full cognitive assessment of the participants they were able to consider the developmental level of the participants as the interview was conducted.

With specific reference to the differences in prevalence rates of ADHD, Leyfer et al. (2006) utilised the ADIS-IV and support for the validity of the ADHD module of the ADIS-IV is limited (see Jarrett, Wolff & Ollendick, 2007). It is, therefore, also possible that the ADIS-IV overestimates prevalence of ADHD. Finally, with reference to differences in prevalence rates of Specific Phobia, the ADIS-IV specifically asks about a wider range of phobias than the K-SADS-PL. For example, parents are specifically asked about phobias of storms, water, going to the doctors or dentist and vomiting in the ADIS-IV but not in the K-SADS-PL. Instead, the K-SADS-PL is more reliant on the parent's free recall of Specific Phobias and provides specific examples to assist with this. It is, therefore, possible that the lower prevalence

rate of Specific phobias in the present research is related to this difference in instruments.

Previous research has not reported prevalence rates of psychotic disorders in WS and, although Leyfer et al (2006) assessed for depression in their cohort of children with WS, no cases of depression have been reported. The prevalence rate of depressive disorders in our entire cohort of individuals with WS was 14% and the prevalence rate for the adult group alone was 25%. This rate is higher than has been reported for adults in the general population (2% - 9%; APA, 2000) or for adults with non-specific intellectual impairment (Whitaker & Read, 2006). The difference in prevalence rates for depressive disorders between the Adult and Child group suggests that Leyfer et al. (2006) found no cases of depression because only children with WS were assessed. With regard to psychotic disorders, one individual in our cohort of 50 met criteria for a psychotic disorder and two additional individuals were described as having experienced definite psychotic symptoms, including auditory command hallucinations and delusions of persecution. In total, 6% of our cohort were reported to have experienced psychotic symptoms, this is closely comparable to the rate reported in the typically developing adult population (King et al., 2005).

The current research also allowed for a comprehensive investigation of psychopathological comorbidity in WS. Approximately one quarter of participants met criteria for more than one diagnosis. The results showed that in addition to the previously noted comorbidity between ADHD and Specific Phobia, depressive and anxiety disorders also commonly co-occurred. This pattern of comorbidity is also commonly reported in typically developing children (Goodman, Schwab-Stone, Lahey, Shaffer, & Jensen, 2000) and adults (Sartorius, Ustun, Lecrubier, Wittchen,

1996), and supports clinical observations of comorbidity between depression and anxiety in WS (Pober & Dykens, 1996).

Overall, our findings support previous research indicating high levels of GAD, Specific Phobia and ADHD (inattentive subtype) in WS. Further to this, the results indicate that adults with WS may be at increased risk for depressive disorders relative to the typically developing population. This profile of psychopathology can be compared with that reported for other developmental disorders. For example, Prader-Willi syndrome is associated with increased rates of affective and psychotic disorders (Soni et al., 2008) and Velocardiofacial syndrome is associated with increased rates of depressive disorders, ADHD and Specific Phobia and increased rates of schizophrenia in adults (Antshel et al., 2006). These findings clearly demonstrate that individuals with certain developmental disorders are at greater risk of developing specific patterns of psychopathology.

Individual difference variables and psychopathology

In order to apply theory and treatment approaches designed for typically developing individuals to the WS population, it is important to consider whether the causes and processes associated with DSM-IV diagnoses are comparable in both populations. As outlined previously, Karmiloff-Smith (1998) highlights that similarities in underlying processes cannot be assumed based on similarities in behaviour, or psychopathological symptoms. Consequently, the second aim of the present research was to examine the relationship between psychopathology and age category (child vs adult), gender and cognitive ability in WS to evaluate whether these relationships were comparable to those reported for typically-developing individuals. Furthermore by examining these relationships, it was also possible to consider potential sources of heterogeneity in the presentation of psychopathology in WS.

Age category.

The results indicated that ADHD was significantly related to age category; all of the participants who met diagnostic criteria were in the Child group and therefore under 18 years of age. Whilst, this finding is in keeping with age-related changes in prevalence for typically-developing individuals (Pineda et al., 1999), alternative explanations for the finding must be considered. Firstly, the K-SADS-PL is designed to assess ADHD in children. As ADHD may manifest differently in adults, it is possible that the K-SADS-PL did not cover the relevant symptoms for adults. The interviewer asked additional questions to overcome this difficulty, but it remains possible that this procedure did not overcome these difficulties entirely. An alternative explanation is that ADHD symptoms remain in adulthood but that these symptoms are less impairing for adults given that they are no longer attending school and are able to choose a pastime that suits their abilities.

Significantly higher prevalence rates of depressive disorders and GAD were found for the Adult group when compared to the Child group; all of the participants who met criteria for GAD and five out of the six participants who met criteria for a depressive disorder were adults. In the majority of cases mid to late adolescence was the most common period for onset of depressive disorders and GAD. These age-related differences are in keeping with those observed in the typically-developing population (Campbell et al., 2003; Lewinsohn et al., 1994). Taken together, these results suggest that there are significant differences in psychopathology in WS depending upon age category (childhood vs adulthood) and that these differences are in keeping with those found in the typically-developing population. Furthermore, the findings suggest that age category may explain some of the heterogeneity of psychopathology in WS.

Gender.

There was a non-significant trend for more male than female participants to meet criteria for ADHD. This finding corresponds to the findings of Leyfer et al. (2006) and reflects the gender pattern for ADHD reported in typically developing children (Gaub & Carlson, 1997). Also consistent with Leyfer et al. (2006), four of the five participants in our cohort who met criteria for GAD were female. This difference did not reach significance; however, this is likely due to the small sample size of individuals meeting criteria for GAD. This gender difference in WS is also consistent with that reported for adults in the general population (Parker & Hadzi-Pavlovic, 2004). Together the findings suggest that gender may also be a source of heterogeneity of psychopathology in WS.

Cognitive ability.

In keeping with previous research, no effect of mental age on psychopathological diagnoses was obtained (Dykens & Rosner, 1999; Leyfer et al., 2006). However, WS is characterised by a cognitive profile of strengths and weaknesses (Bellugi et al., 2000), therefore a general measure of intellectual ability (such as IQ or mental age) is likely to mask large variations in underlying cognitive skills and consequently be somewhat uninformative. To overcome this problem, the relationship between specific cognitive abilities and psychopathology in WS was explored.

No significant relationships were found between specific cognitive abilities and psychopathological diagnoses in our cohort of individuals with WS. However, examination of effect sizes suggests that this may be the result of the small sample size for the diagnosis present groups. The direction of group differences was largely in keeping with those reported for the typically-developing population. For example,

in keeping with the typically-developing population, children with WS who met criteria for ADHD showed poorer short-term memory ability than those without (Willcutt et al., 2005). Similarly, there was some evidence that adults with WS who met criteria for a depressive disorder exhibited poorer processing speed and poorer short-term memory, which is also in keeping with findings for typically developing adults. There was, however, little evidence for a relationship between GAD or Specific Phobia and cognitive ability. However, there is some speculation as to whether a relationship between either of these diagnoses and cognitive ability would be expected, even in typically developing individuals (see Airaksinen et al., 2005).

Although no significant relationships between psychopathology and cognition in WS were found, the pattern of relationships is in keeping with what would be expected based on research with typically-developing individuals. Consistent with the findings for age category and gender, there is no evidence that the relationships are highly divergent between populations. Consequently, at least in regards to age category, gender and cognitive ability, there is no reason to believe that the causes and processes underlying psychopathology in WS are any different to those underlying psychopathology in the typically developing population. These findings support the validity of applying theory and treatment practices developed with respect to the typically developing population, to the WS population.

Examination of the relationship between psychopathology and individual difference variables in WS has further demonstrated that gender and age category may explain some of the heterogeneity apparent in the psychopathological profile of WS. However, there is little evidence for a significant relationship between cognitive heterogeneity and heterogeneity in the psychopathological profiles.

Limitations and future research

A principal aim of the present research was to examine DSM-IV diagnoses in both children and adults with WS. For ease of comparison between children and adults, a child diagnostic interview was utilised. Although this interview is appropriate for the developmental level of all of the participants, it is possible that the symptoms of psychopathology expressed in adults with developmental disabilities differ from the expression of those symptoms in children. However, the K-SADS-PL is semi-structured, which allows the interviewer to ask additional questions to explore whether symptoms may be manifesting differently because of the participants chronological age. For the purposes of the present research, the benefits of utilising a single diagnostic interview outweighed the disadvantages of this methodology. Nevertheless, it remains possible that the K-SADS-PL may have under-diagnosed psychopathology in the adult group. This is of particular relevance for ADHD, as discussed previously. Consequently, it will be of interest for future research to replicate the findings for adults by assessing psychopathology in adults with WS using an interview that is designed for use with adults with intellectual disabilities.

A second limitation of the present research is the reliance on caregiver report. There are a number of difficulties with this methodology, however, as discussed previously, there is little alternative for the assessment of psychopathology in individuals with intellectual impairment as these individuals may lack the insight to describe their emotional experiences and may have difficulties providing accurate accounts of their experiences (Cooper et al., 2003). It is possible, however, that a small number of high-functioning individuals with WS may be able to accurately report their own symptoms and feelings. Consequently, we are currently conducting a small study with a group of high-functioning individuals with WS that utilises self-report.

The findings of the present research highlight a number of areas of interest for future research in this area. Firstly, in light of the high prevalence of GAD obtained in our study, it is of interest that no participants met criteria for Social Phobia. This is inconsistent with the pattern in the general population, where Social Phobia is often reported to be the most prevalent anxiety disorder (Jefferys, 1997). This suggests that individuals with WS do not have a general vulnerability to all anxiety disorders and that the profile of anxiety in WS is atypical. Further exploration of this dissociation between social and non-social anxiety may provide insight into the development of Social Phobia and potential risk and protective factors in the general population. A second area of interest for future research will be to explore other factors that have been shown to underpin psychopathology in typically developing individuals such as maladaptive thoughts or attentional biases. Finally, it will also be of interest for future research to explore the relationship between psychopathology in WS and other individual difference variables not examined within the present study, such as genetic variation.

Conclusion

The present research supports previous findings of high rates of anxiety and attention difficulties in WS and also indicates that the psychopathological profile of children and adults with WS differs markedly. In particular, adults with WS appear to be at increased risk, relative to children to WS, for depressive disorders and Generalised Anxiety Disorder and there is some evidence that ADHD may be more common, or cause more functional impairment, in children than adults with WS. The relationships between diagnoses and age, gender and cognitive ability were largely in keeping with those reported for typically-developing children and adults.

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Table 1

Demographic date for entire sample and child and adult groups.

	N	Gender (M;F)	Age in years M (range)	Mental Age M (range)
Entire Cohort	50	24;26	18.53 (6 – 59)	6.25 (2.16-10.58)
Child group	30	16;14	11.8 (6 – 17)	5.96 (2.16-7.92)
Adult group	20	8;12	27.3 (18 - 50)	6.77 (4.5-10.58)

Table 2

Overall prevalence rates for current DSM-IV Axis I disorders

Diagnosis	Entire Cohort No. (%)	Child Group No. (%)	Adult Group No. (%)
Depressive Disorders	6 (12%)	1 (3%)	5 (25%)
Major Depressive Disorder (MDD)	2 (4%)	1 (3%)	1 (5%)
Depressive Disorder NOS	1 (3%)	0 (0%)	1 (5%)
Adjustment Disorder with Depressed Mood	2 (4%)	0 (0%)	2 (10%)
Schizoaffective Disorder	1 (2%)	0 (0%)	1 (5%)
Psychotic Disorders	1 (2%)	0 (0%)	1 (5%)
Schizophrenia	1 (2%)	0 (0%)	1 (5%)
Anxiety Disorders	19 (38%)	11 (37%)	8 (40%)
Panic Disorder	0 (0%)	0 (0%)	0 (0%)
Obsessive Compulsive Disorder	2 (4%)	1 (3%)	1 (5%)
Separation Anxiety Disorder	0 (0%)	0 (0%)	0 (0%)
Phobia (including agoraphobia) [a]	15 (30%)	11 (37%)	4 (20%)
Generalised Anxiety Disorder	5 (10%)	0 (0%)	5 (25%)
Behaviour Disorder	10 (20%)	10 (33%)	0 (0%)
ADHD [b]	10 (20%)	10 (33%)	0 (0%)
> 1 Diagnosis [c]	10 (20%)	4 (13%)	6 (30%)
No Diagnosis	21 (42%)	11 (37%)	10 (50%)

[a] 3 Blood, Injury Injection subtype, 1 Animal subtype, 9 Natural environment subtype, 2 Situational subtype, 1 Other, 6 Noise related, 1 Agoraphobia [b] 9 inattentive, 3 combined, 1 hyperactive/impulsive [c] 3 x Depressive Disorder/Phobia; 1 x Depressive Disorder/GAD; 1 x Schizoaffective Disorder/Panic Disorder/Phobia/ADHD; 1 x GAD/Phobia; 1 x GAD/Phobia/ADHD; 6 x ADHD/Phobia .

Table 3

Diagnostic Group Differences in Cognitive Abilities and Gender

Diagnostic Group	**Gender**		**GCA**	**Oral**	**S-T**	**Proc.**	**Auditory**	**Visual**	**Comp.**	**Fluid**
			M	**language**	**Memory**	**speed**	**proc.**	**proc.**	**know.**	**reason.**
	M	F	***(SD)***	***M***	***M***	***M***	***M***	***M***	***M***	***M***
				(SD)	***(SD)***	***(SD)***	***(SD)***	***(SD)***	***(SD)***	***(SD)***
Entire Cohort	24	26	6.3	7.1	5.7	6.8	9.82	6.9	7.5	7
			(1.8)	(2.4)	(2.2)	(1.5)	(7)	(2.1)	(2)	(2)
Depressive										
Disorders[a]										
Present	2	3	6.58	7.87	5.8	6.3	11.45	6.26	8.1	6.9
			(1.90)	(3.13)	(1.84)	(1.46)	(9.75)	(1.18)	(2.61)	(1.7)
Absent	8	12	6.83	7.74	6.31	6.9	10.75	6.94	7.98	8
			(1.43)	(2.98)	(2.99)	(0.99)	(7.57)	(1.78)	(2.36)	(1.81)
Effect Size (*d*)			0.15	0.04	0.21	0.48	0.08	0.45	0.05	0.05
Phobia[b]										

Present	6	9	6	7.1	5.7	6.5	9.7	6.6	7.4	6.7
			(1.9)	(2.4)	(1.7)	(1.4)	(8)	(1.8)	(2.2)	(1.8)
Absent	18	17	6.4	7.1	5.7	6.9	9.9	7.1	7.5	7
			(1.7)	(2.4)	(2.3)	(1.5)	(6.6)	(2.2)	(2)	(2.1)
Effect Size (*d*)			0.22	0	0	0.28	0.02	0.25	0.05	0.15
GAD[a]										
Present	1	4	6.9	8.71	6.75	6.83	11.1	7.28	8.7	7.68
			(2.39)	(5.06)	(3.92)	(1.37)	(9.6)	(2.52)	(3.63)	(2.76)
Absent	7	8	6.73	7.45	5.99	6.72	10.86	6.6	7.78	6.74
			(1.21)	(1.99)	(2.33)	(1.07)	(7.63)	(1.32)	(1.88)	(1.3)
Effect Size (*d*)			0.09	0.33	0.24	0.09	0.03	0.34	0.31	0.44
ADHD[c]										
Present	7	3	5.81	6.78	4.66	6.51	9.33	7.18	7.13	6.8
			(1.78)	(1.95)	(1.08)	(2.03)	(7.36)	(2.71)	(1.64)	(1.24)
Absent	19	11	6.04	6.6	5.73	7.03	8.89	6.99	7.02	6.99
			(1.92)	(1.77)	(1.79)	(1.6)	(5.89)	(2.21)	(1.60)	(2.59)

Effect Size (*d*)	0.09	0.72	0.28	0.06	0.08	0.07	0.09	0.12

Note. Cognitive ability values represent age equivalent, in years. Diagnostic group refers to diagnosis present vs diagnosis absent groups. GCA = General Cognitive Ability; S-T = Short-Term; GAD = Generalised Anxiety Disorder.

[a] Adult group only. [b] Entire cohort. [c] Child group only.

*p<0.05