Mental health problems in adults with Williams syndrome

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ABSTRACT

Although many researchers have investigated emotional and behavioral difficulties in individuals with Williams syndrome, few have used standardized diagnostic assessments. We examined mental health problems in 92 adults with Williams syndrome using the Psychiatric Assessment Schedule for Adults with Developmental Disabilities—PAS-ADD (Moss, Goldberg, et al., 1996). Factors potentially associated with mental health problems were also explored. The PAS-ADD identified mental health problems in 24% of the sample. The most common were anxiety (16.5%) and specific phobias (12%). Other diagnoses included depression, agoraphobia, and social phobia. No association was found between the presence of mental health problems and either individual (e.g., age, IQ, language level) or external (life events) variables.
INTRODUCTION

Williams syndrome (WS), a rare genetic disorder caused by a hemizygous deletion of approximately 26 genes at chromosome 7q 11.23 (Peoples et al., 2000), is typically associated with positive behavioral characteristics, such as friendliness and sociability (e.g., Bellugi, Lichtenberger, Jones, Lai, & St. George, 2000; Von Arnim & Engel, 1964). However, emotional and behavioral difficulties are also common and include inappropriate social behaviors, preoccupations and obsessions, impulsivity, distractibility, and anxiety (Einfeld, Tonge, & Rees, 2001; Udwin, Yule, & Martin, 1987). Recently, researchers have investigated these problems in terms of diagnosable psychiatric disorders (Cherniske et al., 2004; Dykens, 2003; Kennedy, Kaye, & Sadler, 2006; Leyfer, Woodruff-Borden, Klein-Tasman, Frick, & Mervis, 2006). Results of these studies indicate that individuals with WS experience a range of anxiety disorders, including specific phobias (35 to 54%), agoraphobia (24%), generalized anxiety disorder (12 to 16%), obsessive compulsive disorder (2 to 12%), separation anxiety (4 to 7%), posttraumatic stress disorder (0.8 to 5%), social phobia (1.7%), and panic disorder with/without agoraphobia (0.8 to 5%). In those studies in which affective disorders were addressed, the incidence of depression was reported as being 10 to 14%; dysthymia, 10%; and manic-depressive disorder, 5%. Cases of attention deficit hyperactivity disorder (ADHD, 43%) and sexual impulse control disorder (5%) have also been reported.

Research into mental health of individuals with WS has been limited by the methods of assessment used. In many cases, reports of psychopathology have been derived solely from parental reports or checklists (e.g., Arnold, Yule, & Martin, 1985; Davies, Udwin, & Howlin, 1998; Udwin & Yule, 1991). Other researchers, although employing more detailed measures, have frequently relied on assessments designed for children (e.g., Dykens, 2003; Kennedy et al., 2006). These child measures may inflate estimates of mental health problems. For example, in the Diagnostic and Statistical Manual (DSM) (1994) criteria for the diagnosis of generalized anxiety disorder in adults, it is stipulated that individuals must find it difficult to control their worry and show at least three out of six symptoms; children need only display one of the six symptoms. Conversely, reliance on informant-based interviews (e.g., Dykens, 2003; Leyfer et al., 2006) may result in underdiagnosis; Moss, Prosser, Ibbotson, and Goldberg (1996) suggested that up to one third of cases may be missed if information is provided by only an informant or the individuals.
themselves. Moreover, many of the instruments that have been employed in studies of individuals with WS have not been validated for use with individuals with intellectual disability.

With occasional exceptions (i.e., Leyfer et al., 2006), most studies have small samples and often very mixed age groups. Cherniske et al. (2004) had a sample of 20 adults with WS (M age = 39 years) and that of Kennedy et al. (2006), 21 individuals ages 7 to 28 years. Although Dykens’ (2003) sample was larger (N = 51), ages ranged from 5 to 49 years. Small samples limit the generalizability of findings to the wider population of individuals with WS. Combining data from young children and adults is also likely to confound the interpretation of results.

Despite these methodological shortcomings, it is evident that there is a high risk of anxiety-related disorder problems in WS and that there is a need to identify the factors that contribute to such problems. In studies of mental health problems in other groups of individuals with intellectual disability, a range of possible risk factors has been identified, including stressful life events, age, sex, and severity of cognitive impairment. However, the findings are often contradictory. Thus, although some investigators (e.g., Hastings, Hatton, Taylor, & Maddison, 2004 [adults with intellectual disability]; Coe et al., 1999 [children with Down syndrome]) reported significant correlations between pathology and negative life events, Mantry et al. (2008) found no significant association between stressful life events and mental health problems in adults with Down syndrome. Hamilton, Sutherland, and Iacono (2005), in a study of individuals with autism, cerebral palsy, Down syndrome, and fragile X, found the strength of the association varied both by diagnostic group and by intellectual level. With regard to age, some researchers reported a positive correlation between age and rates of mental health problems in individuals with intellectual disability (Deb, Thomas, & Bright, 2001); others suggested that such problems are more common in younger individuals or that there are no significant age differences (Cooper, Smiley, Morrison, Williamson, & Allen, 2007; Espie et al., 2003). The role of sex is also uncertain. Although much higher rates of mental health problems have been reported in females in some studies (Cooper et al., 2007; Hastings et al., 2004), others have found no sex-related differences (e.g., Smiley, 2005; Tsakanikos, Bouras, Sturmey, & Holt, 2006). Similarly, with respect to intellectual level, although some researchers have reported a positive association between psychiatric disorder and severity of intellectual impairment (e.g., Cooper et al., 2007;
Whitaker & Read, 2006), others have suggested that individuals with mild–moderate impairments are at greater risk for mental health problems than are those with severe–profound intellectual disability (Deb et al., 2001; Holden & Gitlesen, 2004; Myrbakk & von Tetzchner, 2008).

Data on the relationship between psychiatric disturbance and other factors, such as physical health and communication skills, are equally contradictory. Associations between mental health problems and epilepsy (Espie et al., 2003) or urinary incontinence (Cooper et al., 2007) have been reported by some researchers; others have failed to find such associations (Deb et al., 2001; Matthews, Weston, Baxter, Felce, & Kerr 2008; Moss, Patel, et al., 1993). Espie et al.’s (2003) finding that poorer communication skills were related to emotional–behavioral difficulties has not been replicated (Cooper et al., 2007; Deb et al., 2001; Matson, Terlonge, González, & Rivet, 2006). Finally, lower rates of mental health problems have been reported among those living with family members compared to those in other settings, such as group homes (e.g., Cooper et al., 2007; Deb et al., 2001).

For individuals with WS, the findings are similarly inconclusive. Gosch and Pankau (1997), who explored the effects of age, found no overall differences in parents’ reported rates of behavioral disturbance between individuals with WS ages less than 10 years, 10 to 20 years, or over 20 years. However, rates of overt behavioral problems (e.g., destroys objects, hits others, disobedient, follows strangers) were lowest in the oldest age group, and scores on the withdrawn item were lowest in the under 10 group. Einfeld et al., (2001), in a 5-year follow-up of 53 children and adolescents with WS, reported a small, but nonsignificant decrease in the total behavior problem score on the Developmental Behavior Checklist (Einfeld & Tonge, 1995); scores on the Self-Absorbed subscale had decreased significantly, and repetitive speech had also decreased. Otherwise, the problems noted at the initial assessment (Einfeld, Tonge, & Florio, 1997) had generally persisted. Dykens (2003) found a significant positive correlation between age and participants’ total fear scores on the Fear Survey Schedule for Children–Revised (Ollendick, 1983). Leyfer et al. (2006) found that the proportion of individuals who received a diagnosis of generalized anxiety disorder was highest in the oldest group (ages 11 to 16 years) and lowest in the youngest group (ages 4 to 6 years). With regard to sex differences, Dykens
(2003) reported that females with WS had significantly higher scores than did males on the Fear Survey Schedule for Children–Revised; Leyfer et al. (2006) found no sex differences in rates of mental health problems.

Given the paucity of research regarding mental health in adults with WS, our aims in the present study were to (a) determine the overall rate of mental health problems in adults with WS using an assessment measure designed specifically for individuals with intellectual disability, (b) determine the types of problems and their relative rates in adults with WS, and (c) explore variables (e.g., adaptive functioning skills, IQ, life events, physical health) that are associated with psychopathology in other populations in relation to psychopathology in adults with WS.

METHOD

Participants
Potential participants were identified via the United Kingdom Williams Syndrome Foundation database, and parents of all individuals age 18 and over were contacted regarding participation. All participants with WS in the study had a diagnosis confirmed by FISH test. The total number of potential participants was 108. Of these, 8 families could not be contacted, 1 adult with WS had died, and 7 families did not wish to participate. In total, 92 adults with WS (50 female, 42 male) and their parents (N = 85) or caregivers (N = 7) took part. The mean age of the adults with WS was 32 years (range = 19 to 55 years).

Assessment Measures

Parental interview. Parents/caregivers of the adults with WS were interviewed on a variety of topics within the areas of physical health, independence, education, occupation, communication, social skills, and emotional–behavioral difficulties. Sample questions are provided in the Appendix. This interview has been employed in previous studies of adults with WS (Davies et al., 1998; Udwin, Howlin, Davies, & Mannion, 1998).

We measured expressive and receptive language using the Expressive One Word Picture Vocabulary Test–2000 Ed. (Brownall, 2000) and the British Picture Vocabulary Scale–Second Edition (Dunn, Dunn, Whetton, & Burley, 1997). All of the assessment measures (or earlier versions of them) had been used in our previous study of adults with WS (Howlin, Davies, & Udwin, 1998; Udwin, Davies Howlin, & Mannion, 1998).

Psychiatric assessment. We assessed mental health using the Psychiatric Assessment Schedule for Adults with Developmental Disabilities—PAS-ADD (Moss, Goldberg, et al., 1996). The PAS-ADD is a semi-structured interview based on the Schedules for Clinical Assessment in Neuropsychiatry (World Health Organization, 1994). It is designed for use with individuals who have a range of cognitive impairments (Moss, Patel, et al., 1993; Patel, Goldberg, & Moss, 1993). Key features pertaining to its use with individuals who have intellectual disability are simplified wording and the use of a memorable anchor event from the individual’s own life in order to focus discussion on the previous 4-week period. There are parallel informant–respondent versions that enable PAS-ADD diagnoses to be produced from the combined information from both interviews or from either of the interviews separately. The PAS-ADD has a three-tier structure that makes it suitable for use with individuals who have a range of abilities. The first tier is geared towards putting the individual at ease and enabling the interviewer to gauge his or her linguistic abilities. The second tier consists of conceptually simpler questions that make up the minimum items required for the identification of mental health problems. The third tier consists of the full set of questions. The PAS-ADD enables International Classification of Diseases—ICD-10 (World Health Organization, 1994) research diagnoses to be generated for schizophrenia, undifferentiated psychosis, hypomania, depressive episode, phobic anxiety disorders (agoraphobia, social phobia, specific phobia), panic disorder, generalized anxiety disorder, and nonorganic hypersomnia. Most symptoms are rated on a scale of 0 (no symptoms present) to 4 (symptoms of severe intensity). Based on the information provided by informants/respondents, each item in the PAS-ADD interview is assigned a numerical value. These values are entered into a computer program (CATEGO-5) that generates ICD-10 diagnoses of psychopathology. The PAS-ADD also contains a checklist of life events. Parents/caregivers were asked to indicate whether the individuals with WS had experienced any of these items in the past 2 years.
The PAS-ADD has generally good reliability, with a mean kappa of .65 for individual item codes and .66 for item groups; the correlation between total symptom scores is .74, and the mean kappa agreement on index of definition is .70 (Costello, Moss, Prosser, & Hatton, 1997). It has good validity, with comparisons between PAS-ADD-generated diagnoses and diagnoses by referring psychiatrists reaching 75% agreement (Moss et al., 1997; Moss, Prosser, & Goldberg, 1996).

PAS-ADD Interrater Reliability

In the present study, 20 pairs of interviews (respondent and informant versions) were rated separately by two raters (the first two authors). Item scores from each of the raters were entered separately into the CATEGO-5 diagnostic program. Interrater reliability was assessed using kappas (KappaCom: Robinson, & Bakeman, 1998) and intraclass correlations. Significant substantial agreement was found for any diagnosis, κ = .68, schizophrenia, κ = .77, depression, κ = .63, agoraphobia, κ = .77, social phobia, κ = .64, and generalized anxiety disorder, κ = .77. We found perfect agreement for specific phobia, κ = 1.00, undifferentiated psychosis, κ = 1.00, hypomania, κ = 1.00, mania, κ = 1.00, and panic disorder, κ = 1.00. The mean kappa agreement on item groups was .75. The intraclass correlation between index of definition scores (a measure of the clinical significance of the observed set of behaviors, ranging from 1 to 8) was .83, and the intraclass correlation between total symptom scores was .98.

Procedure

Assessments took place in parents’ homes and at the homes, day centers, and work places of the individuals with WS. Typically, assessments began with the parent/caregiver interview, enabling subsequent assessments to be tailored to suit the ability level of the individual with WS. Assessments were conducted over a minimum of 2 days. Breaks were taken when requested by the individual with WS or parents/caregivers or at the discretion of the examiner.

Because of the number and length of the various assessments conducted, we did not feel that it was appropriate to ask all participants and their parents/caregivers to complete the PAS-ADD. Instead, the general parent/caregiver interview was used as a screen to indicate which individuals should be further assessed on this measure. This interview provided preliminary information on a range of potential mental health problems, with items generally rated on a scale of 0 to 3 (0 = no
problem, 1 = some evidence of difficulty in this area but no evidence of distress/interference in daily life, 2 = evidence of some distress/intrusion in daily life, and 3 = serious problem causing significant distress/disruption to daily life). For those individuals who scored a 2 or 3 on any of the mental health items (n = 75, 83% of total sample), we conducted PAS-ADD interviews separately with the adult with WS (the respondent) and a second person who knew them well (the informant). Informant-based PAS-ADD assessments were mostly completed with parents, but in 4 cases the informant was a caregiver. Two individuals with WS lacked adequate verbal skills to complete the PAS-ADD themselves.

**RESULTS**

*Statistics and Significance Level*

We used the Statistical Package for the Social Sciences Version 15 for Windows (SPSS 15, 2006) to conduct our analyses. Parametric or nonparametric tests (one-way ANOVAs, Mann-Whitney, chi-square tests) were used according to the data analyzed. The level of significance was set at .01.

*Cognitive Characteristics*

Full details of cognitive, language, and adaptive functioning of the adults with WS involved in the study are described in Howlin, Elison, and Stinton (in press). The mean Full Scale IQ of the adults with WS was 56.6 (SD = 7.2); mean Verbal IQ, 61.7 (SD = 7.4); and mean Performance IQ, 58.3 (SD = 6.7). The mean receptive vocabulary age equivalent was 10.6 years (SD = 3.7) and the mean expressive vocabulary age equivalent was 7.4 years (SD = 2.8). The standard score for the VABS Adaptive Behavior Composite was 40.0 (SD = 16.3).

*Emotional–Behavioral Problems*

Data from the parent/caregiver interview indicated that 75 individuals with WS, over 80% of the sample, experienced significant emotional–behavioral difficulties. The most common problems were distractibility (n = 45, 49%), anxiety (n = 41, 45%), and phobias (n = 43, 47%). Other problems included mood disturbances (e.g., elevated and depressed moods, 11 to 13%), obsessive and compulsive behaviors (8%), and psychotic symptoms (e.g., hallucinations, delusions, and paranoia, 5%). Individuals with these problems had significantly higher IQ, F(1, 87) = 9.84, p =
.002, expressive vocabulary, $F(1, 90) = 5.91, p = .02$, receptive vocabulary, $F(1, 90) = 10.72, p = .002$, and Adaptive Behavior Composite scores, $F(1, 89) = 18.07, p < .001$, than those without emotional–behavioral problems.

_PAS-ADD Diagnoses: Informant or Respondent Version_  

On the basis of the information derived from the parent/caregiver interview, we administered the PAS-ADD to 75 individuals. Based on the combined data from the respondent interview and the informant interview (i.e., where a diagnosis came from either interview), we found that 22 adults with WS (24% of total sample) had at least one PAS-ADD diagnosis. The most commonly identified problem was specific phobia (12%) followed by depression (9%). Specific phobias were of storms ($n = 6$), hospitals ($n = 2$), dentists ($n = 1$), heights ($n = 1$), and wasps ($n = 1$). Other PAS-ADD diagnoses are shown in Table 1. Fifteen adults (16% of the total sample) received a PAS-ADD diagnosis for any anxiety disorder.

+++++++ Table 1 here ++++++++  

Comorbidity was common, with 9 adults receiving two or more PAS-ADD diagnoses. Of these individuals, 6 received two PAS-ADD diagnoses, 2 received three diagnoses, and 1 received four PAS-ADD diagnoses (see Table 2). Typically, these were for multiple anxiety disorders or anxiety disorders with depression.

+++++++ Tables 2 and 3 here ++++++++  

_Agreement: Informant Versus Respondent_  

There was little agreement between PAS-ADD diagnoses from respondent and informant interviews. If the PAS-ADD diagnoses obtained from both informant interview and respondent interview were included, 9 adults with WS (9.8% of total sample) received a PAS-ADD diagnosis. The most common problems were depression ($n = 4$) and specific phobias ($n = 3$). There were isolated cases of agoraphobia, panic disorder, generalized anxiety disorder, and undifferentiated psychosis. Five of the sample received a PAS-ADD diagnosis of any anxiety disorder (see Table 1). Two individuals received multiple diagnoses (see Table 2). The level of
agreement for any diagnosis between parent/caregiver and adult with WS was not related to respondents’ sex, $p = .51$ (Fisher’s Exact), IQ, $F(1, 84) = 2.74$, $p = 1.01$, receptive vocabulary, $F(1, 87) = 3.66$, $p = .06$, or expressive vocabulary, $F(1, 86) = 1.95$, $p = .17$), or to whether the adult with WS was living at home with parents, $p = .86$ (Fisher’s Exact).

**Mental Health and Pharmacological Treatments**

The parent/caregiver interview provided information on the medications prescribed for emotional, behavioral, or mental health problems. In total, 11 participants were receiving pharmacological treatments: 6 for depression, 2 for anxiety, and 3 for combined anxiety and depression. The medications prescribed were fluoxetine ($n = 3$), diazepam ($n = 3$), paroxetine ($n = 3$), citalopram ($n = 2$), sertraline ($n = 2$), venlafaxine ($n = 2$), chlorpromazine ($n = 2$), escitalopram ($n = 1$), and carbamazepine ($n = 1$). Three participants were taking more than one type of medication. Because the PAS-ADD does not cover whether medication is taken (which may, of course, prevent overt symptoms), the true rate of mental health problems may have been underestimated. To investigate whether this was the case, we further examined the PAS-ADD diagnoses of individuals who were receiving pharmacological treatment. Five adults who were currently taking medication for mental health problems (3 for depression, 1 for anxiety, and 1 for depression and anxiety) did not receive any PAS-ADD diagnoses. Of the remainder, 2 were taking medication for depression (both received PAS-ADD diagnoses of depression and anxiety); 1 (diagnosis of depression) was taking antidepressants; 1 (diagnosis of depression) was receiving medication for depression and anxiety; 1 (diagnosis hypomania) was receiving medication for anxiety, and 1 (diagnoses anxiety and schizophrenia) was taking medication for depression. If those individuals who were not exhibiting overt symptoms but were taking prescribed medication were included in the assessment of diagnosable mental health problems, then there may have been an additional 4 cases of depression and an additional 2 cases of anxiety. Including individuals who were receiving psychotropic medication as well as those who met PAS-ADD criteria would bring the total number of individuals with diagnosable mental health problems to 27 (29%), giving a rate of 13% ($n = 12$) for depression and 19% ($n = 17$) for any anxiety disorder.
Variables Associated With Mental Health Problems

Life Events

Over the preceding 2 years, 59 participants (69%) had experienced one or more stressful life event. The most common events were death of or serious illness/injury to a close relative/friend, followed by serious problems with a close relative/friend, serious illness/injury to self, move of residence, and break up of relationship (see Table 3). There were no significant differences in the number of life events experienced by individuals who received a PAS-ADD diagnosis and those who did not, \( U = 542, z = -1.36, p = .17 \).

Other Variables

Other factors potentially related to mental health problems were also considered. These were age, sex, expressive vocabulary, receptive vocabulary, IQ, health, adaptive behavior, and residential status. No specific hypotheses were made regarding their impact in view of limited information on predictors of mental health problems in this group. For all analyses, we based diagnosis on combined data (i.e., when a PAS-ADD diagnosis came from either the informant interview or the respondent interview).

Chi-square tests indicated that there were no significant associations between mental health status and sex or living arrangements (see Table 4). One-way ANOVA tests indicated that there were no significant differences between participants who received a PAS-ADD diagnosis and those who did not in terms of age, \( F(1, 89) = .017, p = .90 \), IQ, \( F(1, 86) = .07, p = .80 \), receptive vocabulary, \( F(1, 89) = .43, p = .51 \), expressive vocabulary \( F(1, 88) = .01, p = .95 \), or Adaptive Behavior Composite standard score, \( F(1, 89) = .53, p = .47 \). (see Table 5).

++++++++++++ Tables 4 and 5 here ++++++++

DISCUSSION

Individuals with WS experience more emotional, behavioral, and mental health problems and have higher rates of anxiety disorders (particularly specific phobias) than do the general population and many other groups who have intellectual disability (e.g., Dykens, 2003).
However, previous studies are often limited by methodological issues (e.g., small samples, broad age range of participants, and the use of assessment measures designed for typically developing populations). In this study we addressed these issues and examined factors associated with mental health problems in the largest study to date of mental health in adults with WS.

Parent/caregiver reports indicated that 83% of the adults with WS experienced emotional or behavioral problems that resulted in some degree of distress or disruption to daily life. These included anxiety, fears and phobias, distractibility, hallucinations, and compulsive behavior. Almost one quarter of the sample (24%) met PAS-ADD criteria for any psychiatric disorder and a further 5 individuals were currently receiving psychotropic medication for diagnosed mental health problems. Thus, in total 29% of the cohort had a diagnosable, or currently diagnosed, psychiatric disorder. Consistent with prior research findings, anxiety disorders were common, with 16.5% receiving a diagnosis for any anxiety disorder and 12%, for specific phobia. Other anxiety problems identified were agoraphobia, panic disorder, social phobia, and generalized anxiety disorder (ranges = 1 to 4%). The most common nonanxiety diagnosis was depression (9%). There was a small number of cases of hypomania (3%), schizophrenia (2%), and undifferentiated psychosis (1%). Nine (41%) of the 22 people with a psychiatric disorder had multiple psychiatric diagnoses.

Comparisons With Previous Research

Comparisons of mental health problems across studies are compromised by the lack of consistency in the methods and instruments used. Nevertheless, rates of panic disorder, social phobia, and depression in the present study were similar to those reported previously. Results of the present study also corroborate findings from earlier research indicating higher rates of depression in WS (9 to 14%) compared with individuals who have intellectual disability of mixed/unknown etiology (2 to 7%; Cooper, 1997; Cooper et al., 2007; Deb et al., 2001).

Rates somewhat lower than previously reported were found for other types of mental health problems, although frequency estimates in other studies of WS also vary (from rates of 48 to 65% for any anxiety disorder, 35 to 54% for specific phobias, and 12 to 24% for generalized anxiety disorder: Cherniske et al., 2004; Dykens, 2003; Kennedy et al., 2006; Leyfer et al., 2006).
Differences are likely due to a number of different factors. Sampling is important and because the present study involved a large proportion of the adults identified with WS in the United Kingdom, it provides a more representative sample than do many other studies. Further, this is the only research in which a psychiatric interview specifically designed for adults with intellectual disability was employed.

Other possible reasons for lower rates of some types of mental health problems in the present study compared to prior research, particularly for anxiety, are age of the sample and families’ experiences of dealing with anxiety over a long period of time. Anecdotally, some parents reported that although their son or daughter had experienced anxiety over the years, as parents they had developed strategies to reduce this anxiety (e.g., not giving too much advanced warning about potentially worrying events or changes to regular routine). Some parents also reported that issues that had previously been a source of distress had later become a source of interest. For example, one parent spoke of how her son had become fascinated with cleaning equipment (e.g., vacuum cleaners, washing machines) despite being very upset when he was younger by the noises they made.

Nevertheless, there was also some evidence from the parent/caregiver interview that other disorders, notably specific phobias and generalized anxiety disorder, may have been underdiagnosed by results on the PAS-ADD. For example, on the parent interview, 47% of adults with WS were reported as having fears/phobias, and 45% were reported as having a tendency to worry about seemingly trivial things. However, the severity of these problems did not meet PAS-ADD diagnostic criteria and, as such, these high rates of parent/caregiver reported anxiety may reflect an anxious disposition in adults with WS rather than diagnosable anxiety disorders.

A further problem relating to the PAS-ADD is that it does not cover certain types of mental health problems identified in other studies of individuals with WS. These include ADHD (e.g., Kennedy et al., 2006; Leyfer et al., 2006), dysthymia (Kennedy et al., 2006), manic depression (Cherniske et al., 2004), obsessive compulsive disorder (Cherniske et al., 2004; Leyfer et al., 2006), posttraumatic stress disorder (Kennedy et al., 2006; Leyfer et al., 2006), separation anxiety (Dykens, 2003; Kennedy et al., 2006; Leyfer et al., 2006), and sexual impulse disorder
Formal diagnoses of these disorders were, thus, not possible, although some of these issues arose in the parent/caregiver interview. Indeed, the most frequent problem reported by parents/caregivers was distractibility (49%), a component of ADHD. Approximately 8% of the adults with WS were reported as displaying obsessive and compulsive behaviors (e.g., excessive interest in famous people, insistence on following set routines). Changeable mood was reported as a problem by parents of 11% of the sample. One participant had previously received treatment for posttraumatic stress disorder following a car accident.

Although the PAS-ADD may have underdiagnosed some conditions, rates of agoraphobia (4%) were considerably higher than the less than 1% rates reported by Leyfer et al. (2006) or for individuals with intellectual disability more generally (Cooper et al., 2007; Emerson, 2003). Again, differences in sample selection may account for this finding. For example, rates of agoraphobia in individuals with intellectual disability are approximately twice as high in adults as children (Cooper et al., 2007; Emerson, 2003). Thus, among older adults with WS, rates of agoraphobia are likely to be higher than those found for younger participants with WS.

Other mental health problems (i.e., undifferentiated psychosis, 1%; schizophrenia, 2%; and hypomania, 3%) not previously reported in individuals with WS were identified in the present study. These rates are comparable to those reported for individuals with intellectual disability of unknown etiology in whom schizophrenia occurs in between 1 to 6% and hypomania, in 2 to 7% (e.g., Clarke, 2007; Cooper et al., 2007; Moss et al., 2000). Failure to identify these relatively uncommon problems in other WS studies is most likely due to the small sample sizes involved (e.g., \( N = 20, \) Cherniske et al., 2004; \( N = 51, \) Dykens, 2003; \( N = 21, \) Kennedy et al., 2006). In addition, many of these studies have included children for whom rates of psychotic disorders are even lower (Emerson, 2003).

**Factors Associated With Mental Health Problems in Williams Syndrome**

It is well-established that stressful life events are more common among individuals with intellectual disability than in the general population, and such events are associated with emotional, behavioral, and mental health problems (e.g., Hastings et al., 2004; Hatton & Emerson, 2004). Nevertheless, although nearly 70% of adults with WS in the present study had
experienced at least one such event in the preceding 2 years, there was no significant association with mental health status. In addition, we found no correlation between diagnosed mental health problems and variables such as age, sex, IQ, adaptive functioning, physical health, or residential status. Additionally, Kennedy et al. (2006) found no relationship with a family history of psychiatric disorders. This lack of association with family or environmental factors, together with the high rates of anxiety and attention disorders in WS, led Kennedy et al. (2006) to propose that such problems may be caused by or related to the specific WS genotype. However, not all individuals with WS experience mental health problems and, clearly, such problems cannot be attributed to genetic factors alone. The cumulative effects of other social, environmental, and individual factors (including personality type) that have been shown to be associated with mental health problems in other populations still require systematic research.

Discrepancy Between Respondent and Parent/Caregiver Informant Reports
In the present study, agreement between informant and respondent reports of psychopathology was low. Diagnoses of anxiety disorders (specific phobia, agoraphobia, panic disorder, and social phobia) were more frequently derived from self reports; affective disorders (depression and hypomania) were more frequently identified by informants.

Poor agreement between self and informant reports of mental health problems poses a significant challenge to psychiatric research generally (cf. Heun, Kockler, Papassotiropoulos, & Fimmers, 2006; Kraemer et al., 2003; Rougemont-Buecking et al., 2008). Such problems are likely to be exacerbated if respondents have additional language or cognitive problems that affect their ability to report internal feelings. Moss, Prosser, Ibbotson, and Goldberg (1996) found that in only 41% of cases did diagnoses based on the informant and the respondent information agree, with respondents who have intellectual disability being more likely to report autonomic symptoms and certain aspects of psychosis (e.g., hallucinations) and informants more frequently reporting symptoms of anxiety and depression (e.g., social withdrawal, irritability, and nervous tension). Dykens (2003) also noted that agreement between individuals with WS and their parents was poor, $r = .20$. Freeman, Williams, Farran, and Brown (2008) found that individuals with WS and their parents reported similar levels of difficulties (emotional symptoms) and strengths (prosocial behaviors) on the Strengths and Difficulties Questionnaire (Goodman, 1999), but there were
significant differences in their ratings of peer relationship problems and hyperactivity/inattention. Further, parents reported problems as having a greater impact than did the individuals with WS.

Other researchers have highlighted differences in the types of information that are reported by informants and respondents. Bramston and Fogarty (2000) suggested that certain emotions experienced by people with intellectual disability, such as fear, guilt, and loneliness, may be difficult for another individual to identify. Moss, Prosser, Ibbotson, and Goldberg (1996) noted that informants may have difficulties in identifying anxiety disorders when the PAS-ADD is used because diagnostic criteria include autonomic symptoms of which they may be unaware. In the present study some parents/caregivers reported that they were unable to identify symptoms such as racing heart, dry mouth, and dizziness. There are specific features of the WS phenotype that may further add to these problems. Although concrete language is relatively good, more abstract aspects of language are impaired (Mervis & John, 2008), and certain deficits in “theory of mind” have been identified (Porter, Coltheart, & Langdon, 2008) that could well reduce individuals’ ability to report internal states. On the other hand, there is a suggestion that people with WS have a tendency to over report fears and anxiety, possibly because of their desire to please the interviewer (Dykens, 2003).

Although the current findings indicate the importance of including the perspectives of both informants and respondents, how to overcome potentially conflicting biases of this kind and reach a reliable estimate of mental health problems remains a major challenge. In determining whether to offer interventions (particularly those involving medication or even in-patient treatment), should clinicians rely on informant reports or those of the individual with intellectual disability? For example, if parents are convinced there is a problem and the individual insists that there is none (or vice-versa), what is the appropriate clinical response? In these circumstances a different approach to assessment may be warranted (e.g., employing a measure where the focus is on significant changes in patterns of behavior or mood compared to the individual’s usual symptoms and behavioral repertoire). The Diagnostic Criteria for Psychiatric Disorders for Use with Adults with Learning Disabilities/Mental Retardation—DC-LD (Royal College of Psychiatrists, 2001) and the Schedule for Assessment of Psychiatric Problems Associated with
Autism—SAPPA (Bolton, & Rutter, 1994) both use this approach, although research into the reliability and validity of these instruments remains limited.

Other Methodological Limitations

This study has a number of limitations. The validity of the PAS-ADD has been questioned in relation to anxiety disorders, with some researchers suggesting that anxiety disorders are underdiagnosed using this instrument (Moss et al., 1997) and others that it overdiagnoses them (Gonzalez-Gordon, Salvador-Carulla, Romero, Gonzalez-Saiz, & Romero, 2002). Further, the ICD-10 criteria for psychiatric disorders, on which the PAS-ADD is based, were designed for typically developing populations. Although these criteria may be applicable for individuals with mild intellectual disability (Sovner & Hurley, 1983), they do not allow consideration of behaviors that may form part of the behavioral phenotype of certain genetic disorders (see Mohr & Costello, 2007, for discussion of these and other diagnostic issues related to intellectual disability). Again, further refinement of instruments such as the DC-LD or SAPPA might play an important role here.

There are also limitations in the approach we used to assess life events. We obtained this information from parents/caregivers, but standardized life event schedules have recently been developed for individuals with intellectual disability (e.g., the Bangor Life Events Schedules for Intellectual Disabilities: Williams et al., 2006 and the Lifestress Inventory: Lunksy & Bramston, 2006). These were not available when our study began. A further issue is that life events were measured only in terms of their presence or absence; factors such as the frequency or impact of those events were not considered, although these may have a greater association with emotional, behavioral, and mental health problems (Esbensen & Benson; 2006). Moreover, although life events are generally assumed to be negative, this is not always the case. For example, depending upon the circumstances, a move of residence could be a very positive experience.

The fact that the PAS-ADD diagnostic interviews were only administered if initial screening on the parent/caregiver interview indicated the presence of mental health problems also raises issues. First, we do not know whether a screening interview conducted with the individuals who have
WS would have elicited the same information. Second, because PAS-ADD interviews were only completed for individuals reported as having emotional–behavioral difficulties, this might have biased interviewers towards identifying more mental health problems on this measure. Third, individuals who were not interviewed with the PAS-ADD were included in the no diagnosis group. It is possible that if these individuals had been interviewed with the PAS-ADD, the rates of mental health problems identified would have increased. However, this is unlikely because although over 80% of the adults were described on the parent/caregiver interview as displaying emotional–behavioral difficulties, only about a quarter of the sample met criteria for a psychiatric disorder on the PAS-ADD. This suggests that it is extremely unlikely that individuals who were reported by parents/caregivers as having no significant emotional or behavioral difficulties would have fulfilled PAS-ADD diagnostic criteria. Nevertheless, this possibility cannot be ruled out.

Finally, it is necessary to exercise caution concerning the apparent lack of statistically significant associations between mental health problems and the variables investigated in the present research. First, the number of participants in the diagnosis group was relatively small, thus reducing the statistical power to identify significant associations. Second, the focus on the relationship between individual variables and mental health problems may have masked the cumulative effects of multiple risk factors. The use of binary logistic regression might have proved a solution to this problem, but the sample size was not appropriate for this type of analysis (cf. Peduzzi, Concato, Kemper, Holford, & Feinstein, 1996), and this would have been the case even if all of the possible participants had agreed to take part in the study. Although research in which much larger samples are used is clearly needed to explore the complex relations between mental health and multiple risk factors, this presents further problems when rare disorders are involved.

Despite such caveats, the major strength of this study is that the findings are derived from a large and exclusively adult sample of individuals, all of whom had received a genetic confirmation of WS. In previous studies of emotional and mental health problems, researchers have relied on data from smaller samples (not all of whom have genetic confirmation) and most also involve younger participants or a mix of both adults and children. Rates and types of such disorders can change significantly with age, and data on problems that are specific to adulthood had not previously
been available. Finally, we assessed mental health using a measure designed specifically for individuals with intellectual disability.

In summary, this research adds significantly to the knowledge base regarding mental health in adults with WS. It is clear from parent/caregiver reports that a large proportion of adults with WS experience emotional–behavioral difficulties that cause at least some distress or intrusion into everyday life. Results of the PAS-ADD indicated that anxiety, fears, and phobias—of a severity that meets diagnostic criteria for psychiatric disorder—are relatively common and occur more frequently than in the general population or other groups of individuals with intellectual disability. None of the factors investigated (e.g., life events) was found to be associated with mental health problems, possibly suggesting that WS may be associated with a particular behavioral phenotype that includes a predisposition towards anxiety.
REFERENCES


ACKNOWLEDGEMENT

This research was generously funded by the Baily Thomas Charitable Fund and the Williams Syndrome Foundation, which provided invaluable support in the tracing of families, and the support of John Nelson from this foundation was of enormous benefit throughout the study. Thanks are due to Mark Davies for his help with some of the assessments. Our sincerest thanks go to all of the adults with Williams syndrome and their families, caregivers, supervisors, and employers for taking part in the research and giving up so much of their time.
APPENDIX
Parents/Caregivers Interview: Sample Questions

Depression
Since the age of 18 years, has _____ (participant) ever had any long periods of unhappiness?
Does _____ (participant) often cry for no apparent reason?
Describe how _____ (participant) behaves during such periods.
How long do such periods of unhappiness last?
In the last 3 years, how often has _____ (participant) been depressed?

Anxiety
Is _____ (participant) overanxious? That is, does s/he have a tendency to worry or become anxious over seemingly trivial things?
What sorts of things does _____ (participant) worry about?
Describe how _____(participant) shows such anxiety and how you cope with it.
How often does _____ (participant) become so anxious?

Fears and Phobias
Is (participant) very afraid of any particular things?
What are they?
How does ____ (participant) show their fear?
What do you do to try and help ____ (participant) cope with this?
Table 1. PAS-ADD Diagnoses and Agreement Types and Rates of Diagnoses and Agreement Between Respondents and Informants

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Source of information</th>
<th>Informant only</th>
<th>Respondent only</th>
<th>Informant or respondent</th>
<th>Informant and respondent</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>n %</td>
<td>n %</td>
<td>n %</td>
<td>n %</td>
</tr>
<tr>
<td>Specific phobia</td>
<td></td>
<td>5 5.5</td>
<td>9 10.1</td>
<td>11 12.1</td>
<td>3 3.4</td>
</tr>
<tr>
<td>Depression</td>
<td></td>
<td>7 7.7</td>
<td>5 5.6</td>
<td>8 8.8</td>
<td>4 4.5</td>
</tr>
<tr>
<td>Agoraphobia</td>
<td></td>
<td>1 1.1</td>
<td>4 4.5</td>
<td>4 4.4</td>
<td>1 1.1</td>
</tr>
<tr>
<td>Panic disorder</td>
<td></td>
<td>1 1.1</td>
<td>3 3.4</td>
<td>3 3.3</td>
<td>1 1.1</td>
</tr>
<tr>
<td>Hypomania</td>
<td></td>
<td>3 3.3</td>
<td>0 0</td>
<td>3 3.3</td>
<td>0 0</td>
</tr>
<tr>
<td>Schizophrenia</td>
<td></td>
<td>1 1.1</td>
<td>1 1.1</td>
<td>2 2.2</td>
<td>0 0</td>
</tr>
<tr>
<td>Social phobia</td>
<td></td>
<td>0 0</td>
<td>2 2.2</td>
<td>2 2.2</td>
<td>0 0</td>
</tr>
<tr>
<td>Psychosis</td>
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<td>1 1.1</td>
<td>1 1.1</td>
<td>1 1.1</td>
</tr>
<tr>
<td>GAD⁵</td>
<td></td>
<td>1 1.1</td>
<td>1 1.1</td>
<td>1 1.1</td>
<td>1 1.1</td>
</tr>
<tr>
<td>Any anxiety</td>
<td></td>
<td>7 7.7</td>
<td>13 14.8</td>
<td>15 16.5</td>
<td>5 5.6</td>
</tr>
<tr>
<td>Any diagnosis</td>
<td></td>
<td>1 17.6</td>
<td>15 16.9</td>
<td>22 24.2</td>
<td>9 10.1</td>
</tr>
</tbody>
</table>

Note. From PAS-ADD (Psychiatric Assessment Schedule for Adults with Developmental Disabilities) interviews. Percentages are based on the total sample (N = 92).

ᵃInformation available from 91 parent/caregiver informants. ᵇInformation available from 89 respondents with Williams syndrome. ⁵Generalized anxiety disorder.
Table 2. PAS–ADD Diagnoses: Comorbidity

<table>
<thead>
<tr>
<th>Sex</th>
<th>Informant</th>
<th>Respondent</th>
</tr>
</thead>
<tbody>
<tr>
<td>F</td>
<td>No diagnosis</td>
<td>Agoraphobia, specific phobia</td>
</tr>
<tr>
<td>F</td>
<td>No diagnosis</td>
<td>Agoraphobia, specific phobia</td>
</tr>
<tr>
<td>F</td>
<td>No diagnosis</td>
<td>Schizophrenia, panic disorder</td>
</tr>
<tr>
<td>F</td>
<td>Depression</td>
<td>Specific phobia</td>
</tr>
<tr>
<td>F</td>
<td>Depression&quot;</td>
<td>Depression&quot;, specific phobia</td>
</tr>
<tr>
<td>F</td>
<td>Depression&quot;</td>
<td>Depression&quot;, specific phobia</td>
</tr>
<tr>
<td>F</td>
<td>Depression&quot;</td>
<td>Agoraphobia, panic disorder, specific phobia</td>
</tr>
<tr>
<td>F</td>
<td>Agoraphobia&quot;, panic disorder&quot;</td>
<td>Agoraphobia&quot;, panic disorder&quot;, social phobia</td>
</tr>
<tr>
<td>F</td>
<td>Depression&quot;, generalized anxiety disorder&quot;, undifferentiated psychosis&quot;</td>
<td>Depression&quot;, generalized anxiety disorder&quot;, undifferentiated psychosis&quot;</td>
</tr>
</tbody>
</table>

*Note. From PAS–ADD (Psychiatric Assessment Schedule for Adults with Developmental Disabilities).*

*aPAS–ADD diagnostic criteria reached on both informant and respondent interviews.*
Table 3. Life Events Experienced Over the Preceding 2 Years

<table>
<thead>
<tr>
<th>Type of event</th>
<th>n</th>
<th>% of total sample</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death&lt;sup&gt;a&lt;/sup&gt;</td>
<td>28</td>
<td>32.9</td>
</tr>
<tr>
<td>Serious illness/injury&lt;sup&gt;a&lt;/sup&gt;</td>
<td>26</td>
<td>30.6</td>
</tr>
<tr>
<td>Serious problem&lt;sup&gt;a&lt;/sup&gt;</td>
<td>14</td>
<td>16.5</td>
</tr>
<tr>
<td>Serious illness/injury (to self)</td>
<td>13</td>
<td>15.3</td>
</tr>
<tr>
<td>Move of residence</td>
<td>11</td>
<td>12.9</td>
</tr>
<tr>
<td>Break up of relationship</td>
<td>9</td>
<td>10.6</td>
</tr>
<tr>
<td>Something valuable lost/stolen</td>
<td>8</td>
<td>9.4</td>
</tr>
<tr>
<td>Unemployed/looking for work</td>
<td>7</td>
<td>8.2</td>
</tr>
<tr>
<td>Death (1st degree relative)</td>
<td>6</td>
<td>7.1</td>
</tr>
<tr>
<td>Sacked/laid off</td>
<td>4</td>
<td>4.7</td>
</tr>
<tr>
<td>Problems with police/authorities</td>
<td>3</td>
<td>3.5</td>
</tr>
<tr>
<td>Major financial crisis</td>
<td>3</td>
<td>3.5</td>
</tr>
<tr>
<td>Separation/divorce</td>
<td>1</td>
<td>1.2</td>
</tr>
<tr>
<td>Problem with drugs</td>
<td>1</td>
<td>1.2</td>
</tr>
<tr>
<td>Sexual problem</td>
<td>1</td>
<td>1.2</td>
</tr>
<tr>
<td>Any life event</td>
<td>59</td>
<td>69.4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>No. of life events experienced</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>26</td>
<td>30.6</td>
</tr>
<tr>
<td>1</td>
<td>20</td>
<td>23.5</td>
</tr>
<tr>
<td>2</td>
<td>17</td>
<td>20</td>
</tr>
<tr>
<td>3</td>
<td>9</td>
<td>10.6</td>
</tr>
<tr>
<td>4</td>
<td>8</td>
<td>9.4</td>
</tr>
<tr>
<td>5</td>
<td>4</td>
<td>4.7</td>
</tr>
<tr>
<td>6</td>
<td>1</td>
<td>1.2</td>
</tr>
<tr>
<td>Median</td>
<td>1</td>
<td>–</td>
</tr>
</tbody>
</table>

Note. Information available from 85 parents/caregivers.

<sup>a</sup>For example, close relative or friend.
**Table 4.** Characteristics of individuals with and without PAS–ADD diagnoses.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mental health problem</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>n (%)</td>
<td>No</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>15 (16.5)</td>
<td>35 (38.5)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>7 (7.7)</td>
<td>34 (37.4)</td>
<td></td>
</tr>
<tr>
<td>Health problems</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>17 (19.5)</td>
<td>48 (55.2)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>3 (3.4)</td>
<td>19 (21.8)</td>
<td></td>
</tr>
<tr>
<td>Residential status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>With parents</td>
<td>10 (11)</td>
<td>39 (42.9)</td>
<td></td>
</tr>
<tr>
<td>Supported</td>
<td>10 (11)</td>
<td>26 (28.6)</td>
<td></td>
</tr>
<tr>
<td>Independently</td>
<td>2 (2.2)</td>
<td>4 (4.4)</td>
<td></td>
</tr>
</tbody>
</table>

*Note.* Chi-square analysis. No significant correlations were found for any variable, *p* > .06.
**Table 5.** Characteristics of individuals with and without PAS–ADD diagnoses

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mental health problem</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
</tr>
<tr>
<td>Age&lt;sup&gt;a&lt;/sup&gt;</td>
<td>32</td>
</tr>
<tr>
<td>IQ&lt;sup&gt;a&lt;/sup&gt;</td>
<td>57.00</td>
</tr>
<tr>
<td>Receptive vocabulary&lt;sup&gt;a&lt;/sup&gt;</td>
<td>11.1</td>
</tr>
<tr>
<td>Expressive vocabulary&lt;sup&gt;a&lt;/sup&gt;</td>
<td>7.3</td>
</tr>
<tr>
<td>Adaptive Behavior Composite</td>
<td></td>
</tr>
<tr>
<td>Age equivalent&lt;sup&gt;a&lt;/sup&gt;</td>
<td>7.3</td>
</tr>
<tr>
<td>Standard score</td>
<td>37.91</td>
</tr>
<tr>
<td>Life events</td>
<td>2.05</td>
</tr>
</tbody>
</table>

*Note. Based on ANOVA/Mann-Whitney analyses, there were no significant group differences on any variable, *p* > .05.*

<sup>a</sup>In years. <sup>b</sup>IQs are for 89 of the adults with Williams syndrome. We were unable to obtain WAIS–III IQs for 3 participants.