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Prevalence of Psychiatric Disorders in 4 - 16-Year-Olds with Williams Syndrome

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Abstract

The prevalence of a range of DSM-IV psychiatric disorders in a sample of 119 4 – 16-year-old children with Williams syndrome (WS) was assessed using a structured diagnostic interview with their parents. Most children (80.7%) met criterion for at least one DSM-IV diagnosis. The most prevalent diagnoses were attention deficit/hyperactivity disorder (ADHD; 64.7%) and specific phobia (53.8%). There was a significant shift in predominant type of ADHD as a function of CA, from Combined for the youngest group (ages 4 – 6 years) to Inattentive for the oldest group (ages 11 – 16 years). The prevalence of generalized anxiety disorder (GAD) increased significantly with age. These findings are another step toward defining the behavioral phenotype of WS.

Keywords

Williams syndrome; psychopathology; children; mental retardation; intellectual disability

Introduction

There is increasing evidence that many syndromes involving mental retardation are associated with not only specific medical and cognitive phenotypes but also with particular patterns of behavioral and psychiatric symptoms. These “behavioral phenotypes” often include extreme manifestations of human traits, such as the gregarious nature of children with Williams syndrome (WS) and even bear similarities to psychiatric disorders, such as obsessive-compulsive features in Prader-Willi syndrome and anxiety in individuals with WS. In the present study, we examine the psychiatric component of the behavioral phenotype of WS in a large sample of children, using the DSM-IV criteria (APA, 2000).

WS is a neurodevelopmental disorder caused by a microdeletion of at least 25 genes on chromosome 7q11.23 (Hillier and others 2003). It is associated with mild to moderate

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mental retardation or learning difficulties, a characteristic facies, heart disease (especially supravalvar aortic stenosis), hypercalcemia, and failure to thrive in infancy (Morris, 2005). The cognitive phenotype for WS includes relative strengths in verbal short-term memory and language and extreme weakness in visuospatial construction, including writing, drawing, and pattern construction (e.g., Mervis and others 2000). A number of studies have considered the behavioral and emotional characteristics of individuals with WS (Cherniske and others 2004; Dykens 2003; Einfeld and others 1997, 1999, 2001; Einfeld and Hall 1994; Gosch and Pankau 1997; Klein-Tasman and Mervis 2003; Preus 1984; Sarimski 1997; Switaj 2000; Tomc and others 1990; Tonge and Einfeld 2003; Udwin and Yule 1991). A variety of problem behaviors (e.g., distractibility, restlessness) and personality characteristics (e.g., social disinhibition, excessive talking, mood swings, anxiety) have been identified.

In a study of the personality characteristics of children with WS, Klein-Tasman and Mervis (2003) found that one aspect of the distinctive personality of these children is their tendency toward anxiety. Klein-Tasman and Mervis used the Children's Behavior Questionnaire (CBQ; Rothbart and Ahadi 1994) and Multidimensional Personality Questionnaire – Parent Version (MPQ; Tellegen 1985) to compare personality characteristics of children with WS age 8 – 10 years to those of a comparison group of children with developmental disabilities (DD) of mixed etiologies matched for chronological age (CA) and IQ. The children with WS were significantly less shy, more gregarious, less dominant, more empathic, more sensitive, and more tense than the comparison group.

Einfeld and colleagues (Einfeld and others 1997, 1999, 2001; Tonge and Einfeld 2003) have conducted the most extensive study of the behavioral characteristics of children and adolescents with WS. This research group used the Developmental Behavior Checklist (DBC; Einfeld and Tonge 1995), a parent-report instrument specifically designed to assess behavioral and emotional disturbances in individuals who have mental retardation (MR), to assess 70 children with WS (mean CA: 9.4 years). Comparisons were made to an epidemiologically-derived control group; gender, CA, and level of MR were statistically controlled. The WS group had a significantly higher Total Behavior Problems score. Subscale analyses indicated that the WS group had significantly more problems on the Communication Disturbance and Anxiety subscales. A significantly higher proportion of the parents of children in the WS group endorsed the following items: tense or anxious, overaffectionate, covers ears or avoids particular sounds, overactive, short attention, food fads, obsessed/preoccupied with an idea or activity, overly attention seeking, doesn't mix with own age group/prefers adult company, inappropriately happy or elated, wanders aimlessly, and repeats words or phrases. Based on these findings, Einfeld and his colleagues concluded that WS may have a distinct behavioral phenotype.

Results of two longitudinal comparisons were also reported. Einfeld and colleagues (1999, 2001) presented a 5-year follow-up (Time 2). Although the Total Behavior Problems score for the WS group decreased, the difference was not significant. There was a significant decrease for the WS group for one item (repeats words or phrases). Differences between the WS group and the epidemiological control group remained significant for the Total Behavior Problems score, the Anxiety and Communication Disturbance subscales, and for all but two of the items listed above (overactive, and obsessed /preoccupied with an idea or activity). An 8-year follow up (Time 3; Tonge and Einfeld 2003) indicated that the Total Behavior Problems score decreased significantly in comparison to Time 1 (no comparisons to Time 2 were reported), although it was still significantly higher than for the epidemiological control group. Scores on 3 of the 5 subscales, Disruptive/Antisocial, Self-absorbed, and Anxiety, decreased significantly. The WS group scored significantly higher than the epidemiological control group on the Communication Disturbance subscale; scores

for the two groups did not differ significantly for the other 4 subscales. These findings suggested that behavioral problems in individuals with WS persist over time, although they may become less severe with age.

Switaj (2000) examined anxiety-related behaviors and traits in children with WS and how their manifestations may change over time. The 1500 members of the Williams Syndrome Association who had children ages 6 – 18 years were invited to participate in a mail survey study. Parents of 190 children (12.6%) completed the surveys. The following measures were included: Child Behavior Checklist (CBCL; Achenbach, 1991), Behavior Assessment System for Children (BASC; Reynolds and Kamphaus 1992), the Revised Children's Manifest Anxiety Scale (RCMAS; Reynolds and Richmond 1985) and the Yale-Brown Obsessive-Compulsive Symptom Checklist (Y-BOCS Goodman and others 1986). Results were compared across the following age groups: 6-9, 10-13, and 14-18. The 14-18 group received significantly higher scores on the Anxious/Depressed subscale of the CBCL than the two younger groups. On the RCMAS, the scores for the three age groups were significantly different. The youngest group received the lowest scores, the 10-13 group received significantly higher scores than the 6-9 group, and the 14-18 group received significantly higher scores than the 10-13 group. On the BASC, the 10-13 group received significantly higher scores than the 6-9 group. No age differences were apparent in the YBOCS scores. Overall, this study demonstrated an increase in anxiety-related symptoms with age, in contrast to findings by Tonge and Einfeld (2003).

The studies discussed thus far used questionnaires and behavior rating scales to compare children with WS to a contrast group. Although these measures provide quantifiable information regarding the presence and severity of behaviors and traits, they typically do not solicit information about their frequency, duration, associated impairment, the context in which the behavior takes place, the nature and time of onset, course of illness, or other variables that are essential for the diagnosis of psychiatric disorders (see Dykens 2000). Additionally, the behaviors included in various scales can be arbitrary. For example, subscales with the same names may provide different scores based on the set of items comprising them. In contrast, structured and semi-structured interviews provide specific diagnoses based on a diagnostic system such as the DSM or ICD. Thus, symptoms and behaviors are grouped into diagnostically meaningful clusters and onset, impairment, and other variables are taken into account.

Use of diagnostic interviews for individuals with DD raises the question of the applicability of the existing diagnostic systems to these individuals. Cooper and colleagues (2003) argue that individuals with MR are less likely to meet DSM criteria than individuals in the general population. This is in part due to the lack of understanding of the relationship between DD and psychopathology. Consistent with this concern, Reiss and colleagues (1982) demonstrated that clinicians examining a person with MR often are unable to “see” anything but the DD (“diagnostic overshadowing”). Their research suggested that reported prevalence rates psychopathology may be an underestimate in populations with DD.

To address this question, Sovner and Hurley (1983) reviewed 25 reported cases of affective disorders in individuals with mental retardation using the DSM-III criteria in order to assess the validity of these diagnoses. The authors concluded that individuals with mild and moderate mental retardation can be diagnosed with the full range of affective disorders using DSM criteria. Overall, Sovner and Hurley (Sovner 1986; Sovner and Hurley 1982a; Sovner and Hurley 1982b) suggested that adults with DD disorders have psychiatric disturbances that are conceptually the same as DSM disorders, although they may be less likely to be diagnosed. Brown and others (2004) argued that DSM-IV criteria are applicable to children

and adolescents with mild or moderate MR. Additionally, Sager and O'Brien (2003) stated that DSM-IV criteria for ADHD are appropriate for children with MR.

The first study to use a DSM-based interview to measure psychopathology in WS was conducted by Dykens (2003) to address rates of anxiety disorders. Dykens used the Diagnostic Interview Schedule for Children-Parent (DICA-R; Reich and others 1991), a semistructured interview based on DSM-III-R (American Psychiatric Association, 1987) criteria. The anxiety domain of the DICA-R was administered to caregivers of 51 individuals with WS ranging in age from 5 – 49 years (mean = 15.91 years, SD = 10.31). The anxiety domain of the DICA-R includes separation anxiety disorder, avoidant disorder, overanxious disorder, specific phobia, and obsessive-compulsive disorder (OCD). The interview demonstrated 35% prevalence for specific phobia (mean CA = 15.08 years, SD = 7.37), 16% prevalence for overanxious/generalized anxiety disorder (mean CA = 16.24 years, SD = 8.49), and 4% and 2% prevalence for separation anxiety and OCD respectively. Although this study provided valuable information regarding psychiatric disorders in WS, it also had significant limitations. First, only the anxiety section of the DICA-R was used; other disorders, such as ADHD and oppositional defiant disorder (ODD) were not assessed. Second, this study used an interview based on DSM-III-R criteria. Finally, the study included a very broad age range and utilized a child interview measure not only with children but also with adults.

More data are needed to define the psychiatric phenotype of individuals with WS, based on DSM-IV criteria and using a measure appropriate for the participants' ages. The present study used a structured diagnostic interview, the Anxiety Disorders Interview Schedule for DSM-IV Parent Interview Schedule (ADIS-IV Parent; Silverman and Albano 1996), to determine prevalence rates of a broad range of DSM-IV diagnoses in 4 – 16-year-old children with WS. Differences in prevalence rates as a function of age and sex were also examined.

Materials And Methods

Participants

Participants were 128 children with WS. Of these children, 121 were consecutive participants within the 4 – 16 year age range in an ongoing study of cognitive and language development of individuals with WS at the University of Louisville and the University of Nevada School of Medicine. As part of this study, the ADIS-P is administered to the parents of all children ages 4 years and older. Seven additional children whose parents had completed the ADIS as part of a similar study at the University of Wisconsin-Milwaukee were also included. The WS diagnosis for all children was confirmed by means of a fluorescence in situ hybridization (FISH) test. Nine children were excluded because they met autism or autism spectrum criteria based on clinical judgment following evaluation using the Autism Diagnostic Interview-Revised (Lord and others 1994) and the Autism Diagnostic Observation Schedule (ADOS-G; Lord and others 2000).

For the remaining 119 children, (54 boys and 65 girls), mean CA was 9.1 years (SD = 3.3 years, range = 4.01 – 16.9 years). Mean General Conceptual Ability Score (GCA; similar to IQ) on the Differential Ability Scales (DAS; Elliott 1990a, b) was 59.5 (SD = 13.7, range = <25 – 94). Based on GCA, 20% of the children had intellectual abilities in the normal range, 61% had mild mental retardation, 14% had moderate mental retardation, and 5% had severe mental retardation. WS is associated with a specific cognitive profile involving relative strength in verbal short-term memory and language and extreme weakness in visuospatial construction (Mervis and others 2000). As such, GCA often provides an underestimate of the verbal abilities of children with WS (Meyer-Lindenberg and others 2006). All of the

children, including those with severe mental retardation, were verbal, and of the children 6 years or older, all but one spoke in sentences.

Instruments

ADIS-IV, Child/Parent version—The ADIS, Parent version (Silverman and Albano 1996), is a structured interview designed to diagnose anxiety disorders of childhood and adolescence. It is based on DSM-IV criteria and is used both to determine the diagnosis and its severity. It allows for differential diagnoses among all the DSM-IV anxiety and related disorders and provides data regarding symptomatology, etiology, and the course of the disorder (Silverman 1994). In addition to anxiety disorders, the ADIS assesses for attention deficit/hyperactivity disorder (ADHD), oppositional defiant disorder (ODD), conduct disorder, enuresis, sleep terror disorder, and selective mutism, as well as major depressive disorder and dysthymia. Silverman and others (2001) have found excellent reliability for separation anxiety disorder, social phobia, specific phobia, and GAD as well as excellent test-retest reliability for the interview. Usually it is administered together with the Child Schedule, however in the current study only the parent reports were analyzed, because individuals with developmental disabilities may not be able to provide accurate reports of experiences (Sovner 1986). Additionally, there is evidence suggesting that parents may be able to provide more reliable information about children's psychological and emotional states and behaviors than the children themselves (Edelbrock and others 1985, 1986).

While the validity of the ADIS-P with children with WS has not yet been established, researchers (e.g., Brown and others 2004) have argued that DSM criteria may be used with individuals with mild or moderate MR. Most individuals with WS have mild mental retardation or borderline normal intelligence (Mervis and Klein-Tasman, 2000). Additionally, when making the diagnoses in this sample, several factors beyond the DSM-IV criteria were considered. For example, when assessing for presence of a specific phobia, the child's developmental level was taken into consideration to differentiate between pathological and developmentally appropriate fears. Similarly, the child's developmental level was considered when making diagnoses of ADHD. Overall, the final diagnoses were made based on DSM-IV criteria and judgment by an expert clinician.

Differential Ability Scales (DAS; Elliott 1990 a, b)—The DAS provides an assessment of general intellectual functioning. This measure was designed to provide specific information about an individual's strengths and weaknesses across a wide range of intellectual activities.

There are two levels of the DAS: Preschool and School Age. Following the test author's recommendation for children who are expected to have below average intelligence, the Preschool Level was administered to all children who were 6 years 11 months or younger. The School Age Level was administered to the remaining children unless they were very low functioning; these children completed the Preschool Level and if necessary GCA was calculated using the extended norms, which are available for the Preschool Level through age 13 years 11 months. The GCA is based on performance on the core subtests and has a mean of 100 and a standard deviation of 15.

Procedure

The ADIS-P was administered to the parents in person by a licensed clinical psychologist, a board-certified developmental behavioral pediatrician, a board-certified pediatrician who specializes in children with developmental disabilities, or a doctoral level clinical psychology student who had passed reliability training on the instrument. The training involved four consecutive matches on diagnosis and its severity. All student interviews were

videotaped. The interview protocols were then reviewed with a licensed clinical psychologist. In some cases, the videotapes of the interviews were observed. The participants completed the DAS within a day of the ADIS interview.

Data Analyses

Chi-square tests were used to compare the prevalence rates among the three age groups and between boys and girls. *t*- tests were used to compare the DAS GCA scores for children with and without particular diagnoses.

Results

The prevalence rates of the diagnoses included in the ADIS-P were first calculated for the entire sample. The sample was then divided into 3 age groups (4-6 years, 7-10 years, and 11-16 years), and the prevalence rates were compared across the groups.

Prevalence in the Entire Sample

The prevalence of each of the diagnoses in the entire sample is indicated in Table 1. The most prevalent diagnosis was ADHD (64.7%). Of the children who met criteria, 68.8% had the Predominantly Inattentive type, 25.9% had the Combined type (inattention plus hyperactivity-impulsivity), and 3.9% had the Predominantly Hyperactive-Impulsive type. To determine if there was a relation between the child's intellectual ability and diagnosis of ADHD, we compared the DAS GCA scores for children with ADHD (mean = 59.4, SD = 14.1) and children without ADHD (mean = 59.7, SD = 13.1). The difference was not significant [t (114) = 0.11, p=.91]. We also compared the DAS GCA between the children who had the Predominantly Inattentive type of ADHD (mean = 59.6, SD = 14.5) and those who had either the Predominantly Hyperactive-Impulsive or the Combined type (mean = 57.9, SD = 13.3). The difference was not significant [t (74) = .49, p = .62].

Specific phobia was the second most prevalent diagnosis (53.8%). The types of specific phobias are listed in Table 2. The most common type of specific phobia was phobia of loud noises (27.7%; actually, hypersensitivity to specific sounds). Types of sounds that caused this type of phobia included startling loud sounds (e.g., fire drills, sirens, thunder), motor sounds (e.g., lawn mowers, weed whackers, vacuum cleaners, blenders), noisy settings (e.g., concerts, ballgames), fireworks, crying, and screaming. Other common types of specific phobia were phobia of blood tests or shots (15.9%) and of doctors or dentists (8.4%). The majority of the children who had hypersensitivity to specific sounds also had at least one other specific phobia (60.6%). To determine if there was a relation between the child's intellectual level and specific phobia, we compared the DAS GCA scores for children with specific phobia (mean = 57.4, SD = 12.8) and children without specific phobia (mean = 61.8, SD = 14.4). The difference was not significant [t (114) = 1.76, p=.08], and the effect size was small (d = .29).

We also considered the comorbidity of diagnoses in children with WS. Twenty-six children (21.8%) had no diagnosis, 37 (31.1%) had one diagnosis, 36 (36.4%) had two diagnoses, 19 (15.9%) had three diagnoses, and 1 (0.8%) had four diagnoses. The two most prevalent diagnoses, ADHD and specific phobia, had the highest co-morbidity rate; 38.7% of the group had both ADHD and specific phobia. To determine if there was a relation between the child's intellectual level and the presence of any psychiatric diagnosis, we compared the DAS GCA scores for children with any diagnosis (mean = 59.2, SD = 13.6) and children without a diagnosis (mean = 60.4, SD = 14.2). The difference was not significant [t (114) = 0.38, p=.71].

To address the possibility of sex differences in the prevalence rates of the DSM-IV disorders that were common in the sample (ADHD, separation anxiety, specific phobia, GAD), we compared the proportions of boys and girls who met DSM-IV criteria for each of these disorders. These results are presented in Table 3. No significant difference was found in the prevalence of these disorders as a function of sex.

Stability and Change as a Function of Chronological Age

To determine if the pattern of psychiatric diagnoses for children with WS changes with age, we compared the prevalence rates of the diagnoses across the three age groups (Table 4). A significant difference was found in the prevalence rates of ADHD as a function of age. Examination of the standardized residuals demonstrated that the prevalence rate for the 7-10 group was significantly higher than expected relative to the prevalence for either the 4-6 or the 11-16 groups.

To address the question of whether there were any age group differences in the distribution of the types of ADHD, we combined the Hyperactive-Impulsive type and Combined type, as only 3 individuals had received a diagnosis of ADHD, Hyperactive-Impulsive type. As indicated in Table 4, a significant difference was found in the distribution of the types of ADHD as a function of age. Examination of the standardized residuals demonstrated that children in the 4-6 group who were diagnosed with ADHD of any type had a significantly higher rate of diagnosis of ADHD, Combined or ADHD, Hyperactive-Impulsive type than expected relative to the prevalence for children in the 11-16 group who were diagnosed with ADHD of any type. Children in the 11-16 group who were diagnosed with ADHD of any type had a significantly higher rate of ADHD, Inattentive type than expected relative to the prevalence for children in the 4-6 group who were diagnosed with ADHD of any type.

No significant difference was found in the prevalence rate of specific phobia as a function of age. When the specific phobia of loud noise was removed from the analyses, the difference remained non-significant [$\chi^2(2) = 2.24$, p=.33]. Further, no difference was found in the prevalence of specific phobia of loud noise as a function of age group [$\chi^2(2) = 1.78$, p=.41].

The prevalence of GAD differed significantly among the three age groups. Examination of the standardized residuals indicated that the youngest group had a significantly lower rate of GAD than expected and the oldest group had a significantly higher rate of GAD than expected.

The prevalence rates of *any* diagnosis changed significantly with age. However, although the 7-10 group appeared to have more children with diagnoses than the other two groups, examination of the standardized residuals indicated that none of the differences between pairs of age groups was significant.

Discussion

This is the first study to use a DSM-IV-based diagnostic instrument to assess psychopathology in children with WS. The ADIS-P was administered to the children's parents. Only parental reports were obtained because of the concern that children with WS may not be able to describe their states and feelings accurately. The applicability of DSM-IV criteria to populations with DD has been widely discussed in the literature, with researchers suggesting that they can be utilized to diagnose psychopathology in individuals with mild and moderate levels of intellectual disability (Brown and others 2004). A small proportion (5%) of the sample in this study fell in the severe range of intellectual disability. However, in contrast to most children with severe MR, the children with severe MR in this sample

were verbal and all but one spoke in sentences. The results are discussed in the order of prevalence of the diagnoses in this sample: ADHD, specific phobia, and GAD.

ADHD

ADHD was the most frequent diagnosis in this sample of 119 children with WS. The prevalence rate (64.7%) was far higher than the 3 – 7% prevalence rate for the general population (APA 2000). Myers and Pueschel (1991) reported a prevalence rate (6.1%) similar to that for the general population for a sample of children and adolescents with Down syndrome, using psychiatric and psychological evaluations. Studies of other syndromes or mixed-etiology samples have consistently reported much higher rates. Dekker and Koot (2003) reported 18.9% prevalence of ADHD in a sample of children with mild to moderate MR, using DSM-IV criteria. Hardan and Sahl (1997) reported ADHD in 42% of their sample of children and adults with MR or DD, based on the DSM-III-R criteria. In boys with fragile X syndrome, the prevalence of ADHD has been found to be as high as 72% (Backes and others 2000) as assessed by a structured psychiatric interview, providing diagnoses based both on ICD-10 and DSM-IV criteria.

The majority of the children with WS who received a diagnosis of ADHD (68.8%) were diagnosed with the Predominantly Inattentive type, 25.9% with the Combined type, and 3.9% with the Predominantly Hyperactive-Impulsive type. In children with typical development, the Predominantly Inattentive type of ADHD is also more common than the Combined and Hyperactive-Impulsive types (Graetz and others 2001); the Hyperactive-Impulsive type is rare (Dunn and Kronenberger 2003).

There was no significant difference in prevalence rates of ADHD between males and females in this sample of children with WS. For children with typical development, the findings have varied. Some studies suggest that ADHD is diagnosed significantly more frequently in males than in females (e.g., Graetz and others, 2001). The DSM-IV-TR (APA 2000) reports a male to female ratio ranging from 2:1 to 9:1 depending on setting and type of ADHD. Others suggest that ADHD may become more prevalent in girls in adolescence (Nigg and Casey 2005).

In the present sample of children with WS, there was also no significant difference in prevalence rates of ADHD types as a function of gender. In contrast, for children with typical development, the Predominantly Inattentive type of ADHD is more common in girls, whereas the Combined type is more frequently diagnosed in boys (Dunn and Kronenberger 2003; Hartung and others 2002; Lahey and others 1994).

The prevalence of ADHD differed significantly as a function of age; the 7-10 group had a higher proportion of children receiving a diagnosis of ADHD than expected relative to the 4-6 and 11-16 groups. This pattern is similar to that found in the general population (e.g., Pineda and others 1999). A significant difference was also found in the distribution of the types of ADHD as a function of age, with a higher proportion of children in the 4-6 group receiving a diagnosis of the combined type of ADHD than children in the other two groups. This pattern is also similar to that found in the general population (e.g., Lahey and others 1994).

Specific Phobia

Specific phobias are highly prevalent in children with WS. This study showed a somewhat higher prevalence of clinical specific phobias (53.8%) than the 35% reported by Dykens (2003) for a WS sample with a considerably higher mean CA. However, the rate in the present study is similar to that reported by Cherniske and colleagues (2004) for a group of 20 adults with WS (50%). The prevalence rates in all three studies are much higher than

those previously reported for individuals with MR of other etiologies. For example, using the ICD-10 criteria, Cooper (1997) found specific phobias in only 6.8% of their sample of adults with MR. Myers and Pueschel (1991) reported phobias in only 1.5% of their sample of children and adolescents with Down syndrome. Dekker and Koot (2003) reported 17.5% prevalence in their sample of children with mild to moderate MR. Emerson (2005) reported specific phobia in 1.9% of children with DD.

The most prevalent phobias in the WS sample were those of loud noises, shots and/or blood tests, and doctors/dentists unrelated to shots and blood tests. The fear of doctors and blood tests/shots may be related to the physical problems frequently associated with WS and hence more frequent exposure to these situations.

The highly prevalent fear of loud noises was expected based on previous findings regarding hypersensitivity to sound in individuals with WS (Einfeld and others 1997; Johnson and others 2001; Levitin and others 2005; Marler and others 2005; Van Borsel and others 1997). For example, in the study by Levitin and colleagues (2005), hypersensitivity to loudness of sounds (odynacusis) was found in 79.8% of their group with WS, as reported by parents on a researcher-designed questionnaire. Furthermore, 90.6% of the parents of children with WS reported that their children had auditory aversions. Hypersensitivity to certain sounds is also often found in other developmental disorders, including autism (Sinha and others 2004) and fragile X syndrome (Reiss and Freund 1992).

It is possible that the hypersensitivity to sounds in WS is related to sensorineural hearing loss, a condition associated with damage to the inner ear or neural pathways from the inner ear to the brain (Johnson and others 2001; Marler and others 2005). Johnson and colleagues administered audiologic testing to 9 individuals with WS in the age range of 9-25 years, finding sensorineural hearing loss in 3 of them. Marler and colleagues (2005) have reported sensorineural hearing loss in 78% of 18 school-aged children with WS (median age 11.4 years). Cherniske and colleagues (2004) reported sensorineural hearing loss in 75% of 20 adults with WS (mean age 38.8 years).

GAD

Approximately 12% of the present sample was diagnosed with GAD. This rate is similar to that reported by Dykens (2003) for overanxious disorder in a study using DSM-III-R criteria. In contrast, studies using DSM-III or DSM-III-R criteria have found a much lower rate of GAD in children with typical development (2-4%; Achenbach and others 1989; Anderson and others 1987; Bowen and others 1990). Studies of children with MR/DD have also shown a much lower rate of GAD. For example, in Dekker and Koot (2003), no child was diagnosed with GAD, and in Emerson (2005) only 1.5% of the children with DD were reported to have GAD. In the present study, the prevalence of GAD was significantly higher than expected in the oldest WS group (ages 11 – 16) relative to the youngest group. This finding is consistent with the results obtained by Switaj (2000) using anxiety rating scales and checklists. It also is similar to the pattern found in the general population, where the mean onset of GAD has been reported to be between 10 and 13 years of age (Last and others 1987; Strauss and others 1988).

The context of worries and their manifestation in individuals with WS is different from that for individuals with typical development. In general, our clinical experience has been that a large proportion of children with WS worry in anticipation of a variety of events, but that once the events begin, the worry dissipates. Furthermore, this anticipatory worry is not limited to events or activities they dislike (such as a doctor's visit), but also pertains to enjoyable events or activities and is perseverative in nature. The quality of the anticipation is such that some parents resist the term “worry” to describe their child's anticipation. The

anxiety may be manifested through asking repeated questions about the upcoming activity. The behavior appears to lie at the intersection of worry and obsessiveness. While this anxiety oftentimes takes up a significant amount of time and parents consistently report it as impairing, it is not captured by the GAD criteria.

Conclusion—The present study is the first to examine a broad range of psychiatric disorders in WS using a categorical diagnostic instrument based on the DSM-IV criteria. Our results indicate that specific phobias and ADHD are a part of the psychiatric phenotype of WS and suggest the need either to modify the definition of GAD or create a new category of anxiety to capture the "anticipatory" anxiety evidenced by a large proportion of children with WS. Toward this goal, systematic description of this type of anxiety is critical.

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Table 1

Prevalence of psychopathology in children with WS (N=119)

Diagnosis	N	%
ADHD	77	64.7
Inattentive	*53*	*68.8*
Combined	*20*	*25.9*
Hyperactive-Impulsive	*3*	*3.9*
Separation anxiety	8	6.7
Social phobia	2	1.7
Specific phobia	64	53.8
Panic disorder w/Agoraphobia	1	0.8
GAD	14	11.8
OCD	3	2.5
PTSD	1	0.8
ODD	4	3.4
No diagnosis	26	21.8

Table 2

Types of specific phobia present in the sample (N=119)

Type of phobia	N	%
Blood-Injection-Injury Type		
Blood tests/shots	19	15.9
Sight of blood	1	0.8
Animal Type		
Animals or Insects	7	5.9
Natural Environment Type		
Heights	6	5.0
Thunderstorms	5	6.3
Darkness	3	2.5
Water	1	0.9
Situational Type		
Elevator/Escalator	1	0.8
Doctor/dentist	10	8.4
Other		
Loud noises	33	27.7
Choking	1	0.8
Vomiting	4	3.4
Bicycles	1	0.8
Washing hair	1	0.8
Costumed characters	1	0.8

Table 3

Sex differences in the prevalence rates of psychiatric disorders in children with WS

Diagnosis	Male (N=54)	%	Female (N=65)	%	χ^2
ADHD	38	70.4	39	60.0	$\chi^2(1)=1.39$, $p=.24$
Inattentive	*26*	*48.1*	*27*	*41.5*	
Combined or Hyperactive-Impulsive	*12*	*22.2*	*12*	*18.5*	$\chi^2(2)=4.60$, $p=.20$[a]
Separation anxiety	5	9.3	3	4.4	Fisher exact $p=.47$
Specific phobia	29	53.7	35	53.8	$\chi^2(1)<0.001$, $p=.99$
GAD	4	7.4	10	15.4	$\chi^2(1)=1.81$, $p=.18$

[a]Type of ADHD as a function of sex

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Table 4

Prevalence of psychopathology by age group in children with WS

Diagnosis	Ages 4 -6 years		Ages 7 -10 years		Ages 11 – 16 years		χ^2
	N = 40	%	N = 44	%	N = 35	%	
ADHD	22	55.0	35	79.5	20	57.1	$\chi^2(2)=6.77$, $p=.034$*
Inattentive	*11*	*50.0*	*22*	*62.9*	*17*	*85.0*	
Combined	*9*	*40.9*	*8*	*22.9*	*1*	*5.0*	$\chi^2(2)=11.76$, $p=.003$[a]*
Hyperactive-Impulsive	*2*	*9.1*	*1*	*2.9*	*0*	*0*	
Separation anxiety	2	5.0	4	9.1	2	5.7	
Social phobia	0		0		2	5.7	
Specific phobia	18	45.0	27	61.4	19	54.3	$\chi^2(2)=2.26$, $p=.323$
Panic disorder w/Agoraphobia	0		1	2.3	0		
GAD	0		6	13.6	8	22.9	$\chi^2(2)=9.63$, $p=.008$*
OCD	0		2	4.5	1	2.9	
PTSD	0		0		1	2.9	
ODD	2	5.0	2	4.5	0		
No diagnosis	14	35.0	5	11.4	7	26.9	$\chi^2(2)=6.96$, $p=.03$*

[a] Type of ADHD as a function of age group

* Difference is significant

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