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Characterizing associations and dissociations between anxiety, social, and cognitive phenotypes of Williams syndrome

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Abstract

Williams syndrome (WS) is a neurogenetic disorder known for its "hypersocial" phenotype and a complex profile of anxieties. The anxieties are poorly understood specifically in relation to the social-emotional and cognitive profiles. To address this gap, we employed a Wechsler intelligence test, the Brief Symptom Inventory, Beck Anxiety Inventory, and Salk Institute Sociability Questionnaire, to (1) examine how anxiety symptoms distinguish individuals with WS from typically developing (TD) individuals; and (2) assess the associations between three key phenotypic features of WS: intellectual impairment, social-emotional functioning, and anxiety. The results highlighted intensified neurophysiological symptoms and subjective experiences of anxiety in WS. Moreover, whereas higher cognitive ability was positively associated with anxiety in WS, the opposite pattern characterized the TD individuals. This study provides novel insight into how the three core phenotypic features associate/dissociate in WS, specifically in terms of the contribution of cognitive and emotional functioning to anxiety symptoms.

Keywords

Anxiety; Williams Syndrome; Neurodevelopmental Disorder; Maladaptive Behaviors; Intellectual Impairment; Social Behavior

1. Introduction

Williams syndrome (WS) is a genetic disorder that stems from a microdeletion on chromosome 7q.11.23 (Korenberg et al., 2000), with prevalence ratings ranging from 1 in 7,000 – 20,000 individuals (Jones & Smith, 1975; Stromme, Bjomstad, & Ramstad, 2002). WS is typified by a multitude of medical and physical abnormalities, e.g., supravalvular aortic and pulmonary stenoses, hypercalcemia, hypotonia, and distinct elfin-like facial features (Pober, 2010). Furthermore, WS is typically associated with mild to moderate

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cognitive impairment; however, upon meeting a person with WS, these disabilities may not at first be apparent. Specifically, the intellectual impairment of WS is characterized by drastic deficits in visuospatial construction contrasted with markedly higher verbal abilities (Mervis & John, 2010; Searcy et al., 2004). Thus, the non-verbal cognitive deficits are masked by relatively strong expressive language capabilities (Mervis & Velleman, 2011), and engaging social-interactive, verbal and non-verbal communicative behaviors (Järvinen-Pasley, Bellugi, Reilly, Mills, & Galaburda, 2008; Reilly, Bernicot, Vicari, Lacroix, & Bellugi, 2005; Reilly, Klima, & Bellugi, 1990; Reilly, Losh, & Bellugi, 2004).

Individuals with WS exhibit a range of unique social attributes including diminished fear to approach strangers (Doyle, Bellugi, Korenberg, & Graham, 2004; Järvinen-Pasley et al., 2008; Haas et al., 2009), an intensified attraction to faces (Jones et al., 2000), and an exaggerated use of affective and linguistic devices to socially engage others (Losh, Bellugi, & Anderson, 2001). We have pioneered in the development of measures attempting to capture the nature of the unusual social behavior of WS in real-life, e.g., the Salk Institute Sociability Questionnaire (SISQ) (Doyle et al., 2004; Järvinen-Pasley et al., 2010; Jones et al., 2000; Zitzer-Comfort, Doyle, Masataka, Korenberg, & Bellugi, 2007). Our studies and those of others have consistently indicated that individuals with WS demonstrate higher global sociability and approachability toward strangers as compared to any other group tested (Autism, Down syndrome, language impairment, unilateral focal lesions, typical development (TD)). The prosocial nature characterizing WS is well defined by both neuroimaging and behavioral research (Järvinen-Pasley et al., 2008; Golarai et al., 2010; Gothelf et al., 2008; Haas et al., 2012, 2010, 2009; Haas & Reiss, 2012; Meyer-Lindenberg et al., 2005) with some hints from genetic studies (Dai et al., 2009; Jabbi et al., 2012; Karmiloff-Smith et al., 2012; Mervis et al., 2012). Yet these distinctive social traits typically coexist with a multitude of general anxieties and other maladaptive behaviors, as well as intellectual impairment, and it is currently poorly understood how the major phenotypic characteristics of WS may relate to each other.

An accumulating literature consistently indicates that psychopathologies pertaining to anxieties and abnormal fears are among the most common diagnoses within the WS population, and these symptoms also appear relatively stable across development (Dykens, 2003; Dykens, Rosner, Ly, & Sagun, 2005; Einfeld, Tonge, & Florio, 1997; Einfeld, Tonge, & Rees, 2001; Leyfer, Woodruff-Borden, Klein-Tasman, Fricke, & Mervis, 2006; Leyfer, Woodruff-Borden, & Mervis, 2009; Woodruff-Borden, Kistler, Henderson, Crawford, & Mervis, 2010). For example, in a large-scale study, Leyfer et al. (2009) examined the prevalence of anxiety disorders in a sample of 132 children with WS by administering the Anxiety Disorder Interview Schedule (ADIS-IV) to their caregivers. Compared to children with developmental disabilities, those with WS were more likely to meet criteria for specific phobia, general anxiety disorder, and separation anxiety, with over 60% of the participants likely to have at least one type of anxiety disorder. In another study, Cherniske et al. (2004) reported that over 60% of the 20 adults with WS tested exhibited moderate to severe anxiety and simple phobias. Notably, studies assessing anxiety in WS have predominantly focused on indexing such individuals' experiences of fear and worry across different contexts (e.g., Dykens, 2003); yet no known studies have elucidated whether anxiety in individuals with WS may actually constitute physiological symptoms (e.g., palpitations, shakiness,

abdominal discomfort). This is important as such features are largely incorporated in diagnoses of anxiety and specific phobia disorders (DSM-IV, 4th Edition). Considering that those with WS experience significant cardiovascular and gastrointestinal abnormalities including hypertension, supravalvular aortic stenosis, and diverticular disease (Pober, 2010), which may contribute to their anxiety features, investigations attempting to disentangle the characteristic anxiety in WS as a function of psychological and physical characteristics is of significance. While elevated anxieties in WS have been consistently documented relative to controls with intellectual impairment of unspecified origin (Dykens, 2003; Gosch & Pankau, 1994) as well as other genetic disorders (e.g., Prader Willi Syndrome, Down Syndrome, Fragile X) (Dykens et al., 2005; Einfeld, Tonge, Turner, Parmenter, & Smith, 1999; Sarimski, 1997), comparisons with healthy controls with normal intellectual function are virtually non-existent. This is of important for being able to clarify whether the anxiety features that are typically elevated in individuals with WS may generally pertain to psychological states of worry or fear as noted in the aforementioned research, or whether they may actually closely relate to the physiological symptomatology, or both. Moreover, these comparisons are necessary to understand the potential convergences and divergences between anxiety features, cognitive ability, and social-emotional functioning in WS, as virtually all neurodevelopmental disorders are associated with some degree of social dysfunction as well as atypical cognition.

Only a handful of existing studies have directly examined the association between anxiety and cognition in WS. In one such study, Leyfer and colleagues (2006) documented no differences in general intellectual functioning between children and adolescents with WS who either met or did not meet the diagnosis of specific phobia. In a similar vein, Woodruff-Borden et al. (2010) reported a lack of association between composite intelligence quotient (IQ) and anxiety in children and adolescents with WS. A recent study by Riby et al. (2013) similarly reported no association between anxiety and cognitive ability in their sample of participants with WS. It is noteworthy here, however, that the study of Riby and colleagues (2013) did not include a comprehensive assessment of cognitive skill but only utilized single measures tapping into receptive vocabulary (British Picture Vocabulary Scale II) and non-verbal reasoning (Ravens Coloured Progressive Matrices) for a subset of the participants. Moreover, the sample was characterized by a broad age range (6-36 years). It is thus possible that the lack of significant association between anxiety and IQ reflects a developmental effect in light of evidence suggesting that subdomains of intellectual functioning may not reach stability until adolescence (Hopkins & Bracht, 1975). Interestingly, and Porter (2009) tested 20 adults with WS who either met or did not meet the diagnosis of general anxiety, and the groups did not significantly differ in their performance on the Woodcock Johnson Test of Cognitive Ability-Revised. However, upon examining the descriptive trends within the WS sample, the five adults with WS who were diagnosed with general anxiety disorder achieved greater average cognitive scores as compared to those without the anxiety diagnosis. More developmental research evaluating the relationship between cognitive ability and anxiety in WS is thus needed to illuminate the potentially moderating effect of IQ on the severity of internalizing symptomatology, and the current study is aimed at addressing this gap particularly in the steady state.

Two recent studies have addressed the link between social functioning and anxiety profiles in individuals with WS. First, Riby et al. (2013) employed the Spence Children's Anxiety Scale (SCAS-P) and the Social Responsiveness Scale respectively, and found a positive correlation between the severity of anxiety and deficits in general social function. Those with WS with high anxiety showed more deficits in social awareness, social cognition, and social communication than their counterparts with low anxiety. However, as no differences in scores between high versus low anxiety individuals with WS emerged in social motivation and autistic mannerisms, this suggests that increased anxiety in WS was specifically linked to poorer aptitude in social reciprocity. However, it is unclear which specific components of anxiety may be related to social functioning in individuals with WS as diverse measures of internalizing symptoms were collapsed to obtain a single metric value. In the second study, Kirk and colleagues (2013) examined the link between visual attention as indexed by eye tracking to social affective faces and anxiety in individuals with WS. The findings showed a negative association between anxiety, as measured by total score on SCAS-P, and the fixation to the eye region of threatening faces (fear, anger) in individuals with WS. Further, interestingly, there was a positive correlation between anxiety and attention to mouths of fearful faces in these participants. The authors interpreted their findings as suggesting that anxiety in WS may have an influential role in the allocation of attention to social stimuli. Moreover, such finding suggests that a particularly amplified hypersocial and socially disinhibited profile in WS may camouflage increasing anxieties. These studies offer initial clues of the relationship between the anxiety and social phenotypes in WS.

The above findings may appear surprising in light of literature suggesting that the nature of anxiety in WS is primarily non-social, which has also been linked to abnormal amygdala processes (Meyer-Lindenberg et al., 2005; Meyer-Lindenberg, Mervis, & Berman, 2006). However, the differential focus, purpose, and design of the studies, together with the use of non-overlapping measures (e.g., Dykens, 2003; Kirk et al., 2013; Riby et al., 2013; Sarimski, 1997) may explain the apparent inconsistency concerning whether the anxiety in WS may be more social or non-social in nature. Moreover, as anxiety is an important phenotypic characteristic of WS, it may not even be possible or useful to separate the anxiety symptomatology from the social aspects of the syndrome, as both are inherent to the condition. Other investigations have provided further support to the idea that the fears experienced by individuals with WS may not relate to social contexts. For example, Sarimski (1997) reported an elevated prevalence of environment-based phobias in individuals with WS. A study by Dykens (2003) employed the Diagnostic Interview Schedule for Child-Parent and the Child Behavior Checklist, and found that specific fears exhibited by individuals with WS pertained largely to the natural environment subtype (e.g., fear of thunderstorms, high places). Regarding neurobiological correlates of anxiety, studies have found that anxiety scores from the Beck Anxiety Inventory (BAI; Beck, Epstein, Brown, & Steer, 1988) were negatively associated with gray matter surface area in insula, orbitofrontal cortex, and other frontal-temporal regions in individuals with WS (Meda, Pryweller, & Thornton-Wells, 2012), providing specific neural substrate for the increased anxiety in WS. Another study further linked the degree of alteration in the insula with levels of anxiety in participants with WS (Jabbi et al., 2012).

Thus, to date, the scarce studies attempting to address the relation between the key phenotypic characteristics of WS pertaining to intellectual impairment, social features, and anxiety characteristics have provided inconsistent evidence. This topic is important in the context of recent evidence suggesting that the intellectual impairment associated with WS is linked to social vulnerability (Jawaid et al., 2012). Consequently, the current study addresses the question of how the intellectual impairment (and indirectly social vulnerability) relates to anxiety profiles and real-life social-emotional functioning in individuals with WS, and to begin to understand how they together may impact the daily life functioning of those with the disorder. Specifically, understanding the associated triggers of anxiety in WS is of significant clinical and practical importance as the internalizing symptoms potentially impact multiple areas of life, such as social-emotional functioning, with disruptive effects on social interactions and relationships (Udwin & Yule, 1991), and on seeking and maintaining employment (Davies et al., 1998; Jawaid et al., 2012). It is also currently poorly understood how the intellectual impairment may relate to the anxiety and social-emotional functioning profiles of individuals with WS, although it is known that it predisposes such individuals to social vulnerability (Fisher et al., 2013; Jawaid et al., 2012). Consequently, understanding the associations between emotional disturbance and social-emotional functioning on one hand, and the potential additional effect of the intellectual impairment on another, are essential to develop therapies that could improve the overall quality of life of those with WS.

To this end, the current study was aimed at examining the following questions: (1) does the anxiety characterizing WS comprise symptomatology that is largely psychological in nature (i.e., subjective experience of stressful events being intensified), or alternatively, would it better be described by physiological symptomatology; and (2) how the intellectual impairment linked to social vulnerability and social-emotional functioning of individuals with WS may relate to the severity of anxiety experienced. To address these questions, for the dimension of anxiety, the test battery included the Brief Symptom Inventory (BSI; Derogatis, 1993) to isolate psychological anxieties into categories of general versus phobic anxieties. In addition, the BAI was administered as it enables distinctions between psychological and physiological stressors to be characterized in adult populations. To assess intellectual functioning, standardized IQ tests (Wechsler, 1981, 1997, 1999) were employed, which afford the associations between verbal and non-verbal IQ profiles and individual anxiety symptoms to be examined. Importantly, the application of such cognitive assessments yields sub-indices of IQ scores that are normed together within each test, rather than having separate standardized measures for verbal and non-verbal cognitive functioning. Finally, for the social-emotional dimension, we utilized the SISQ (Doyle et al., 2004; Zitzer-Comfort et al., 2007) due to extensive prior literature on this measure underscoring its reliability as a measure of capturing real-life social-behavioral tendencies (see Järvinen-Pasley et al., 2010). In line with the previous research, we predicted that individuals with WS would present greater physiological and psychological anxieties relative to TD individuals. Regarding the potential associations between anxiety and IQ on one hand, and anxiety and sociability on the other, while the current evidence is both slight and inconsistent, we hypothesized that the anxieties of individuals with WS may relate to both the intellectual impairment and the social-emotional profile associated with the syndrome.

Finally, as an explorative effort, we evaluated a small subset of individuals with developmental delay (DD) to provide a description of the nature of their anxiety to contrast with that reported in WS.

2. Method

2.1. Participants

A mature sample of participants in the present study was recruited through the Laboratory for Cognitive Neuroscience at the Salk Institute for Biological Studies. For participants with WS who participated in a multicenter research study the diagnosis was confirmed by a fluorescent in situ hybridization (FISH) test. The remaining participants with WS were recruited through the biennial conventions hosted by the William Syndrome Association and completed the FISH test through physicians external to our research team. However, we also administered a Diagnostic Score Sheet for WS for all participants (American Academy of Pediatrics Committee on Genetics, 2001) to further verify the presence of the condition.

Our TD comparison individuals were recruited through The Salk Institute. All were local to the San Diego County. The following exclusionary criteria were employed: significant history of neurological or central nervous system disorder, substance use, and/or past psychiatric problems. Participants with DD were also recruited locally, as part of a pilot study within a large multi-site program project. These individuals were screened for the following exclusionary criteria: presence of severe motor, visual, and auditory impairment; diagnosed with a history of traumatic brain injury, epilepsy/seizures, multiple sclerosis, autism spectrum disorder, or any genetic disorder such as Down syndrome. Thus, this sample represented individuals with developmental delays without any specific etiology and neurological trauma. Given that the main aim of the current study was to provide a comparison of anxiety symptoms between individuals with WS and TD, and that the sample size of the DD participants was significantly smaller than both the WS and TD groups, their data were not included in the global statistical analysis. Instead, the results from the DD group are reported descriptively as reference.

Table 1 displays the characteristics (CA and gender) of the two main participant groups, alongside the descriptive sample of individuals with DD, with the Ns provided across the administered tests. Participants were administered the Wechsler Adult Intelligence Scale Revised or Third Edition (WAIS-R/III; Wechsler, 1981; Wechsler, 1997), or the Wechsler Abbreviated Scale of Intelligence (Wechsler, 1999) to determine their level of intellectual functioning. A proportion of participants with WS were administered the WAIS-R/III due to the length and on-going nature of the current program of studies and the release of the WAIS-III. Similarly, as a result of time constraints with respect to participants' schedules and the publication of a briefer test (i.e., WASI), in the TD participant group, 53% of participants were administered the WAIS-R/III with the remaining 47% of participants completing the WASI. Notably, the WAIS-III and WAIS-R have been reported to assess similar constructs despite newly added subtests, and yield correlation in the excess of .90 for the respective VIQ, PIQ, and FIQ indices (Tulsky, Zhu, & Prifitera, 2000). Likewise, investigations of large samples of over 200 participants have provided evidence that the WASI and WAIS-III yield a higher than 0.84 correlation across the three IQ composites (for

review of psychometrics information see Kamphaus, 2005). Consequently, although not ideal, indices of intellectual functioning were measured across the different Wechsler tests. As expected, individuals with WS showed mild cognitive impairment and scored significantly lower than TD comparison individuals across all domains (*ts* >16.41, *ps* < . 001).

2.2 Materials and Procedures

To maintain consistency with the existing literature (Järvinen-Pasley et al., 2010), caregivers of individuals with WS were instructed to complete the questionnaires below according to their personal interactions and observations with the participant. TD participants were requested to complete the inventories with a close family member or a spouse, and in an event of a disagreement, respond in accordance of the rating of the "other" informant.

2.2.1. Brief Symptom Inventory (BSI)—BSI is a 53-item inventory used to evaluate psychiatric symptoms tapping into the following nine traits: hostility, obsessive compulsion, interpersonal sensitivity, somatization, paranoid ideation, depression, psychoticism, phobic anxiety, and anxiety. Specifically, six of the items are related to common anxieties, e.g., "Feeling fearful", while five items reflect phobic anxieties, e.g., "Feeling afraid to travel on buses, subways, or trains". Each item required a response on a five-point Likert-type scale assessing whether the symptom was present and elicited distress in the past week. The responses were: 0 (*Not at all*), 1 (*A little bit*), 2 (*Moderately*), 3 (*Quite a bit*), 4 (*Extremely*).

2.2.2. Beck Anxiety Inventory (BAI)—All of the 54 participants who completed the BSI also completed the BAI, with the exception of 5 individuals (2 WS, 3 TD). The BAI consists of 21 items indexing four subtypes of anxiety symptoms: subjective, neurophysiological, autonomic, and panic. Examples of items in the subjective subscale included symptoms such as "Terrified" and "Nervous". The neurophysiological index of anxiety included statements such as "Shaky" and "Hands trembling". The autonomic sub-measure of anxiety comprised of physiological symptoms such as "Indigestion or discomfort in abdomen". Symptoms typical to panic attacks such as "Heart pounding or racing" and "Difficulty breathing" were included in the panic subscale. Psychometric reports have supported the four-scale model of the BAI (Osman, Kopper, Barrios, Osman, & Wade, 1997). Respondents self-rated on a 4-point Likert-type scale each of the items as follows: 0 (*Not at all*), 1 (*Mildly*), 2 (*Moderately*), and 3 (*Severely*). Raw scores for each subscale were converted into t-scores for analyses.

Both the BSI and BAI were originally administered to participants in an effort to characterize the broader anxiety symptomatology in WS. However, the BAI and BSI provide divergent characterizations of anxiety. Namely, whereas the BAI offers a detailed catalogue of symptoms associated with anxiety disorders, together with subscales of physiological and psychological features, the BSI provides a broader index of the severity of anxiety, yielding only a general T-score for the general anxiety domain. In an effort to reduce the number of caregiver-administered inventories within our larger multi-site study of individuals with WS, and to specifically target gaps in the current literature, the BSI was

discontinued. Consequently, while all but five participants in the study have scores for the BAI, as noted, some are missing them for the BSI.

2.2.3. The Salk Institute Sociability Questionnaire (SISQ)—The SISQ was administered to all participants WS and TD, similarly to the BAI and BSI, to assess overt affiliative tendencies and behaviors in social settings, as well as social-emotional characteristics. This measure requires informants to rate the participant's social behaviors using a seven-point Likert scale with low, mid, and high endpoint labels tailored to each individual item. Additionally for some items, descriptions of social behavior are requested, resulting in both quantitative and qualitative data. Questionnaire items were designed to assess two aspects of sociability, namely approach behavior and social-emotional behavior. Items targeting social approach behavior index approach toward both familiar (e.g., My child would spontaneously greet or approach an adult friend/acquaintance of the family; with a scale of 1 = very rarely to 7 = very often) and unfamiliar people (e.g., My child would spontaneously greet or approach an unfamiliar adult; with a scale of 1 = very rarely to 7 = very often). The social-emotional scale indexes emotional responsivity towards others, empathic tendencies, and the desire to please others (e.g., How likely is your child to comment on the emotional state of other individuals? with 1 = not very likely to comment, 7 = extremely likely to comment). Higher scores are indicative of increased social behaviors within each domain.

The SISQ has been employed in various investigative contexts. This instrument has been shown to sensitively distinguish unique features of sociability in WS relative to comparison groups, despite age, IQ, and cultural background. Results consistently highlight elevated global sociability as well as Approach Strangers score, in individuals with WS as compared to participants with various other neurodevelopmental disorders (e.g., Down syndrome) and TD, whether it was employed in investigations with child, adolescent, or adult participants (Doyle et al., 2004; Jones et al., 2000; Zitzer-Comfort et al., 2008). Importantly, this inventory has also been used cross-culturally in the United States and Japan (Zitzer-Comfort et al., 2008). The results showed a general effect of elevated sociability in individuals with WS as compared to TD, as indexed by Global Sociability. Additionally, a cultural trend of increased sociability in the American participants with WS as compared to their counterparts in Japan was found, suggesting the SISQ was sensitive to detect cultural effects in addition to differences in social behavior attributable to the genetic anomaly. Finally, the SISQ has been utilized in investigations with functional magnetic resonance imaging (fMRI), which showed that those with WS who scored higher in the SISQ Approach Strangers also demonstrated reduced amygdala response to fearful faces (Haas et al., 2010). Taken together, the SISQ has been employed in diverse methodological settings to delineate the distinguishing features of sociability in WS both at the group and individual levels. As such, this measure was selected as an index of social functioning. The specific psychometric properties are outlined in Doyle et al. (2004) and Zitzer-Comfort et al. (2008).

3. Results

3.1. BSI

Independent samples t-tests were employed to explore group differences in psychiatric symptoms as measured in the BSI. Individuals with WS scored higher in anxiety (M_{WS} = 52.42, M_{TD} = 44.17), hostility (M_{WS} = 49.46, M_{TD} = 43.33), and phobic anxiety (M_{WS} = 54.17, M_{TD} = 45.03) as compared to TD individuals, *ts* > 2.25, *ps* < .05. Notably, within these four scales, participants (3 WS, 2 TD) reached the floor of the converted T scores according to the BSI scoring manual (e.g., T < 34 in hostility)(Derogatis, 1993). Among these individuals, one participant with WS and one TD individual obtained the lowest possible T score in the BSI scoring manual for hostility, one TD participant for anxiety, and one participant with WS and two TD individuals for phobic anxiety. Given the converted scores are lower than the denoted subscale's T-score (e.g., T < 41), we conducted the analysis by applying these data as one lower than the denoted value. For example, if a participant scored the lowest T value for a given subscale (e.g., T < 32) we counted the data value as one lower than the T score (e.g., 31). As such, considering that a greater number of TD participants scored in the lowest possible range across the subscales, the resulting differences in the three subscales (hostility, anxiety, phobic anxiety) is likely even greater. In the opposite end, within anxiety, six participants scored in clinical range (T > 65)(5WS, 1TD). For hostility, all three participants whose scores were in the clinically significant range had the diagnosis of WS. Finally, within phobic anxiety, all five individuals that surpassed the clinical threshold had the diagnosis of WS. In brief, both generalized and phobic anxiety symptoms were found to be more prevalent in individuals with WS as compared to TD individuals.

Mann Whitney U-tests were applied to further examine differences in anxiety profiles across groups. Table 2 summarizes the occurrence of anxiety symptoms on the BSI in percentages for the WS and TD groups. Significant group difference in anxiety subscale was driven by greater symptom ratings of spells of terror or panic, (z = 2.30), and tense or keyed up (z = 2.12, *ps* < .05), for participants with WS as compared to TD individuals. Those with WS scored significantly higher across phobic symptoms: Fear of traveling on buses, subways and trains (z = 2.87), avoidance of places, things, and activities (z = 3.86), and nervousness when alone (z = 3.16, *ps* < .01). No other group differences were found.

Pearson correlations (two-tailed) between the BSI phobic and general anxiety scores and the VIQ, PIQ, and FIQ measures were computed to assess relationships between intellectual function and anxiety across both groups. Twelve TD participants did not complete the SISQ, thus the reported associations for the TD group are from the 18 remaining participants. Table 3 summarizes the relationships between anxiety symptoms with all IQ and SISQ subscales. In the WS group, phobic anxiety correlated negatively with the approach toward familiar people ($r(24) = -.46$, $p < .05$). By contrast, no associations were observed for the TD group. Taken together, these results suggest that greater experiencing of phobic fears on the BSI is linked to decreased affiliative tendencies toward familiar individuals in individuals with WS. In the section below, the BAI physiological and psychological symptoms of anxiety are examined in a to further elucidate the relationships between intellectual

functioning and the specific nature of anxiety symptoms in individuals with WS contrasted with TD.

3.2. BAI

No between-group differences were found for the BAI composite and sub-measures of anxiety (M_{WS} = 6.94, M_{TD} = 5.20)($t(139) = 1.61$, $p = .11$); however, differences in the severity of anxiety were observed. Specifically, while 61.3% of participants with WS were classified as experiencing minimal anxiety symptoms, 21.0% as experiencing mild anxiety symptoms, and 17.7% as experiencing moderate anxiety symptoms, for the TD individuals, greater occurrence of minimal anxiety symptoms (74.7%) relative to the WS group was documented. However, the pattern for the TD group masked a different distribution of anxiety symptoms as compared to that for the WS group: 19.0% of participants with anxiety reported mild anxiety symptoms, 5.1% moderate anxiety symptoms, and 1.3% severe anxiety symptoms. Thus, whereas over 35% of participants with WS demonstrated mild-to-moderate anxiety symptoms, correspondingly, approximately 25% of the TD participants reported somewhat more serious, moderate-to-severe forms of anxiety. No group differences in neurophysiological (M_{WS} = 0.20, M_{TD} = 0.15), autonomic (M_{WS} = 0.33, M_{TD} = 0.32), or panic symptoms (M_{WS} = 0.21, M_{TD} = 0.18) of anxiety were evident ($ts < 0.34$, $ps > .31$). However, participants with WS were classified as experiencing greater subjective feelings of anxiety as compared to the TD individuals (M_{WS} = 0.56, M_{TD} = 0.35)($t(139) = 2.47$, $p < .05$). Thus, while individuals with WS were associated with increased anxiety symptoms overall as measured by the BAI relative to the TD individuals, the intensity of the anxiety symptoms differed between the groups, with those with WS reporting milder symptoms overall.

Table 4 summarizes the group differences in the BAI scores across individual anxiety symptoms. Unexpectedly, over 66% of the BAI items elicited no group differences in anxiety symptoms. Items yielding significant results stemmed from the BAI neurophysiological and subjective anxiety subscales. Mann Whitney U-tests indicated that within the neurophysiological subscale, individuals with WS showed increased instances of shakiness ($z = 2.88$) and greater frequency of trembling hands ($z = 2.09$, $ps < .05$). By contrast, the TD group reported slightly increased episodes of fainting ($z = -2.01$, $p < .05$). On the subjective experience subscale, participants with WS were reported to experience more severe episodes of terrified ($z = 2.54$, nervous ($z = 2.53$), and scared emotional states ($z = 4.37$, $ps < .05$), as compared to the TD individuals. Taken together, individuals with WS showed greater somatic and physiological symptoms of anxiety as compared to the TD group.

Finally, correlations were applied to the data to examine between-group differences in the anxiety domains and intellectual functioning. Of the 141 participants, 59 individuals with WS and 64 TD individuals had data across all inventories; thus, data from these participants were included in this analysis. As shown in Table 5, the WS and TD groups were characterized differing patterns of association between intellectual functioning, social-emotional behavior, and anxiety symptoms. The only significant correlations for the WS group indicated a positive association between the BAI subjective anxiety t-score and VIQ

and FIQ. By contrast, for the TD group, surprising negative correlations between BAI neurophysiological and panic anxiety t-scores with all IQ measures, as well as between BAI subjective anxiety t-score and PIQ, emerged. Similar to the results from the BSI, no significant associations between social-emotional functioning and anxiety measures were found for the TD individuals.

Descriptive Comparisons with DD Participants

Descriptive analyses were applied to the BAI and BSI data that were obtained through caregiver reports. Given the significant discrepancy in sample size of our WS and DD groups, Welch's t-tests were applied to examine group differences. On the BSI, the DD participants' scores on phobic anxiety (M=57.09) and general anxiety (M=56.09) were not significantly different to those reported for the WS sample (ts < 1.24, ps > .27). On the BAI, the DD participants' scores on the neurophysiological (M=0.40), autonomic (M=0.56), subjective (M=0.57), and panic symptoms (M=0.31) symptomatology of anxiety did not differ from those of the WS group (ts < 1.49, ps > .11). Of the 12 DD adults, five individuals (41.7%) were characterized by scores of mild anxiety, five (41.7%) with minimal anxiety, one (8.3%) with moderate anxiety, and one participant (8.3%) with severe anxiety. Thus, the DD sample showed a similar distribution of the intensity of anxiety symptoms as those with WS, with most demonstrating mild to moderate forms of anxiety.

Pearson correlations were applied between anxiety measures and social and cognitive indices for the DD group. No significant correlations emerged between panic and general anxiety subscales of the BSI and either SISQ or IQ measures. For the BAI, subjective symptoms of anxiety were negatively correlated with the SISQ Approach Strangers score ($r(12) = -.58$, $p < .05$). However, due to the small sample size, the results for the individuals with DD should be interpreted with caution, and are provided as a descriptive reference..

4. Discussion

The goals of the present study were first, to elucidate the nature of the increased general anxieties commonly associated with WS, and second, to examine their relations to the level of intellectual ability and social-emotional functioning of such individuals. As intensified anxiety, intellectual impairment, and increased social-emotional behavior represent some of the core features of WS (e.g., Jabbi et al., 2012), the current study was aimed at clarifying the associations between the key components of the phenotype of WS at the "basal" level.

The main findings showed firstly, that in line with previous literature (e.g., Dykens, 2003; Einfeld et al., 1997, 1999, 2001; Gosch & Pankau, 1994; Leyfer et al., 2006, 2009; Sarimski, 1997; Switaj, 2000; Woodruff-Borden et al., 2010), individuals with WS relative to TD individuals displayed increased anxiety symptoms overall as measured by both the BAI, including neuropsychological/somatic (hands trembling and shaky) and subjective (terrified, nervous, scared) symptoms of anxiety, and the BSI, encompassing generalized anxiety (terror and panic, tense or keyed up) and phobic anxiety (avoidance of feared places and things, nervous when alone, fear of traveling in different vehicles). However, surprisingly, the intensity of the anxiety symptoms reported differed between the groups, with the WS group demonstrating milder symptoms overall. Thus, in the few cases of TD individuals,

when present, the anxiety symptoms were more severe in nature than those reported for the WS group. However, as an underreporting effect in relation to anxiety prevalence has been noted in the WS population particularly in conjunction with parental reports (Dykens, 2003), it is possible that the current findings reflect a similar effect also in terms of severity. Individuals with WS relative to TD may also be less capable of verbalizing/expressing their anxieties, particularly when they consist of mental states rather than more easily/objectively measurable physical symptoms. Indeed, the current result showing an association between higher intellectual ability and increased subjective anxiety in individuals with WS supports this view.

In addition, interestingly, the current results indicated elevated aggression in individuals with WS relative to the TD group, as indexed by higher Hostility ratings. Although the present literature into aggression in WS is limited, the current findings are consistent with prior observations that implicate increased anger and aggression in the WS population. For example, previous studies have suggested that over 40% of adult participants with WS demonstrate frequent outbursts of anger (Davies et al., 1998), and that emotion dysregulation of negative affect is common in such individuals (Phillips, 2008). The present pattern of findings may reflect two features of altered social-emotional function in WS. First, relative to TD individuals, those with developmental disabilities may generally exhibit more dysregulated emotional responses thereby demonstrating amplified aggressive behaviors (cf. Dykens, 2000). Secondly, the greater tendency for aggressive behaviors in adults with WS may pertain to their reactions toward social rejection and interpersonal circumstance; however, a more detailed examination of these possible explanations is beyond the scope of the current study. Future research is needed to clarify whether externalizing behaviors such as aggression may more frequently be observed in response to social than nonsocial events in individuals with WS.

Regarding the nature of anxiety symptoms, our results replicated previous studies (Dykens, 2003) suggesting that particularly subjective anxiety may be a distinguishing feature of the anxiety profile associated with individuals with WS as compared to TD individuals. Specifically, those with WS were reported to experience negative affective states such as fear, nervousness, and terror more adversely than is the case in normative development. Indeed, as these anxiety symptoms were unrelated to social functioning in both groups, and as atypically augmented neurobiological and behavioral responding to non-social fears has been identified as a unique characteristic of the WS phenotype (Meyer-Lindenberg et al., 2005; Thornton-Wells et al., 2011), the current finding showing increased subjective/psychological anxiety in WS may reflect the underlying amygdala dysfunction (Haas et al., 2009, 2010; Martens, Wilson, Dudgeon, & Reutens, 2009; Meyer-Lindenberg et al., 2005). Considering that the existing literature suggests that those with WS express negative social emotions with reduced intensity as compared to TD individuals (e.g., Meyer-Lindenberg et al., 2005), it is further possible that the current results, although significant, may reflect an underestimation of both the amount and intensity of negative affect they experience.

An additional finding from the present study suggested that greater verbal ability in individuals with WS may be associated with increased psychological/subjective anxiety symptoms as indexed both by the BAI. The contrasting pattern was found for the TD group

suggesting that stronger cognitive capacities may be protective against both neuropsychological/somatic and panic/psychological anxieties. In contrast, more normal intellectual functioning (i.e., greater IQ) in individuals with WS was associated with a greater erisk of experiencing of psychological anxiety. This may reflect the fact that higher cognitive skill allows such individuals to be more aware of and better consider potential dangers and threats, which may feed into their anticipatory anxiety; a phenomena that has been previously noted in the WS literature (Leyfer et al., 2006). It is further plausible that individuals with WS may be more capable of expressing their anxiety through higher verbal skill, thereby appearing to endorse more negative emotions, whereas those with reduced intellectual functioning may instead internalize these affective states due to difficulties in conveying their experience. By contrast, the protective effect of intelligence in TD individuals may suggest that higher intellectual capacity may enable enhanced cognitive control and rational reasoning about dangers/threats, as well as the development of more effective stress coping strategies reflected as reduced biological symptoms of anxiety. However, future studies should further elucidate the adaptive/maladaptive contribution of aspects of cognitive function to anxiety in individuals with WS.

The differential associations between intellectual capacity and severity of anxiety symptoms in individuals with WS contrasted with TD participants may further be influenced by our selection of the comparison group. As the comparison group of the current study included TD individuals without any neurological or genetic condition or intellectual deficiency, average or above-average intellectual skill may have acted as a protective factor, by increasing such individuals' resilience to mental health problems and stressful life experiences. However, given that our participant groups do not allow for the examination of these relationships in individuals with compromised intellectual functioning (i.e., moderate to severe intellectual impairment), it is unknown whether intellectual ability may only protect those with higher cognitive functioning, and in turn, increase vulnerability in individuals with lower IQ regardless WS diagnosis. However, it is noteworthy here that while existing literature suggests a high prevalence of anxiety disorders in individuals with intellectual disability (Emerson, 2003), a study specifically into WS further implicated augmented anxieties in such individuals relative to participants with other with developmental disabilities of mixed etiology (Dykens, 2003). Thus, future research would benefit from the inclusion of both individuals with TD with normative IQ scores, and those with intellectual impairment without specific medical etiology, to parse the potential role of the WS gene deletion in the association between IQ and anxiety as observed in the current study.

No significant relationship between social-emotional functioning and anxiety characteristics as indexed by the BAI emerged for either the WS or TD groups. However, the results from the BSI indicate that increased phobic anxieties are related to less frequent affiliative overtures toward familiar peers. It is important to note that the items that composed the BSI construct of phobic anxiety centered on specific situations that underpin anxiety, rather than tapping into general physical and psychological symptoms of anxiety. In contrast, the BAI measures comprised both somatic and cognitive symptoms of anxiety. Consequently, the current association may suggest that individuals with WS who demonstrate situational fears are likely to socially interact with familiar peers. Notably, however, when applying an

inventory catered specifically toward clinical diagnosis of anxiety, this relationship is not significant. Consequently, the differences in strength of this association between social approach and anxiety may differ in individuals with WS as a function of the specific features of anxiety evaluated, whereby this association is pervasively insignificant in TD individuals. The results from the BAI are in line with those of Riby et al. (2013), which showed no group difference between individuals with WS with high and low anxiety in social motivation, indicating that the drive to socially engage with others may not be associated with the anxiety profile in these individuals. In their study, the SCAS-P was utilized, which measures situational, somatic, and psychological characteristics of anxiety; thus, the reported lack of relationship between anxiety and social behaviors may be due to the all-encompassing construct of anxiety. In the present study, anxiety symptoms were divided according to psychological and somatic categories, thereby providing a more detailed examination. When we evaluated the relationship between social behaviors as indexed by SISQ and the overall score of anxiety on the BAI of individuals with WS (rs < .24, ns), our results converge with those of Riby and colleagues (2013). Nonetheless, further systematic research are required to further elucidate whether symptom clusters of anxiety may be associated with real-life social behaviors in individuals with WS, or alternatively, whether their social and anxiety profiles may be independent in this syndrome.

The current findings suggest that the anxiety symptoms associated with WS may specifically originate from fear-based mechanisms together with physiological responses related to the medical features of the genetic condition. Specifically, our findings from the BAI indicated that participants with WS reported greater incidences of shakiness, trembling, and feelings of nervousness, fright, and terror, as compared to TD individuals. As mentioned above, this atyical profile may stem from the altered neurobiological processing of fear (Haas et al., 2009; Meyer-Lindenberg et al., 2005). Moreover, muscular problems are a common feature in the medical profile of WS; these may represent a further contributing factor to the increased physiological anxiety in WS. For example, it is possible that shaking of the body is linked to hypotonia, a lack of general muscle tone that is prevalent in infancy in WS (Mervis & Morris, 2007), while the trembling of hands may be associated with the cerebellar ataxia documented in older adults with WS (Nakaji et al., 2001). Thus, the defining physiological/medical characteristics of WS may also be important contributing factors to the anxiety phenotype.

Surprisingly, no between-group differences emerged in the occurrence of phobic and autonomic symptoms of anxiety. These findings are surprising in the context of literature reporting increased incidence of phobic anxieties in the WS population (e.g., Leyfer et al., 2006, 2009; Sarimski, 1997). Moreover, WS is associated with atypical autonomic nervous system (ANS) functioning particularly in response to social-emotional stimuli (e.g., Doherty-Sneddon et al., 2009; Järvinen et al., 2012; Riby et al., 2012; for a review, see Järvinen & Bellugi, 2013), which may be expected to contribute to at least certain types of anxieties. However, these seemingly contradictory findings may reflect the fact that previous studies have rarely utilized the measures selected for the current study, namely the BSI and the BAI, of which particularly the latter has been widely employed in psychiatric research in general (Beck & Steer, 1991; Steer, Ranieri, Beck, & Clark, 1993) Moreover, many existing

studies have involved clinically diagnosed cases (e.g., Leyfer et al., 2006, 2009; Woodruff-Borden et al., 2010), while the current study was experimental in nature. Only one known study of individuals with WS utilized the BAI (Meda et al., 2012), and interestingly, results highlighted that the presence of anxiety symptoms correlated negatively with surface area in the insula, orbitofrontal cortex, and other frontal-temporal regions in individuals with WS. It is thus of interest to further explore the nature of anxiety symptoms behaviorally in WS utilizing a variety different anxiety instruments in order to obtain a comprehensive picture of the anxiety profile of WS. With regard to the lack of between-group differences in the ANS-based anxiety symptoms, future studies should directly relate ANS activity of participants to their anxiety profiles, to determine the extent to which ANS function may contribute to types of internalizing disorders in WS versus TD. Such investigations are critical considering that ANS dysfunction may not be clearly reflected in overt behaviors.

Finally, data from a small sample of DD participants were included as an exploratory and descriptive effort, to provide a crude comparison to the anxiety symptoms reported for individuals with WS. The results suggested that the participants with DD exhibited a similar degree of anxiety to those with WS. Notably, however, participants with DD as compared to their counterparts with WS yielded different associations among anxiety, IQ, and social functioning. Namely, whereas individuals with WS showed an association between subjective anxiety and cognitive ability particularly within the verbal domain, such a relationship was not observed in the DD group. Further, while for individuals with DD a correlation between greater subjective experiences of anxiety and lower Approach Strangers score, as indexed by the BAI and SISQ respectively, was found, no such association was evident in the WS group. It is thus possible that anxiety does not interfere with the motivation to socially engage with others in WS, whereas fears and worries may serve as cues of potential stranger-related threat for individuals with DD. As such, anxiety may increase social withdrawal or inhibition in those with DD, yet exert no such influence in individuals with WS. These data offer preliminary evidence suggesting that anxiety may differentially impact social behavior of individuals with WS and DD. However, given the modest sample size of DD individuals in the current study, the interpretation of these data should be taken with caution. Taken together, the current study highlights the importance of understanding the mechanisms underlying the documented anxiety symptomatology in different neurodevelopmental populations, which should be addressed in future studies in systematic and detailed fashion.

5. Conclusions

The current study aimed at delineating the specific nature of the anxiety symptoms, and examining linkages between anxiety, social functioning, and cognitive capacity, in individuals with WS relative to TD comparison individuals. Notably, the present study extends the current literature by examining patterns of anxiety in individuals with WS contrasted with those with normative development. Further, in contrast with previous research, we employed an in-depth analysis of symptoms that are associated with WS, rather than focusing on the general level of anxiety and personality traits that characterize such individuals. By assuming a dimensional approach, our results outlined the specific symptoms that contribute to the commonly noted increases of anxiety symptoms in the WS

population, instead of merely classifying the individuals with WS on the basis of whether they meet the overall diagnostic criterion. Subsequently, our findings highlighted a distinct profile of anxiety for individuals with WS, together with a differential pattern of association between cognitive ability and anxiety symptoms between the groups. Specifically, the altered neurobiological processing of fear may be driving at least some of the common anxiety symptoms experienced by individuals with WS.

Future studies are thus warranted to further elucidate the specific nature of anxieties, both qualitatively and quantitatively, in individuals with WS and comparison groups of TD individuals and those with intellectual disability of unspecified origin, as well as those with other neurodevelopmental disorders. Empirical investigations utilizing larger sample sizes, longitudinal approaches, and measures of real-life social functioning are needed to elucidate the aspects pertaining to the associations among the cognitive, anxiety, and social profiles that may be unique to WS, and those that may also be observed in other neurodevelopmental conditions. Further studies should also address the question of whether the increased anxiety in the WS population may reflect a greater tendency to endorse anxiety symptomatology, an increased frequency of experiencing a limited range of anxiety symptoms, and/or more severe subjective experiencing of negative states. Finally, an importation limitation of the current study design that should be considered in prospective investigations pertains to the fact that different report methods were used for the WS and TD groups. This is important in light of a study by Dykens (2003), who reported that caregivers tend to underestimate fears and phobias experienced by individuals with WS. Thus, it may be that the present findings reflect an underestimation of anxiety symptomatology in WS. However, the use of self-report method with populations with intellectual disabilities raises validity issues, with such individuals often showing difficulties with understanding the items and/or scales (Emerson, Felce, & Stancliffe, 2013). Further, previous investigations have shown that self-report and reports by proxy are low in concordance rates for items pertaining to subjective experiences or internalized feelings, and yet high for items that are pertaining to more obective or observable attributes (Perry & Felce, 2002), which may explain the parents' underestimation of their children's fear in Dykens' study (2003). Taken together, it is vital for researchers investigating individuals with intellectual disabilities, such as WS, to consider extensive methodological approaches when targeting phenotypic features, given the complexity of the syndrome.

Evidently, it is also of significant interest to disentangle the potential contribution of the neurobiological alterations implicated in the unique profile of processing fear in individuals with WS. Such investigations promise to clarify whether individuals with WS would derive the most benefit from interventions/treatments emphasizing on moderating the physiological and psychological experience of anxiety (e.g., mindfulness-based stress reduction training), or techniques targeting at reducing the variety of fears (e.g., cognitive behavioral psychotherapy, exposure therapy). Nevertheless, the present study contributed to the extant literature in WS by providing a detailed characterization of the specific psychological and physiological anxieties that are elevated in individuals with WS relative to those without the genetic abnormality.

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Highlights

- Anxiety is a core feature of the Williams syndrome (WS) phenotype
- The study examined the specific nature of anxieties in WS contrasted with typical development (TD)
- Associations between cognitive/social functioning and anxiety were also examined
- Increased physiological and subjective anxieties characterized individuals with WS
- Increased cognitive but not social functioning was associated with anxiety only in WS

Table 1
Participant Characteristics Across Inventories Administered

	Mean ± Standard Deviation [range]		
	Williams Syndrome	**Typical Development**	**Developmentally Delayed**
Beck Anxiety Inventory (BAI)			
N	**62**	**79**	**12**
Gender	27M, 35F	36M, 43F	6M; 6F
Age (years)	32.65 ± 9.58 [18.02-53.52]	27.10 ± 8.76 [18.10-51.71]	25.82 ± 9.46 [18.68-46.77]
VIQ	71.35 ± 9.05 [53.00-91.00]	106.90 ± 11.44 [83.00-139.00]	64.17 ± 10.29 [55.00-85.00]
PIQ	66.56 ± 7.94 [53.00-91.00]	106.35 ± 13.84 [75.00-148.00]	61.00 ± 5.89 [53.00-72.00]
FIQ	67.32 ± 8.47 [49.00-82.00]	107.30 ± 11.47 [82.00-137.00]	59.58 ± 8.78 [51.00-77.00]
N (with SISQ)	**59**	**64**	**12**
Approach	5.15 ± 1.32 [1.60-7.00]	3.91 ± 1.12 [1.00-6.60]	3.19 ± 1.63 [1.00-6.40]
Strangers			
Approach	6.69 ± 0.49 [5.33-7.00]	6.06 ± 1.18 [1.00-7.00]	5.97 ± 1.58 [2.33-7.00]
Familiars			
Social-Emotionality	5.67 ± 0.80 [3.33 -7.00]	4.82 ± 0.83 [3.00-7.00]	4.50 ± 1.18 [2.50-6.25]
Brief Symptom Inventory (BSI)			
N	**24**	**30**	**11**
Gender	10M, 14F	13M, 17F	3M; 8F
Age (years)	32.16 ± 9.14 [18.02-48.04]	22.27 ± 5.37 [18.10-39.98]	26.58 ± 9.55 [18.74-46.78]
VIQ	68.29 ± 9.02 [54.00-91.00]	110.46 ± 9.66 [88.00-128.00]	64.73 ± 10.59 [55.00-85.00]
PIQ	63.83 ± 6.68 [53.00-77.00]	113.26 ± 11.42 [89.00-148.00]	63.91 ± 7.80 [54.00-81.00]
FIQ	63.63 ± 7.60 [51.00-80.00]	113.20 ± 7.82 [98.00-126.00]	61.55 ± 8.71 [51.00-77.00]
N (with SISQ)	**24**	**18**	**10**
Approach	5.35 ± 1.37 [2.20-7.00]	3.84 ± 0.78 [2.40-5.60]	3.43 ± 2.01 [1.00-7.00]
Strangers			
Approach	6.72 ± 0.48 [5.67-7.00]	6.31 ± 0.60 [4.67-7.00]	6.11 ± 1.27 [4.00-7.00]
Familiars			
Social-Emotionality	5.53 ± 0.86 [3.75-6.75]	4.99 ± 0.50 [4.00-6.00]	4.69 ± 1.10 [3.25-6.25]

Note. SISQ subscores per participant pool for the BAI and BSI are reported to reflect the consistency in the within-group ratings despite the sample sizes across BAI and BSI.

Table 2

Percentage of Williams Syndrome and Typical Developing Participants with the Presence of BSI Anxiety Symptoms (N=54)

	Williams Syndrome		Typical Development		
	No	Yes	No	Yes	*z*
Nervousness or shakiness (A)	54.17	45.83	63.33	36.67	0.94
Scared without reason (A)	83.33	16.67	96.67	3.33	1.59
Fearful (A)	54.17	45.83	76.67	23.33	1.78
Tense or keyed up (A)	50.00	50.00	73.33	26.67	2.12*
Spells of terror or panic (A)	83.33	16.67	100.00	0.00	2.30*
Restless (A)	66.67	33.33	73.33	26.67	0.80
Afraid in open spaces or streets (P)	83.33	16.67	93.33	6.67	1.20
Afraid to travel on buses, subways, trains (P)	75.00	25.00	100.00	0.00	2.87**
Avoid things, places, activities because of fear (P)	58.33	41.67	100.00	0.00	3.86**
Uneasy in crowds (P)	83.33	16.67	93.33	6.67	1.15
Nervous when left alone (P)	70.83	29.17	100.00	0.00	3.14**

(P) = Phobic Anxiety

(A) = Anxiety

* $p < .05$

** $p < .01$

Table 3

Correlations Among Mean Phobic Anxiety and General Anxiety BSI Scores and IQ Measures in Williams Syndrome (N = 24) and Typical Development (N = 18)

	Williams Syndrome		Typical Development	
	Phobic Anxiety	**Anxiety**	**Phobic Anxiety**	**Anxiety**
VIQ	.24	.17	−.14	.04
PIQ	.05	.11	.50*	−.19
FIQ	.20	.17	.09	−.24
Social-emotionality	−.40	−.30	−.17	.20
Approach Strangers	−.03	−.02	.08	.24
Approach Familiars	−.46*	−.26	−.10	−.12

Table 4

Percentage of Williams Syndrome and Typical Developing Participants with the Presence of BAI Symptoms (N=141)

	Williams Syndrome		Typical Development		
Neurophysiological	**No**	**Yes**	**No**	**Yes**	***z***
Numbness or tingling	87.10	12.90	78.48	21.52	−1.34
Wobbliness in legs	88.71	11.29	92.41	7.59	0.80
Dizzy or lightheaded	83.87	16.13	78.48	21.52	−0.84
Unsteady	79.03	20.97	84.81	15.19	0.84
Hands trembling	79.03	20.97	91.14	8.86	2.09*
Shaky	70.97	29.03	89.87	10.13	2.88**
Faint	100.00	0.00	93.67	6.33	−2.01*
Subjective					
Unable to relax	58.06	41.94	56.96	43.04	0.13
Fear of the worst happening	66.13	33.87	69.62	30.38	0.53
Terrified	77.42	22.58	92.41	7.59	2.54*
Nervous	33.87	66.13	48.10	51.90	2.53*
Fear of losing control	87.10	12.90	89.87	10.13	0.26
Scared	48.39	51.61	83.54	16.46	4.37**
Panic					
Heart pounding	69.35	30.65	69.62	30.38	0.37
Feelings of choking	91.94	8.06	94.94	5.06	0.70
Difficulty breathing	91.94	8.06	89.87	10.13	−0.47
Fear of dying	87.10	12.90	91.14	8.86	0.81
Autonomic					
Feeling hot	75.81	24.19	64.56	35.44	−1.55
Indigestion/discomfort in abdomen	58.06	41.94	72.15	27.85	1.62
Face flushed	82.26	17.74	81.01	18.99	−0.17
Sweating	74.19	25.81	83.54	16.46	1.30

Table 5

Correlations Among BAI Subscale Scores and IQ Measures in Williams Syndrome (N = 59) and Typical Development (N = 64)

	Williams Syndrome				Typical Development			
	Neurophysiological	**Subjective**	**Panic**	**Autonomic**	**Neurophysiological**	**Subjective**	**Panic**	**Autonomic**
VIQ	.17	.28*	.12	.17	−.27*	.03	−.27*	−.15
PIQ	.12	.21	.00	.05	−.36**	−.25	−.30*	−.19
FIQ	.17	.27*	.08	.12	−.38**	−.13	−.34**	−.22
Social-emotionality	.03	−.01	.10	.20	−.01	.01	.01	.05
Approach Strangers	.13	.21	.19	.23	−.05	.11	.08	.10
Approach Familiars	−.11	−.05	−.13	−.02	.03	.09	.02	−.03

*Significant at $p < .05$

**Significant at $p < .01$