Symposium Title: Salient Aspects of the Williams Syndrome Phenotype in Adulthood: Mental Health, Behavior, Cognition, and Sociability

Overview: Williams syndrome (WS), estimated to occur in 1 in 7500 births, is a complex neurodevelopmental disorder caused by a deletion of 26-28 genes on chromosome 7q11.23 (Hillier et al., 2003). WS is associated with a distinct cognitive-behavioral phenotype, including hypersociability, anxiety, and attention problems (Martens et al., 2008). Further, although there is a wide range of cognitive functioning, most individuals with WS present with developmental delays in early childhood and mild to moderate intellectual disability come the school age years (e.g., Mervis & John, 2010). While a large body of research describes the development of individuals with WS throughout childhood, much less is known about how the behavioral profile changes (or stays the same) in adulthood. The four presentations in this symposium will address a few of the salient aspects of the Williams syndrome phenotype at an understudied point of development--adulthood. The first presentation will use EEG to examine the auditory sensitivities in WS and relate these auditory sensitivities to emotional and behavioral difficulties. The second presentation will address the patterns of adaptive and functional behavior in adulthood, and how such behavior relates to social and cognitive profiles. The third presentation will analyze changes in the behavioral and emotional profiles of adults with WS, extending our understanding childhood behavioral profiles into adulthood. Finally, the fourth presentation will compare the social behaviors of adults with WS to those without disabilities and then relate those social behaviors to social vulnerability. Collectively, these presentations highlight that adults with WS continue to display distinct areas of behavioral strengths and weaknesses, while providing important avenues for novel interventions.

Paper 1 of 3

Paper Title: Neural and Behavioral Associations among Auditory Sensitivities, Attention Problems, and Anxiety in Adults with Williams Syndrome

Introduction: Williams syndrome (WS) is a neurodevelopmental disorder caused by the deletion of 28 genes on chromosome 7. WS is associated with a distinct cognitive-behavioral phenotype, including hypersociability, anxiety, and attention problems (Martens et al., 2008). Additionally, sensitivities to sounds are extremely common in WS, affecting around 90% of individuals. In particular, many individuals with WS are reported to being able to distinguish between similar types of sounds and to having sound aversions. However, the neural correlates of these auditory sensitivities and how they relate to other aspects of the WS are poorly understood.

Methods: Participants included 23 adults with WS and 20 typically developing (TD) age- and gender- matched adults. Participants completed an oddball paradigm in which they heard 288 instrumental tones of three different musical timbres (42% cello, 42% trumpet, 16% piano). Participants were instructed to press a button whenever they heard the piano timbre. EEG was recorded with a high-density array throughout the paradigm. Cluster-randomization procedures were used to identify significant differences in EEG amplitude to the different timbres for the WS and TD groups. Additionally, parents of participants with WS completed the Child Behavior Checklist, a broad band screener of behavioral and emotional symptoms. Parents also completed the Sensitivity to Sounds scale, which asked how bothered/frightened their child was to five different sound characteristics and 21 different specific sounds on a 7-point Likert scale.

Results: In both WS and TD participants, a central-parietal cluster of electrodes revealed significantly greater amplitude to the target piano timbre compared to the non-target cello and trumpet timbres consistent with a P300 response typically seen to target stimuli in an oddball paradigm (latency ~250-600 ms, $p<.05$). For the WS group only, there was also a central-parietal cluster of electrodes differentiating the two non-target timbres, with a greater P300 amplitude response to the cello versus trumpet timbre (latency 324-606 ms, $p=.06$). In the WS group,

Sensitivities to Sound Characteristics and Specific Sounds were associated with CBCL Attention and Internalizing Problems (r's=0.45-.59, p's<.05). Additionally, greater P300 amplitude responses to the non-target cello versus trumpet timbre were associated with greater CBCL Attention and Internalizing Problems (r's=.49-.59, p's<.05).

Discussion: To our knowledge, this is the first study to directly examine neural responses of timbre perception in WS. While individuals with WS demonstrated a P300 response, reflecting attentional orienting and memory updating for the target stimuli, they also showed a differential response to the non-target stimuli, indicating atypical attentional and sensory processing. This suggests individuals with WS were unable to inhibit an attentional response to the non-target stimuli, consistent with prior questionnaire studies of poor auditory filtering and EEG studies of poor auditory inhibition in WS (e.g., John et al., 2010). Moreover, building on prior questionnaire studies suggesting relationships between sensory sensitivities and behavior problems in WS (John et al., 2010), this is the first study to demonstrate a relationship between neural responses to auditory stimuli and behavioral and emotional problems. Implications for examining mechanisms of sensory dysfunction and their role in behavior difficulties and the development of intervention strategies will be discussed.

References/Citations:

- John, A.E. & Mervis, C.B. (2010). Sensory modulation impairments in children with Williams syndrome: American Journal of Medical Genetics Part C, 154C, 266-276.
- Martens et al. (2008). Research Review: Williams syndrome: a critical review of the cognitive, behavioral and neuroanatomical phenotype. Journal of Child Psychology and Psychiatry, 49(6), 576-608.

Paper 2 of 3

Paper Title: Functional Ability and Social Skills in Adults with Williams Syndrome

Introduction: Williams syndrome (WS) is a neurodevelopmental disorder caused by the deletion of 26-28 genes on the 7th chromosome, with an estimated prevalence of one in 7,500 live births. While some studies have examined behavior and functioning in adults with WS (e.g. Elison, Stinton, & Howlin, 2010), it is not yet known how social, intellectual, and adaptive functioning are related in this population. The present study examined patterns of functional abilities, social responsiveness, and IQ among a sample of adults with WS.

Methods: The present sample included 28 participants (25% female) with WS who were attending a week-long residential summer camp. Participants ranged in age from 20 to 51 (mean = 28.46, SD = 9.13). Participants with WS completed the Kaufman Brief Intelligence Test, Second Edition (KBIT-2), and parents completed the Social Responsiveness Scale (SRS) and Vineland Adaptive Behavior Scales, Second Edition. Descriptive statistics, bivariate correlations, and t-tests were used to analyze levels of functioning, as well as relationships among variables.

Results: There were no significant differences in IQ, social responsiveness, or adaptive functioning by gender. Though the mean adaptive behavior scores from the Vineland subscales (communication = 55.73, daily living skills = 62.15, social = 67.58) appeared slightly higher than previous studies, there were significant negative correlations with age. Specifically, higher scores in communication skills (r = -.48) and daily living skills (r = -.63) were associated with younger age, as was overall adaptive behavior (r = -.50). Social adaptive behavior (r = .40) and total adaptive behavior (r = .40) were significantly correlated with IQ. Additionally, certain functional skills were related to social responsiveness.

Discussion: These analyses reveal important patterns of functional abilities among adults with WS. Though the mean Vineland scores appeared somewhat higher than those reported in other samples (Elison, Stinton, & Howlin, 2010), all still fell in the "low" range of adaptive behavior skills. Additionally, all but one subscale score were

negatively correlated with age, which contradicts earlier findings that younger adults have lower levels of adaptive skills. Interestingly, social cognition scores (e.g. understanding and interpreting social cues, such as facial expression), but not other scales of social responsiveness, were related to communication and social adaptive skills. This suggests that, for adults with WS, the ability to read and interpret social cues plays a more important role in overall adaptive functioning than the social motivation or social communication skills. Implications for future research and clinical practice will be discussed.

References/Citations:

- Elison, S., Stinton, C., & Howlin, P. (2010). Health and social outcomes in adults with Williams syndrome: Findings from cross-sectional and longitudinal cohorts. Research in Developmental Disabilities, 31, 587 - 599.

Paper 3 of 3

Paper Title: A Profile of Behavior in Adults with Williams Syndrome

Introduction: Although individuals with Williams syndrome are considered to have distinct behavioral characteristics, such as outgoing personalities, high distractibility, and anxiety, most studies have evaluated these characteristics primarily in children (Greer et al., 1997). Less is known about whether these behavioral characteristics are consistent throughout adulthood, or whether they vary with age. In this study, we evaluated differences in behavioral profiles for adults with Williams syndrome across age and gender.

Methods: Participants included 74 adults with Williams syndrome between the ages of 18 and 59 years (median = 25). The Child Behavior Checklist (CBCL), a standardized measure of behavioral and emotional problems, was completed for all participants. Each item was rated on a scale from 0, not true, to 2, very true or often true. We calculated sub-scale scores by averaging raw scores across the following areas: Anxious; Somatic; Thought; Attention; Rules; Aggressive; Withdrawn; Social; Internalizing, and Externalizing. Using these scores, we examined differences across subscales, age groups, and gender, using repeated measures t-tests and ANOVAs.

Results: Comparing internalizing to externalizing behavior for all participants, internalizing behavior ratings were significantly higher, $t(73) = 5.38$, $p < .001$. Within subdomains, respondents rated the Attention sub-scale significantly higher than all others, with a mean of .604 (SD=.365), $F(1,73) = 18.38$, $p < .001$. There were no significant differences between males and females on CBCL total or sub-domain scores. Results of ANOVAs also did not show significant differences between age groups across sub-scales, indicating behavior problems remain relatively stable throughout adulthood.

Discussion: These preliminary results provide some initial evidence for ongoing attentional and internalizing problems for adults with Williams syndrome, similar to problems reported in childhood. Our results supports and updated findings from Davies and colleagues (1998), who found through caregiver interviews that distractibility and concentration problems limited the independence of adults with Williams syndrome. These findings are important in understanding the behavioral needs of adults with Williams syndrome so that appropriate supports and services can be provided across the lifespan. Additional research is needed to build on these cross-sectional findings by looking at longitudinal changes in behavior within, rather than across, individuals with Williams syndrome.

References/Citations:

- Davies, M., Udwin, O., & Howlin, P. (1998). Adults with Williams Syndrome. British Journal of Psychiatry, 172, 273-276.

- Greer, M. K., Brown, F. R., Pai, G., S., Choudry, S. H., & Klein, A. J . (1997). Cognitive, adaptive, and behavioral characteristics of Williams Syndrome. American Journal of Medical Genetics, 74, 521-525.