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Relations Between Lab-Based and Parent-Reported Executive Functioning in Children and Adolescents with Williams Syndrome

Gregor Nathanael Pau Schwarz
University of Wisconsin-Milwaukee

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by

Gregor Nathanael Pau Schwarz

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ABSTRACT

RELATIONS BETWEEN LAB-BASED AND PARENT-REPORTED EXECUTIVE FUNCTIONING IN CHILDREN AND ADOLESCENTS WITH WILLIAMS SYNDROME
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Gregor Nathanael Pau Schwarz

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Williams syndrome (WS) is a rare genetic disorder characterized by lowered cognitive abilities and significant attention and executive functioning (EF) difficulties. The current study constitutes the first investigating the relevance of performance on an EF task measuring one or more of the "core" EF's (inhibition, shifting, working memory) to EF behaviors observed by parents of youth with WS. Parent-ratings of their children indicated more EF difficulties in all domains compared to the general population. Performance on the EF task (correct trials during the last phase of the Dimensional Change Card Sort) predicted parent reported general EF difficulties, metacognition, working memory and inhibition difficulties but not shifting difficulties after controlling for age, gender and nonverbal ability. Performance on this EF card sorting task appears to have some relevance to everyday executive functioning difficulties of youth with WS.

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Introduction

Williams syndrome (WS) is a rare genetic disorder caused by a hemizygous deletion of 26 genes on chromosome 7q11.23 (Ewart et al., 1993; Hillier et al., 2003). Many children with WS have cognitive abilities in the mild to moderate intellectual disability range together with significant attention and executive functioning difficulties associated with common occurrence of Attention Deficit Hyperactivity Disorder (ADHD). Executive functions allow for the regulation of behavior and thought processes. They are critical for functioning at school and work and are important at home and for social functioning. Whereas executive functioning deficits on tasks in laboratory contexts have been investigated in Williams syndrome, particularly in samples that combine child and adult participants, the examination of executive functioning skills in daily lives of children with WS has been relatively neglected. In addition, even less attention has been given to questions about how relevant deficits in laboratory tasks are for the everyday functioning of children and adolescents with Williams syndrome. The current study aims to: 1) comprehensively describe the difficulties with executive functioning related behaviors as observed by parents; and 2) examine relations with lab-based performance on an executive functioning task, taking into account the contribution of intellectual functioning.

Description of Williams Syndrome

Williams syndrome (WS) occurs in about 1 in 7500 live births (Stromme, Bjornstad, & Ramstad, 2002) and has a unique cognitive phenotype characterized by extreme weakness in visuospatial constructive skills (Mervis et al., 2000). Cognitive abilities are variable (with IQs ranging from 30 to 100) with the average IQ of individuals with WS being around 70. Therefore, most individuals with WS have intellectual functioning falling in the borderline to moderate

intellectual disability range of cognitive functioning (Mervis & John, 2010; Mervis et al., 2000). The behavioral phenotype of WS includes broad-ranging inhibition difficulties reflected in elevated rates of ADHD (~50%), very high levels of friendliness and social approach as well as anxiety and emotion regulation difficulties (Davies, Howlin, & Udwin, 1997; Klein-Tasman & Mervis, 2003; Leyfer, Woodruff-Borden, Klein-Tasman, Fricke, & Mervis, 2006a; Mervis & John, 2010). There is increasing evidence for deficits in a variety of domains of executive functioning in Williams syndrome based on lab-based tasks measuring working memory, inhibition, shifting, and planning as detailed below. There is some evidence that the GTF2I family of genes of general transcription factors may play a role in the cognitive phenotype of WS, including the generally lower cognitive functioning (Meyer-Lindenberg, Mervis, & Berman, 2006; Porter et al., 2012). Some preliminary evidence suggests that the GTF2IRD2 gene of this GTF2I family of genes may contribute to some of the executive functioning difficulties observed in WS (Porter et al., 2012). However, the exact mechanisms are not clear, as these transcription factors appear to interact with a variety of proteins and DNA, particularly in the brain, including during the developmental phases; this likely affects a variety of processes. There is also mixed evidence in regard to the deletion size and severity of symptoms (Morris & Mervis, 2000; Porter et al., 2012). These genes may be related to the lower activation of the striatum, dorsolateral prefrontal cortex and anterior cingulate cortex during an inhibition task in individuals with WS (Mobbs et al., 2007).

Lab-based Assessment of Executive Functions in Williams Syndrome

Working Memory in WS. There are clear and broad impairments in working memory in WS beyond what would be expected, based on lower general cognitive ability, that may also be

partially accounted for by short-term memory deficits. Individuals with WS demonstrate consistently worse working memory performance compared to CA-matched individuals (Rhodes, Riby, Park, Fraser, & Campbell, 2010; Rhodes et al., 2010; Sampaio, Sousa, Férnandez, Henriques, & Gonçalves, 2008; Sampaio et al., 2008; Zarchi et al., 2014). Cognitive ability (overall IQ, verbal, spatial, and nonverbal IQ) accounts for some of the working memory performance deficits observed in WS, as evidenced by significantly smaller effect sizes when comparing performance to MA-matched controls instead of CA-matched controls. Working memory generally remains significantly worse even when comparing to MA matched controls (Carney, Brown, & Henry, 2013; Costanzo et al., 2013; Menghini, Addona, Costanzo, & Vicari, 2010; O'Hearn, Courtney, Street, & Landau, 2009; Rhodes, Riby, Matthews, & Coghill, 2011; Rhodes et al., 2010; Rhodes, Riby, Fraser, & Campbell, 2011). Therefore, working memory performance deficits appear to be more pronounced than expected based on the lower general cognitive ability observed in WS. Given the accumulating evidence that short-term memory and working memory are highly related (perhaps psychometrically indistinguishable) constructs (Dang, Braeken, Colom, Ferrer, & Liu, 2014), short-term memory difficulties may also account for some of the working memory deficits observed in WS; several studies have found short term memory deficits in WS (Menghini et al., 2010; Menghini et al., 2010; Sampaio et al., 2008). Most studies included broad age ranges of participants between 10-30 years of age. Overall, broad deficits in working memory have been consistently observed in individuals with WS, and these deficits likely are partially accounted for by lower IQ and deficits in short term memory.

Inhibition in WS. Individuals with WS also show broad deficits in inhibition and seem to favor speed over accuracy more so than controls; this is consistent with broader inhibitory

behavior difficulties in WS (very high social approach). Individuals with WS show significant deficits in inhibitory control compared to chronological age matched individuals as well as mental age matched children (Atkinson et al., 2003; Carney et al., 2013; Menghini et al., 2010; Mobbs et al., 2007; Porter, Coltheart, & Langdon, 2007; Zarchi et al., 2014), indicating that those with WS may show more difficulties with inhibitory control than expected based on cognitive impairments. Studies of inhibition in WS have included children as young as 4 years of age. It is notable that high rates of non-completion of study tasks are reported in the literature, and several investigators also noted that relatively large proportions of participants (30-50%) had significant difficulties learning and understanding the inhibition tasks and were excluded from the analyses (Atkinson et al., 2003; Mobbs et al., 2007). In sum, consistent with observations of behavior difficulties that may be related to inhibition (i.e. indiscriminate social approach), individuals with WS demonstrate broad inhibition difficulties.

Planning in WS. Although only very few studies have investigated planning abilities in WS, individuals with WS show consistent impairments in planning task performance. In a study using the Tower of London task, individuals with WS showed impaired planning performance compared to CA-matched, MA-matched and MA-matched ADHD male controls both in regard to solving items under time constraints and solving them with minimal moves and attempts (Menghini, Rhodes 2010, Rhodes 2011). Similar to what was seen for the working memory domain, IQ accounted for some of the planning deficits, as indicated by significantly lower effect sizes when compared to MA-matched controls (Rhodes 2010). As seen on the inhibition tasks, there is also some indication of a bias for speed over accuracy on planning tasks as well (Costanzo et al., 2013; Menghini et al., 2010). The very limited literature on planning deficits in

WS indicates significant impairments in planning beyond what would be expected based on the general cognitive deficits and ADHD frequently observed in WS.

Shifting/Flexibility in WS. As with studies of planning, there are only a few studies of cognitive flexibility or set-shifting in individuals with WS (Carney et al., 2013; Costanzo et al., 2013; Menghini et al., 2010; Osório et al., 2012; Rhodes et al., 2010; Zarchi et al., 2014). The studies included primarily combined child and adult samples ranging from 8 to 34 years old. Shifting was measured with a variety of tasks (Wisconsin Card Sort, Trail-Making Test, DKEFS Alternative Category Fluency Task). The current evidence on set-shifting abilities in WS suggest consistent deficits in a variety of shifting tasks, including both shifting speed and accuracy, when compared to chronological age matched controls. Deficits appear less severe and consistent when comparing performance of individuals with WS to mental-age matched controls or when mental age is statistically controlled, suggesting that general cognitive deficits account for some of the set-shifting difficulties observed. Deficits were observed during tasks with both implicit and explicit rules, on tasks measuring accuracy, speed or switching cost, and on tasks with different definitions of mental age across studies (i.e., verbal, nonverbal or overall mental age).

Parent Report of Executive Functioning

Parent report measures of executive functioning are a compliment to lab-based performance measures of executive functioning, with arguably higher ecological validity (Isquith, Roth, & Gioia, 2013). Parent reported behavior-rating measures permit a systematic way of measuring parental observations of a child's executive functioning related behaviors in the everyday context. Lab-based performance measures are generally conducted in quiet environments with friendly and patient examiners in a 1-1 setting. However, children are not

frequently exposed to such "optimal conditions," and parent report allows measurement of the child's functioning under less optimal conditions. One frequently-used measure of executive functioning related behaviors, the Behavior Rating Inventory of Executive Function (BRIEF), permits comparison to the general population. This measure includes several indices: The BRIEF Behavioral Regulation Index consists of Inhibit, Shift and Emotion Control scales. The BRIEF Metacognition Index consists of Working Memory (which also reflects inattention symptoms), Planning/Organization, Organization of Materials, Initiation, and Monitor scales. The General Executive Composite reflects includes both the Behavioral Regulation Index and Metacognition Index.

Parent Reported Executive Functioning in Williams Syndrome. Evidence from two investigations indicates that parents of individuals with Williams syndrome commonly observe significant difficulties with executive functioning and relate to sensory difficulties and anxiety. In a small sample (N=18) of 16-39 year olds, Hocking, Menant, Kirk, Lord, and Porter (2014) found that both the BRIEF Metacognition Index and the General Executive Composite were significantly elevated in the individuals with WS compared to chronological age matched controls. On both indices, mean executive functioning difficulties fell in the clinical range. The only other study examining BRIEF performance of children with Williams syndrome was Mervis and John's (2010) study of sensory modulation difficulties among 78 4-11 year olds with WS. They found that parents of children in the high sensory modulation group reported, on average, clinical-range difficulties in shifting, emotional control, initiation, working memory, planning, and monitoring. Even in the low sensory modulation difficulty group, mean parent ratings were in the clinical range for monitoring and working memory and in the subclinical range for

planning. Descriptive statistics regarding parent ratings for the sample as a whole were not reported, but it is nevertheless evident that EF difficulties were observed, as both groups showed elevations. In sum, there is some evidence for executive functioning difficulties in everyday life for young children as well as for adults with WS, as observed by parents.

Relations between Lab-Based and Parent-Reported Executive Functioning in Other Populations. Although several studies have found relations between parent-reported executive functioning (particularly the BRIEF) and lab-based executive functioning, results are mixed and several reasons may account for this inconsistency (for a detailed review & table of studies see: McAuley, Chen, Goos, Schachar, & Crosbie, 2010). Although most studies found some relations between lab executive functioning performance and BRIEF ratings, performance on tasks of a given domain did not consistently relate to the BRIEF scale of the corresponding domain (i.e. an inhibition task not consistently relating to the BRIEF inhibit scale). In addition, when performance on a task of a given domain related to scores on the BRIEF, it related to several different scales, not just one. Possible reasons for these results include task impurity, "behavior impurity," diverse populations sampled (ADHD, PKU, TBI, epilepsy), and lack of power for small to medium effect sizes (Isquith et al., 2013; McAuley et al., 2010; Miyake et al., 2000). Task impurity relates to the problem that performance on any given executive functioning task generally taps several EFs at the same time. Similarly, "behavior impurity" reflects the problem that any given executive functioning related behavior in everyday life likely relies on more than one EF. In addition, some studies examined relations of lab-based tasks to specific BRIEF scales, whereas others only examined relations between lab-based tasks and the three BRIEF indexes (General Executive Composite, Behavioral Regulation Index, and Metacognition Index). In

conclusion, although the precise nature of the relation between lab-based and parent-rated executive functioning has yet to be delineated, some evidence exist for relations.

Relations between Lab-Based and Parent-Reported Executive Functioning in Williams Syndrome. There is only one study that has investigated relations between parent-reported executive functioning and lab-based executive functioning among individuals with WS (Hocking 2014). The study investigated the relationship between dual task performance (digit span or verbal fluency while walking) and parent-reported EF. Dual task cost was defined as the difference in walking quality while performing a second task compared to walking quality without a second task. Specifically, reductions in walking quality, due to performing another task (digit span, verbal fluency) simultaneously, were related to parent report of EF. In the individuals with WS (N=18, age 16-39), parent rated general executive functioning problems (BRIEF GEC) predicted higher walking quality costs during both the verbal fluency task and the digit span task conditions. Ratings of behavioral regulation problems were associated with more walking quality cost only during the verbal fluency condition. In conclusion, while this study suggests some relation between dual task performance and parent rated executive functioning, no study to date has investigated the relationship between parent-report and lab-based measures of core executive functions (working memory, inhibition, set shifting) in Williams syndrome.

Limitations of Prior Research and Extension of Prior Research

Very few studies have examined executive functioning in a narrow age range with children with WS (Carney et al., 2013; Tager-Flusberg, Sullivan, & Boshart, 1997; Vicari, Bellucci, & Carlesimo, 2003). The vast majority of studies included very large age ranges with young children up to young or middle-aged adults when comparing performance to typically

developing children and adults. Therefore, very few participants were represented at a particular age, such that the representativeness of the sample is often unclear due to likelihood of significant variability at each age. Additionally, although there has been increasing interest in the study of executive functioning in Williams syndrome over the last few years, investigations of parent/caregiver-reported executive functioning difficulties in daily life have been relatively neglected. Further, with an average group sample size of 15-20, most studies to date have been significantly underpowered to detect large and, in particular, medium effect sizes. Moreover, the relation between "foundational" executive functions measured in the lab and parent reported executive functioning has not been investigated yet in Williams syndrome.

Conclusion and Rationale for Current Study

In summary, there is growing evidence for significant difficulties in various executive functioning domains for individuals with WS. The very limited literature on executive functioning related behaviors (as reported by parents) suggests that executive functioning problems are common in everyday contexts. The large majority of studies on Williams syndrome are significantly underpowered and have not permitted more nuanced analysis of patterns of executive functioning difficulties. Executive functioning is critical for purposeful behavior at school, work, home and in social situations. Knowledge of executive functioning difficulties in everyday life of youth with Williams syndrome can inform early intervention services and parent education on the potential for executive functioning difficulties in a child with Williams syndrome. In addition, in regard to ecological validity, it is important to understand the degree to which lab-based performance on executive functioning tasks is relevant to the everyday executive functioning behaviors that parents observe in children with Williams syndrome.

Brief Study Description

The current study intends to describe the executive functioning related behaviors of youth with Williams syndrome as reported by their parents, as well as relations of parent-reported EF to an executive functioning task intended to measure inhibition and set-shifting (the Dimensional Change Card Sort). In particular, the current study examines the degree to which lab based executive functioning performance predicts parent reported executive functioning difficulties in youth with Williams syndrome while controlling for age and nonverbal ability.

The current study provides the first comprehensive description of parent rated executive functioning difficulties in youth with Williams syndrome, with a substantial sample size (n ~ 80). The current study will have sufficient power to examine relative differences in parent reported executive functioning difficulties across domains to describe the pattern of everyday executive functioning difficulties in Williams syndrome. This study will investigate how relevant performance on a frequently-used task of developing executive function (Dimensional Change Card Sort) is to executive functioning difficulties in daily life observed by parents of children with Williams syndrome. The current sample is sufficient to detect medium effect sizes instead of only very large effect sizes; this permits effective examination of relations between lab based executive functioning performance and parent rated executive functioning (as such relations will likely be of medium but not large effect). Further, due to the (relatively) narrow age range of 8-15 years with the relatively large sample size of about 80, this study adds to the very limited literature about executive functioning in children and adolescents with WS and permits meaningful description of age effects of EF in youth with WS during this time period.

Method

Participants

The sample used includes archival data from both Child Neurodevelopment Research Lab at UW-Milwaukee and the Neurodevelopmental Sciences lab at the University of Sciences Lab at the University of Louisville. 81 children aged 8-15 years with Williams syndrome (M=11.18, SD=2.51) were included in the study (44 girls, 37 boys; (see Table 1 for descriptives). Inclusion criteria consisted of being native English language speakers and having tested positive genetically for Williams syndrome. There were no specific exclusion criteria. KBIT-2 IQ Composite standard scores ranged from 40 to 106, and KBIT-2 Nonverbal standard scores ranged from 42 to 110.

Materials

The measures selected are appropriate for young children and adolescents and were selected to provide information about participants' overall cognitive functioning, lab-based performance on an executive functioning task, and parent reported executive functioning related behaviors.

Kaufman Brief Intelligence Test – 2. (Kaufman & Kaufman, 2004) is a brief measure of overall cognitive abilities that includes subtests assessing verbal as well as nonverbal domains. The verbal domain includes a subtest on receptive vocabulary and a word-reasoning task in the form of "riddles". The nonverbal domain consists of a matrices task that measures comprehension of relationships and patterns of shapes. The KBIT-2 has demonstrated good reliability and validity. This measure of cognitive ability is helpful to estimate overall verbal and nonverbal ability without using visual-spatial construction tasks (like the block design task in the Wechsler tests), on which individuals with Williams syndrome show a significant relative

weakness. The KBIT-2 is therefore a good measure of overall cognitive functioning in Williams Syndrome.

The Dimensional Change Card Sort. (DCCS, Zelazo 2006) is a measure of the emerging executive functioning and flexible rule use in particular. It was developed as a measure of executive functioning for children, based on the Wisconsin Card Sort, a measure of executive functioning used primarily with adults. However, the DCCS, through the explicit statement of card sorting rules and repetition of the relevant rules, has been shown to be sensitive to development of EF from preschool age through adulthood. Given that the cognitive abilities of individuals with WS are frequently in the intellectual disability range, the DCCS provides an appropriate floor. During the first phase (pre-switch), participants are instructed to sort cards along the dimension of color, during the second (post-switch) phase, participants are asked to sort cards according shape, and in the third phase, sorting according to the two rules switches back and forth in a random manner. Sorting rules are explicit and are stated once before pre-switch and post-switch phases and during every trial of the border phase. Performance on the DCCS has been shown to be impaired in children with ADHD and autism who tend to have significant executive functioning difficulties (see Zelazo 2006). A computerized version is also now available in the NIH Toolbox (Bauer & Zelazo, 2014) .

The Behavior Rating Inventory of Executive Function. (BRIEF, Gioia, Isquith, Guy, & Kenworthy, 2000) is a behavior rating questionnaire of executive functioning related behaviors of school-age children as observed by parents at home or at school by teachers. Parents rate on a three point Likert-type scale (never, sometimes, and often). There are eight subscales (Inhibit, Shift, Emotional Control, Initiate, Working Memory, Plan/Organize, Organization of

Materials, Monitor). Inhibit, Shift, and Emotional Control contribute to the Behavioral Regulation Index. The remaining scales contribute to the Metacognition Index. The General Executive Composite reflects both the Behavioral Regulation Index and Metacognition Index. The BRIEF has good internal consistency, test-retest reliability and good external validity with a variety of other questionnaires. We used percentages to illustrate the proportion of youth with Williams syndrome who scored in the "at risk" and "clinical" ranges of each BRIEF scale and index, and we included for comparison the frequency of elevations to the proportion that would be expected in the general population ("at risk"but not clinical ~ 9%, "clinical" ~9%). The BRIEF has slightly different percentiles associated with the same T-score based on age- group, gender and scale; this is likely a norming issue of using empirical percentiles instead of theoretical percentiles, and therefore we used the average across age and gender groups of the BRIEF GEC Composite as benchmark for percentages. As discussed previously, relations between executive functioning performance tasks in the lab and BRIEF ratings have been somewhat inconsistent, likely relating to underpowered studies, differences in various external factors between lab-based performance assessment, and observations outside the laboratory.

Procedure

For all participants, examiners obtained parental informed consent. Data were collected at the Child Neurodevelopmental Research Lab at the University of Wisconsin Milwaukee, at Williams Syndrome Association Conferences (for families with children with Williams syndrome), and as part of a longitudinal study of Williams syndrome at the Neurodevelopmental Sciences Lab at the University of Louisville. Trained examiners administered the Kaufman Brief Intelligence Test 2nd edition and Dimensional Change Card Sort to the participants. For the

longitudinal data, the visit with the first DCCS administration was included in the current study. A mother, father or other caregiver completed the Behavior Rating Inventory of Executive Function.

Statistical analysis, testing for normality and outliers was conducted with R version 3.2.3. Potential univariate outliers for independent t-tests were identified as values with extreme z-scores (+-3.29) as recommended by Tabachnick and Fidell (citation 2007). Potential bivariate outliers for bivariate correlations were identified as having studentized residuals higher than +-2. Multivariate outliers were identified in two steps. First, participants with extreme studentized residuals (+-) and Cook's distance values higher than 4/N were identified as potential influential values for the overall regression model. If the overall regression model or the variable that was added in either the multiple hierarchical regression or in the final full model for each coefficient had a change in significance level (<.05, 0.5 <p<.10, non-significant), or if the overall R2 value was much larger, the model without these values was reported. In addition to the examination of potential influential values for individual regression coefficients, models were computed that also excluded values with high standardized DFBETA values (2/sqrt(N)) for each added coefficient to the hierarchical regressions and for all coefficients in the final model. If removing those values changed the significance level, this was indicated in the table.

Study Aims, Hypotheses, and Analytic Strategy

Aim 1: ***Describe patterns of problems of executive functioning behaviors as reported by parents in youth with Williams syndrome (largest sample to date), including mean severity of difficulties and percentage of children rated in the at-risk and/or clinical range and relations to age.*** One-sample t-tests were used to examine whether WS mean T-scores are statistically

significantly above the population average of 50. It was expected that on the vast majority of scales, the WS group would be rated on average above 50. Given the current evidence on lab performance deficits in these domains, it was expected that mean scores on Working Memory, Shifting, and Planning scales would be above 50. In addition, the only study that detailed parent reported executive functioning in individuals with Williams Syndrome on the BRIEF scale level suggested that the Shift, Emotional Control, Initiation, Working Memory, Plan/Organize and Monitor scales likely would be elevated (John & Mervis, 2010).

We used percentages to illustrate the proportion of youth with Williams syndrome that scored in the "at risk" and "clinical" ranges of each BRIEF scale and index, and we included the proportion that would be expected to fall in each range in the general population ("at risk" but not clinical ~ 9%, "clinical" ~9%) for comparison . To examine any differences between scales, we conducted within group t-tests between the scales representing skills primarily researched (working memory, inhibition, shifting and planning). To examine relations of parent reported executive functioning problems to age, Pearson correlations were conducted between age and BRIEF General Executive Composite, Behavioral Regulation Index, Metacognition Index and Working Memory standard scores. Based on the BRIEF normative data for the general population, it was expected that age would not be correlated with executive functioning difficulty levels in relation to same-aged peers (standard score).

Aim 2: Describe patterns of performance on a task measuring emerging executive functioning and in particular flexible rule use in youth with Williams syndrome. To examine whether the DCCS is sensitive to changes in executive functioning skills as children with WS mature, Pearson correlations between participant age and DCCS performance (# of

phases passed, # of correct border trials) were examined. It was expected that increased participant age would be associated with increased DCCS performance (# of phases passed, # of correct border trials). To examine whether the relation between age and DCCS performance is nonlinear, regression models using quadratic and logarithmic curves were tested to determine whether they provide a statistically significant improvement in model fit. There is no clear hypothesis, but such a fit might suggest a leveling off of performance at a certain age.

Aim 3: Examine the extent to which executive functioning performance in the lab as measured by the DCCS predicts parent rated everyday executive functioning behaviors on the BRIEF, after controlling for nonverbal ability. To examine whether gender should also be controlled, models predicting the BRIEF General Executive Functioning composite were conducted with the added gender predictor. Since gender significantly predicted BRIEF GEC above and beyond nonverbal ability and DCCS performance, gender was included as a covariate in the remaining analyses. To examine the unique contribution of the DCCS after controlling for cognitive ability (either nonverbal standard score or raw score) in predicting BRIEF ratings, a series of multiple regression models with the following format were conducted.

a. BRIEF scale standard score = KBIT 2 Nonverbal Standard Score + DCCS # passes/DCCS # of correct border trials (only for BRIEF GEC as outcome variable)

b. BRIEF scale standard score = KBIT Nonverbal raw + DCCS # passes/DCCS # of correct border trials

Given that performance on the DCCS is intended to reflect cognitive flexibility, we expect that the DCCS will predict BRIEF Shift scores above and beyond the other control variables. Given likely inhibitory control and working memory involvement (in particular during

the "border" phase), it is also expected that DCCS performance will be a significant unique predictor of BRIEF Inhibit and Working Memory raw scores. As there is literature indicating that performance on one EF task tends to relate to several BRIEF scales (McAuley et al., 2010) , the DCCS performance may also be related to other BRIEF scales. Based on the previous literature and the abilities that the DCCS likely measures, it is expected that DCCS performance predicts BRIEF General Executive Composite, BRIEF Metacognition, BRIEF Inhibit, BRIEF Shift and BRIEF Working Memory standard scores.

Results

R 3.2.3. and IBM SPSS 23 for Windows were used for the analyses. A p-level of .05 was considered statistically significant. Effect sizes for mean level differences (Cohen's D) were interpreted as .3=small, .5=medium and .8=large; for correlations, .1=small, .3=medium, .5 large effect; for R2, .01=small, .09=medium and .25 large effect. Assumptions of normality were fulfilled for all analyses. Several outliers were identified with elevated studentized residuals and Cook's distance values, particularly when gender and DCCS were added as predictors. After following the procedure described above in the methods section (when appropriate because of significant changes in the model), most regression coefficients were stable (i.e., did not significantly change when further potentially influential values specific to the coefficient were removed). In the few cases that the significance level changed again by removing data points with high DFBETAS values, the change in significance level is noted in the respective table.

Patterns of Parent-rated Executive Functions.

Mean Level Differences to General Population. As expected, parents with children and adolescents with Williams syndrome rated their children's executive functioning difficulties

higher than the general population (see Table 2, all p's <.001), including on the BRIEF General Executive Functioning Composite, Behavior Regulation Index, and Metacognition Index as well as on the Inhibit, Shift, Emotion Control, Initiate, Working Memory, Plan/Organize, Organization of Materials and Monitor scales. All effect sizes were large. Of note, the lower end of the mean level rating confidence interval was above T=60 for all but two scales (Shift and Emotion Control), indicating that, with these exceptions, the scales had mean levels above the subclinical threshold.

Mean Level Differences between BRIEF domains. To examine differences in mean levels of parent reported executive functioning across the domains, several within-group T-tests were conducted for the variables primarily researched previously with performance tasks (Inhibition, Shifting, Working Memory, Planning). Variables were first ranked by mean value (see Table 2) resulting in the following ordering (from the highest): Planning, Working Memory, Inhibition, Shift (See Figure 1). The highest mean, Planning, was not statistically significantly higher than the next highest, Working Memory scale (p=.132). However, the Planning mean was statistically significantly higher than the BRIEF Inhibit scale (t(80)=2.57, p=.012, d=.21), with small effect, and the BRIEF Shift scale with medium effect (d=.33). The BRIEF Working Memory scale was not significantly higher than the Inhibit Scale mean (p=.155) but statistically significantly higher than the BRIEF Shift scale (t(80)=4.26, p<.001, d=.52) with medium effect. The Inhibit mean was significantly higher than the Shift mean (t(80)=2.70, p=.008, d=.30), with small effect. Overall, medium effect sizes were seen for most differences between scales, with particular difficulties in and least difficulties with shifting.

Proportions in normal, subclinical and clinical ranges. With regard to overall parent rated executive functioning (BRIEF General Executive Composite), only 11.1% of participants scored in the normal range, whereas 25.9% scored in the subclinical range (T score = 60-64) and 63% scored in the clinical range (T score 65+, see Figure 2). There was some variability in parent rated executive functioning difficulties by domain. Differences in mean levels between BRIEF domains is also reflected in the proportion of participants who scored in the clinical range. Whereas 37% of participants scores in the clinical range on the Shift scale, 64.2% did so on the Plan/Organize scale.

Age effects. Age was not correlated with any of the BRIEF T-scores, including General Executive Composite, Inhibition, Shifting, Working Memory, and Plan/Organize (r's -.08 to .12, $.289<p<.956$). Age was significantly correlated with Inhibition raw scores (r=-.24, p=.033, without 3 outliers) and Working Memory raw scores (r=-.37, .001). This is consistent with the norms from the BRIEF, which include a decrease in expected raw scores for Inhibit and Working Memory raw scores with age, but not for Shift and Planning/Organization raw scores. Although the norms also suggest a decrease in General Executive Composite raw scores, no significant correlation was found with age.

Patterns of Performance on DCCS.

Age effects. Because the variable DCCS Phases passed only included three values (1,2,3), a regression was computed using dummy codes for the DCCS Phases variable and age as the outcome variable in order to examine the relation with age. DCCS phases significantly predicted Age (converted effect r=.35, p=.006), with medium effect. The number of correct border trials was initially only marginally correlated with age (r(62)=.24, p=.052), but was

significantly positively correlated after removing two outliers (r(60)=.33, p=.009), with medium effect. After removing two outliers, logarithmic and quadratic models did not significantly improve model fit of a linear model.

Prediction of Parent Reported Executive Functions.

DCCS phases passed as main predictor. Several hierarchical multiple regression models were computed to examine the relative predictive contribution of the number of DCCS phases passed to prediction of general executive functioning difficulties (BRIEF General Executive Composite T score), metacognitive difficulties (BRIEF Metacognition T score), inhibition, shifting, and working memory difficulties (See Tables 4 and 6). The multiple regression models controlled for the contributions of age, nonverbal ability (KBIT-2 raw) and gender. Predictors were entered simultaneously.

The regression models accounted for 12-24% of the variance in BRIEF scores (see Tables 4 and 6). The overall models predicting general executive functioning difficulties, shifting, and metacognition were statistically significant; however, the models predicting inhibition and working memory reached only trend level. After controlling for age, absolute nonverbal ability and gender, the number of DCCS phases passed did not predict general executive functioning difficulties or shifting difficulties. However, DCCS phases passed significantly predicted working memory difficulties with medium effect. In addition, although initially not significant, the number of DCCS phases passed also predicted Inhibit significantly and Metacognition at a trend level after removing coefficient specific extreme values. Similarly, in an additional multiple regression model including relative nonverbal ability (KBIT-2 Standard Score) instead of absolute nonverbal ability (KBIT-2 nonverbal raw score), DCCS did not

predict general executive functioning difficulties after controlling for the other variables in the model (age, nonverbal ability and gender). Of note, gender significantly uniquely predicted General Executive Composite, Shift, and Metacognition scores. Age only significantly predicted Shift scores after controlling for the other variables in the models. Age predicted General Executive Composite scores at a trend level (after removing coefficient specific extreme values).

DCCS number of border trials as main predictor. Several simultaneous multiple regression models were computed to examine the relative contribution of correct DCCS border trials (during phase 3) after controlling for age, nonverbal ability (KBIT-2 raw) and gender in predicting general executive functioning difficulties (BRIEF General Executive Composite T score), metacognitive difficulties (BRIEF Metacognition T score), inhibition, shifting, and working memory difficulties (See table 4 and 5). Predictors were entered simultaneously (See Table 4 and Table 5).

The regression models including the DCCS number of border trials as a predictor accounted for 14-31% of the variance in BRIEF T-scores of the various scales. Models predicting General Executive Composite, Metacognition, Inhibition, and Shift T-scores overall yielded significant results, but the model predicting Working Memory scores did not.

After controlling for age, absolute nonverbal ability (K-BIT-2 nonverbal raw), and gender, DCCS correct border trials predicted all scales (General Executive Composite, Inhibition, Working Memory, Metacogntion) significantly with medium effect except for the Shift scale scores. Gender uniquely predicted General Executive Composite, Shifting (after further removal of coefficient specific extreme values), and Metacognition scores. After removal of coefficient-specific extreme values, age no longer uniquely predicted General Executive

Composite scores and predicted Shift scores only at a trend level. Gender uniquely predicted General Executive Composite scores, Metacognition, and Shift scores (for shift: after removing coefficient specific extreme values; for all: boys with higher values). When KBIT-2 nonverbal standard scores were used to control for nonverbal ability instead of raw scores (after removing coefficient specific extreme values), gender predicted General Executive Composite scores only at a trend level. This indicates that some of the gender effect observed in the models appears to be accounted for by the differences in IQ observed between boys and girls in this sample.

Discussion

The study of executive functioning related behaviors in everyday life and the relevance of laboratory based tasks of executive functioning for the daily functioning of youth with Williams syndrome has been neglected. Executive functions are critical for functioning at school and work as well as at home and in relationships. A growing body of research has documented broad deficits in various executive functioning domains for individuals with Williams syndrome in comparison to chronological and mental age matched controls based on lab-based tasks. The current study adds to the existing literature by examining parent-observed difficulties in executive functioning at home in children and adolescents with Williams syndrome in a detailed manner. Additionally, the current study represents a contribution to the literature by investigating the degree to which lab-based executive functioning performance in children and adolescents with Williams syndrome is relevant to parent-observed executive functioning in everyday settings. Parents of children and adolescents with WS reported high levels of executive functioning difficulties, and several executive functioning domains were predicted by lab-based performance.

Patterns of Parent-rated Executive Functions

Consistent with our hypothesis, parents' ratings of youth with WS indicated high levels of executive functioning difficulties across all domains (inhibition, shifting, emotion regulation, initiating, working memory, planning, organization of material, and monitoring). This is consistent with findings of elevated scores on the Behavior Regulation Index and Metacognition Index in a very small sample of primarily adults (16-39 years old) with Williams syndrome (Hocking et al., 2014). The current findings from a sample of 8-15 year old youth are also consistent with previous findings for a large sample of 4-10 year old children with Williams syndrome. The current study scale means (for the scales that were reported in prior work) were usually between the previously reported averages for the two participant groups they included. Therefore, the extent of parent reported difficulties appears similar to the published literature about both younger children and adults with Williams syndrome. These parent-report findings are also consistent with the literature on broad executive functioning difficulties measured with lab-based tasks in working memory, inhibition, shifting, and planning in individuals with WS (Carney et al., 2013; Costanzo et al., 2013; Porter et al., 2007; Vicari, Bellucci, & Carlesimo, 2006; Zarchi et al., 2014).

In the current study, very few parents (11%) rated their child having overall executive functioning difficulties in the normal range. Whereas previous lab-based evidence documented on average lower performance, the current study also quantifies the proportion of children who show normal executive functioning behaviors (at least in the population of youth with Williams Syndrome that typically participates in research studies). These highly frequent, pervasive executive functioning difficulties put an additional burden on youth with Williams syndrome to

function in everyday contexts, in addition to the burden created by significant general cognitive difficulties, adaptive functioning challenges, elevated risk for anxiety disorders, and to a lesser degree autism spectrum disorders.

Although the previous literature on lab-based executive functioning in WS has documented deficits in various executive functioning domains, there has been little investigation of relative difficulties between various domains of executive functioning (likely because of a lack of power in these typically very small samples). The current findings add information about the relative difficulties between various domains of executive functioning in everyday contexts. The exploratory analysis of relative executive functioning difficulties across domains indicates that parents observed particular difficulties with: 1) working memory and planning-related behaviors compared to shifting difficulties, and 2) to a somewhat lesser degree, inhibition difficulties compared to planning and working memory difficulties. Nevertheless, still about half the youth with WS were rated as having subclinical or clinical range difficulties with shifting. This finding of particular elevations on the Planning/Organization and the Working Memory scale is consistent with the high prevalence of ADHD in WS (Leyfer, Woodruff-Borden, Klein-Tasman, Fricke, & Mervis, 2006b) and the working memory and planning difficulties that are frequently found in individuals with ADHD (Toplak, Bucciarelli, Jain, & Tannock, 2008). In addition, many of the Working Memory scale items on the BRIEF include inattention symptoms from the diagnostic criteria for ADHD, and this scale has been found to be elevated in samples of children with ADHD (Gioia et al., 2000; Toplak et al., 2008).

Using age-normed scores, there were no age effects for parent ratings of executive functioning. On a positive note, whereas children with Williams syndrome tend to fall further

behind their peers over time in certain adaptive functioning skills (motor skills, community living skills, Mervis & Morris 2007), there does not seem to be a decline in parent observed executive functioning in comparison to same-aged peers with age. This is also consistent with a lack of association with age and general cognitive abilities in a large cross-sectional sample (Pitts & Mervis 2016), as well as with a generally stable IQ scores across childhood in youth with Williams syndrome in a longitudinal sample (Mervis, Kistler, John, & Morris, 2012). Similarly, as would be expected based on the norms, age was significantly correlated with inhibition and working memory raw scores, suggesting that older youth with WS tend to show better parent observed executive functioning in these domains, as would be expected.

Patterns of Performance on executive functioning task

Consistent with our hypothesis, performance on the executive functioning task improved with age, both with regard to how many phases passed and, for those who reached the third phase, the number of correct border trials. This is consistent with prior research showing improvement on the task in preschool age. Curve estimation suggests that this improvement in performance during the border trial, during which sorting rules can change on a trial-by-trial basis, is linear, and that improvement did not seem to level off even in our older participants (i.e., 15-16 year olds). Hongwanishkul and colleagues (2005) conducted a study with the DCCS with 98 3-5 year olds. Of the 4 year olds, 83% passed the second phase and 8% passed the third phase. Of the 5 year olds, 96% passed the second phase and 48% passed the third phase. When comparing DCCS performance of the current sample of youth with WS to the sample of typically developing preschoolers of Hongwanishkul and colleagues (2005), the 8-15 year olds showed equivalent performance in the ability to switch to a new rule (DCCS Phase 2). With regard to the

ability to switch task rules on a trial-by-trial basis, the 8-9 year-olds with WS in this sample performed much more poorly than the typically developing 5 year olds described in the literature. This is expected given the significantly lower overall cognitive abilities of individuals with WS and the frequent finding that executive functioning deficits were somewhat attenuated in WS when comparing to mental age-matched controls (instead of chronological aged matched controls) or when controlling for IQ (Osório et al., 2012; Rhodes et al., 2010). However, even the oldest participants with WS in our sample (15-16 years old) did not appear to perform better than the 5- year-olds at rapidly switching between task rules. Hence, EF abilities as measured by this lab-based task were clearly delayed.

Prediction of Parent Reported Executive Functions.

It was expected that performance on the card sort task would predict parent reported executive functioning after controlling for age, nonverbal ability and gender. Using the number of DCCS phases passed as a measure of executive functioning performance, DCCS performance significantly predicted parent reported inhibition and working memory, but not parent reported shifting difficulties, metacognition difficulties, or general executive functioning difficulties. However, gender significantly predicted general executive functioning difficulties, shifting, and metacognition difficulties, with boys having more executive functioning difficulties than girls compared to their peers (even though gender-based norms were used). These gender differences remained even when accounting for nonverbal ability with the standard score.

A larger amount of the variance in parental report of executive functioning difficulties was accounted for when using the number of trials during the 3rd phase (border phase), during which participants had to switch back and forth between the two sorting rules. Consistent with

our hypothesis, DCCS border performance significantly predicted parent-reported general executive functioning, metacognition, inhibition and working memory ratings, but not shifting difficulty ratings, after controlling for age, nonverbal ability and gender. The lack of significant prediction of shifting difficulties is somewhat surprising, as our task is often considered a "switching" or "cognitive flexibility" task. Of note, the difference in findings is not subtle; DCCS border performance accounted for 10-12% of parent ratings of inhibition and working memory but only 1% of shifting.

One possible explanation is that different aspects of shifting may be measured by the lab task and the behavior ratings of parents. The BRIEF manual defines the BRIEF Shift scale as assessing "the ability to move freely from one situation, activity, or aspect of a problem to another as the circumstances demand. Key aspects of shifting include the ability to make transitions, problem-solve flexibly, switch or alternate attention…" (p18, Gioia, Espy, & Isquith, 2003). Therefore the BRIEF behavioral definition of shifting is significantly broader than the ability to quickly switch between two rules of a problem. These findings are also consistent with the prior literature on inconsistent relations between lab-based tasks and BRIEF scores (McAuley et al., 2010). In previous studies, performance in a given domain (i.e., inhibition) did not consistently predict parent ratings in this same domain in previous studies, or performance on a task measuring a specific aspect of executive functioning was related to several parent-rated domains of executive functioning.

It is also possible that the DCCS reflects multiple cognitive processes. Lezak and colleagues (2012) argue that intact attention is a first condition for focused behavior and that attention is measured in the context of a specific activity (i.e., here, the rule switching task).

They further state that while the constructs of short-term memory, working memory and attention may be separable theoretically, empirically this separation is more difficult, that attentional difficulties may reflect more "simple" and global difficulties or more "complex" and task-specific attentional difficulties. One of the causes of rule-switching performance in this study may be simple attentional lapses, which may have prevented even a reduced working memory ability to function properly and correctly decide which rule to employ in a given trial. Given that, based on primarily parent and teacher report, the attentional difficulties of youth with Williams syndrome are rather pervasive (citations), it is likely that more global and less task-specific attentional difficulties have significant impact on attentional functioning outcomes. Attentional functioning outcomes may also depend on the domain of the task (primarily verbal, visual), as youth with Williams syndrome frequently show better performance on verbal tasks than primarily nonverbal tasks. The DCCS appears to involve both verbal elements (rules repeated verbally at every border trial) and nonverbal elements (response to sort by color or shape, although this could also be partially verbally mediated). Relations to parent rated executive functioning may differ for executive functioning tasks that rely on either mostly verbal or mostly nonverbal modalities.

There is also evidence that performance on one task may reflect different abilities depending on the developmental level of the person. For example, in a large study with 7-21 year olds, working memory was the strongest predictor of Wisconsin Card Sort Test performance (Huizinga, Dolan, & van der Molen, Maurits W, 2006), whereas in young adults, shifting performance was the strongest predictor of WCST performance (Miyake et al., 2000). Performance on the DCCS for individuals with WS may not primarily reflect shifting, but rather

inhibition and working memory/attention functioning. Since border trial performance predicted both inhibition and working memory as well as broader indices of executive functioning such as metacognition and general executive functioning ratings, it appears likely that performance on the DCCS for youth with Williams syndrome reflects several executive functions.

Taking into consideration that DCCS performance in youth with Williams syndrome likely appears to tap into several executive functions, the DCCS may be a useful "complex executive functioning" task to measure general emerging executive functioning, particularly in older children and adolescents with Williams syndrome. Of note, instructions and rules are quite straightforward and are frequently repeated, which is not always the case with executive functioning tasks. In studies of executive functioning, several authors have noted that large proportions of their samples of individuals with Williams syndrome (20-50%) needed to be excluded because participants did not appear to understand the nature of the task (Atkinson et al., 2003; Jarrold, Baddeley, & Hewes, 1999; Mobbs et al., 2007; Rhodes et al., 2011).

There was significant multivariate variability in the multiple regression models in the current study sample. First, for many models, 2 or 3 participants had a large impact on the overall multiple regression model. Further, particularly for age, but also for gender and DCCS performance, 3-5 participants at times significantly changed given coefficients and caused effects to appear or disappear. The results reported reflect the patterns for the vast majority of the sample (~90-95%). However, it is noteworthy that there is a sizeable number of youth who performed and were rated quite differently from group trends. This is consistent with the variability in functioning commonly described in the literature in WS (Mervis et al., 2012; Woodruff-Borden, Kistler, Henderson, Crawford, & Mervis, 2010).

Limitations and Future Directions

One limitation was the difference in IQ between boys and girls in the sample. Gender differences in general cognitive functioning in individuals with Williams syndrome are not commonly reported (Pitts & Mervis, 2016). Another limitation included the lack of a comparison group. Different comparison groups would provide different information. A comparison group with either typically developing children or children with other genetic disorders with cognitive difficulties (i.e., Down syndrome) would have permitted a description of the extent of DCCS performance difficulties more clearly in Williams syndrome. It would have also permitted examination of whether a diagnosis of Williams syndrome moderates the relation between performance on the DCCS and the BRIEF parent ratings of executive functioning. A control group with typically developing youth would allow comparison of executive functioning in youth with WS to typical development. Inclusion of a control group with similar intellectual abilities at the same chronological age would help examine the extent to which the executive functioning difficulties observed in WS are related to generally lower and delayed cognitive development seen in individuals with intellectual disability range cognitive functioning. This would also elucidate the extent to which executive functioning difficulties observed in WS are unique to WS. In addition, a mental-age matched comparison group of youth with ADHD might allow examination of the degree to which executive functioning deficits of youth with WS are related to lower general cognitive functioning and ADHD diagnosis.

Investigation of the developmental trajectories of executive functioning performance and everyday context behaviors is warranted. Although relations between age and parent rated executive functioning difficulties were not found in the current study, this was a "whole group"

result, and longitudinal investigations could delineate if significant variability in developmental trajectory of parent-rated (and performance based) executive functioning exists in WS. A study of cognitive functioning in youth with Williams syndrome found stable IQ scores over time but also significant variability in the slopes of scores, indicating that while some children improved and many remained similar compared to their peers, some children continued to fall further behind their peers in regard to general cognitive functioning (Mervis et al., 2012).

Only one task was used to examine lab-based executive functioning. Ideally, a battery of tasks assessing in particular inhibition, working memory and set-shifting would be helpful to more closely examine which executive functioning tasks appear most relevant to executive functioning related behaviors in everyday life. With sufficient sample size and a battery of tasks, the factor structure of performance on the battery could be examined. This factor structure then could be compared to the factor structure of EF task performance in typically developing youth and adults found in previous studies (Brydges, Reid, Fox, & Anderson, 2012; Friedman et al., 2006; Huizinga et al., 2006; Miyake et al., 2000; Rose, Feldman, & Jankowski, 2011; Wiebe, Espy, & Charak, 2008). It may be possible that inhibition, working memory and shifting tasks may actually primarily load onto a single factor (similar to findings in young typically developing children) or to more than one factor. This large sample also could give information about whether the BRIEF factor structure in WS is the same as in the general population, since executive functioning behaviors may be related to each other in WS differently in comparison to the general population. Recently, a study of parent reported anxiety using the MASC in youth with autism indicated such a difference in symptom factor structure (White et al., 2015). Furthermore, using a battery of tasks and a latent variable approach would address the problem

that any task reflects a combination of skills and may elucidate why relations between executive functioning performance tasks and parent observed executive functioning behaviors have been found rather inconsistently (McAuley et al., 2010). Such an analysis might show whether, for example, it is primarily a common performance EF factor that predicts parent reported EF, as well as the degree to which individual performance EF domains map onto their parent report equivalents. The previous literature on relations between performance based EF and parent rated EF has only included studies using, at most, a few EF tasks with small samples and not permitted such analysis (McAuley et al., 2010).

Conclusion

The current study provides a detailed examination of parent reported executive functioning difficulties and the relevance of a lab-based executive functioning task to such difficulties with a large sample given the rarity of Williams syndrome. Results indicate that parents of youth with Williams syndrome observe significantly more executive functioning difficulties in a variety of domains in their children. Very few children and adolescents with Williams syndrome showed normal levels of executive functioning behavior difficulties, and a large majority showed clinical level difficulties. There is some variability in the extent of difficulties depending on the domain that parents observed. Working memory and planning difficulties appeared to be of particular concern to parents, along with inhibition difficulties and, to a lesser degree, shifting and emotion regulation difficulties. Nonetheless, about half of the parents still reported subclinical or clinical level concerns about their child's executive functioning related behavior for the latter two domains. The extent of the executive functioning difficulties relative to peers in the general population was independent of age. The performance

on the laboratory task, particularly the successful back-and-forth switching of rules, significantly predicted parent reported executive functioning in a variety of domains. Boys with Williams syndrome appeared at somewhat higher risk for executive functioning difficulties even after already using gender-based norms, suggesting that the gender difference in executive functioning related behaviors in Williams syndrome is somewhat larger than in the general population. Although age, gender, nonverbal ability and lab-task performance predicted up to a third of the variability in parental observations of executive functioning difficulties, the majority of variability remained unexplained. Future research directions include: 1) comparing relations between lab-based EF performance and parent ratings of youth with WS to typically developing youth and youth with similar general cognitive difficulties; 2) examination of longitudinal trajectories of executive functioning; and 3) examination of the factor structure of executive functioning and representative tasks of EF development in WS.

Table 1
Descriptive Statistics

Measure/*Subscale*		**Full Sample**	**Girls**		**Boys**				
	N	M(*SD)*	N	M(*SD*)	N	M(*SD*)	***t***	*p*	*d*
Age			44	11.64 (*2.62)*	37	10.17 (*2.28*)	-1.81	.074	.40
KBIT-2[a] IQ Composite	81	73.02 (*14.68*)	44	76.94 (*14.38*)	37	68.84 (*13.34*)	-2.42	.018	.54
KBIT-2 Nonverbal SS	81	76.16 (*16.78*)	44	80.30 (*17.91*)	37	71.24 (*14.04*)	-2.54	.013	.56
DCCS[b] # Border Trials correct	64		39	8.26 (*2.58*)	25	7.52 (2.28)	-1.20	.236	.30

[a]Kaufmann Brief Intelligence 2nd Edition IQ Composite
[b]Dimensional Change Card Sort

Table 2
BRIEF[a] Mean Scores Difference to T=50.

Index/*Subscale*	M	SD	Conf. Int 95%		*t*	*d*
General Executive Composite	68.54	8.58	[66.65	70.44]	19.45	2.16***
Behavior Regulation Index	67.36	9.90	[65.17	69.55]	15.78	1.75***
Inhibit	64.95	12.68	[62.15	67.76]	10.61	1.18***
Shift	61.22	11.90	[58.59	63.85]	8.49	0.94***
Emotion Control	61.74	10.98	[59.31	64.17]	9.62	1.07***
Metacognition Index	69.31	7.93	[67.56	71.06]	21.91	2.44***
Initiate	64.35	10.17	[62.10	66.59]	12.70	1.41***
Working Memory	66.90	10.08	[64.67	69.13]	15.09	1.68***
Planning/Organize	68.49	8.65	[66.58	70.41]	19.25	2.14***
Organization of Materials	63.79	11.04	[61.35	66.23]	11.24	1.25***
Monitoring	64.79	10.06	[62.57	67.02]	13.23	1.47***

[a]Behavior Rating Inventory of Executive Function
*** <.001 of single-group T-test comparing to T=50

Table 3
DCCS[a] cumulative percentages of phases passed by age group.

Age	N	Phase 1	Phase 2	Phase 3	95%CI Ph1		95%CI Ph2		95%CI Ph3	
8-9	35	100%	69%	14%	[88%	100%]	[51%	83%]	[5%	31%]
10-11	17	100%	71%	29%	[77%	100%]	[44%	89%]	[11%	56%]
12-13	13	100%	92%	62%	[72%	100%]	[62%	100%]	[32%	85%]
14-15	16	100%	100%	38%	[76%	100%]	[76%	100%]	[16%	64%]

[a]Dimensional Change Card Sort

Table 4

Overall model statistics of multiple regression of DCCS performance as predictor of BRIEF ratings after controlling for age, gender and nonverbal ability[d].

DCCS Variable Type/ *Dependent variable*	R^2	F	Num DF	Den DF	Model P	Extreme Vle. rem.[b]
DCCS Border[c]						
General Executive Composite	0.31	6.43	4	57	0.000	2
Inhibit	0.26	4.91	4	56	0.002	3
Shift	0.18	2.88	4	54	0.031	5
Metacognition (2)	0.22	4.09	4	57	0.006	2
Working Memory	0.14	2.36	4	59	0.064	0
General Executive Composite KBIT-SS[e]	0.22	4.01	4	57	0.006	2
DCCS Phases passed						
General Executive Composite	0.239	4.59	5	73	0.001	2
Inhibit	0.125	2.09	5	71	0.076	5
Shift	0.184	3.15	5	70	0.013	5
Metacognition (2)	0.166	2.90	5	73	0.019	2
Working Memory	0.123	2.10	5	75	0.075	0
General Executive Composite KBIT-SS[e]	0.239	4.58	5	73	0.001	3

[a]Behavior Rating Inventory of Executive Function
[b]Number of values with extreme studentized residuals and cook values
[c]Dimensional Change Card Sort
[d]Kaufmann Brief Intelligence 2nd Edition Nonverbal raw
[e]Kaufmann Brief Intelligence 2nd Edition Nonverbal SS

Table 5

Simultaneous multiple regression model statistics of multiple regression models predicting BRIEF[a] ratings using DCCS[f] correct border phase trials as predictor.

	General Executive Composite[a] (2)[b]			**Metacognition[a] (2)[b]**			**General Executive Composite[a] by NV SS[c] (2)[b]**		
	β	R^2chg	P chg	β	R^2chg	P chg	β	R^2chg	P chg
Age	0.84	.06	0.036(3,NS)[d]	0.30	.01	0.434	0.48	.02	0.235
KBIT-2 NV raw/SS[e]	0.09	<.01	0.579	0.30	.05	0.070	0.23	.02	0.196
Female	-6.65	.14	0.001	-5.09	.10	0.010	-0.47	.07	0.0237(2,†)[d]
DCCS Border[f]	-1.24	.11	0.004	-1.11	.10	0.008	-1.26	.12	0.004
	Inhibit[a] (3)[b]			**Shift[a] (5)[b]**			**Working Memory[a] (0)[b]**		
	β	R^2chg	P chg	β	R^2chg	P chg	β	R^2chg	P chg
Age	0.80	.03	0.154	1.33	.11	0.011(3,†)[d]	0.44	.01	0.418
KBIT-2 NV raw[e]	-0.40	.03	0.119	-0.22	.02	0.324	0.15	.01	0.515
Female	-3.81	.02	0.180	-4.82	.05	0.070(2,*)[d]	-1.51	<.01	0.572
DCCS Border[f]	-1.60	.10	0.008	-0.41	.01	0.458	-1.64	.12	0.005

[a]Behavior Rating Inventory of Executive Function

[b]Number of participants removed due to extreme studentized residuals (>|2|) and cook values (>4/N) for given model, if removal changed significance level of either entire model

[c]Multiple regression model controlling for the KBIT-2 Nonverbal Standard Score instead of KBIT-2 NV raw score

[d]If removal of additional coefficient specific participants with high standardized DFBETA values (2/sqrt(N)) caused change in significance level, significance level indicated (NS p>.1, †.10<p<.05, *p<.05), along with number of additional participants removed

[e]Kaufman Brief Intelligence Test 2nd edition Nonverbal raw score except in the model predicting GEC using the Standard Score instead (3rd model on top)

[f]Number of correct 12 Dimensional Change Card Sort Border trials

Table 6

Simultaneous multiple regression model statistics of multiple regression models predicting BRIEF[a] ratings using DCCS[f] number of phases passed as predictor.

	General Executive Composite[a] (2)[b]			**Metacognition[a] (2)[b]**			**General Executive Composite[a] by NV SS[c] (3)[b]**		
	β	R^2chg	P chg	β	R^2chg	P chg	β	R^2chg	P chg
Age	0.85	.05	0.034 (5,†)	0.22	0	0.548	0.88	.06	0.017(3, †)
KBIT-2 NV raw/SS[e]	0.04	<.01	0.822	0.25	0.03	0.103	<.01	<.01	>.99
Female	-6.11	.12	0.001	-4.61	0.09	0.006	-6.06	.12	0.001
DCCS Passes[f]		.05	0.110		0.05	0.100 (4,†)		.04	0.130
1-2 Phase	0.62		0.791	-0.78		0.713	0.77		0.746
1-3 Phase	-4.06		0.186	-5.01		0.075 (3,*)	-3.69		0.230

	Inhibit[a] (5)[b]			**Shift[a] (5)[b]**			**Working Memory[a] (0)[b]**		
	β	R^2chg	P chg	β	R^2chg	P chg	β	R^2chg	P chg
Age	0.83	.02	0.202	1.15	0.05	0.035	0.34	.01	0.513
KBIT-2 NV raw[e]	-0.15	<.01	0.595	-0.41	0.04	0.073	0.16	.01	0.455
Female	-4.81	.03	0.104	-6.63	0.09	0.008	-0.63	<.01	0.787
DCCS Passes[f]		.04	0.180 (4,**)		<.01	0.92		.10	0.020
1-2 Phase	1.95		0.613	1.22		0.705	-3.87		0.209
1-3 Phase	-4.61		0.360 (4, †)	1.57		0.706	-11.13		0.006

[a]Behavior Rating Inventory of Executive Function

[b]Number of participants removed due to extreme studentized residuals (>|2|) and cook values (>4/N) for given model, if removal changed significance level of either entire model

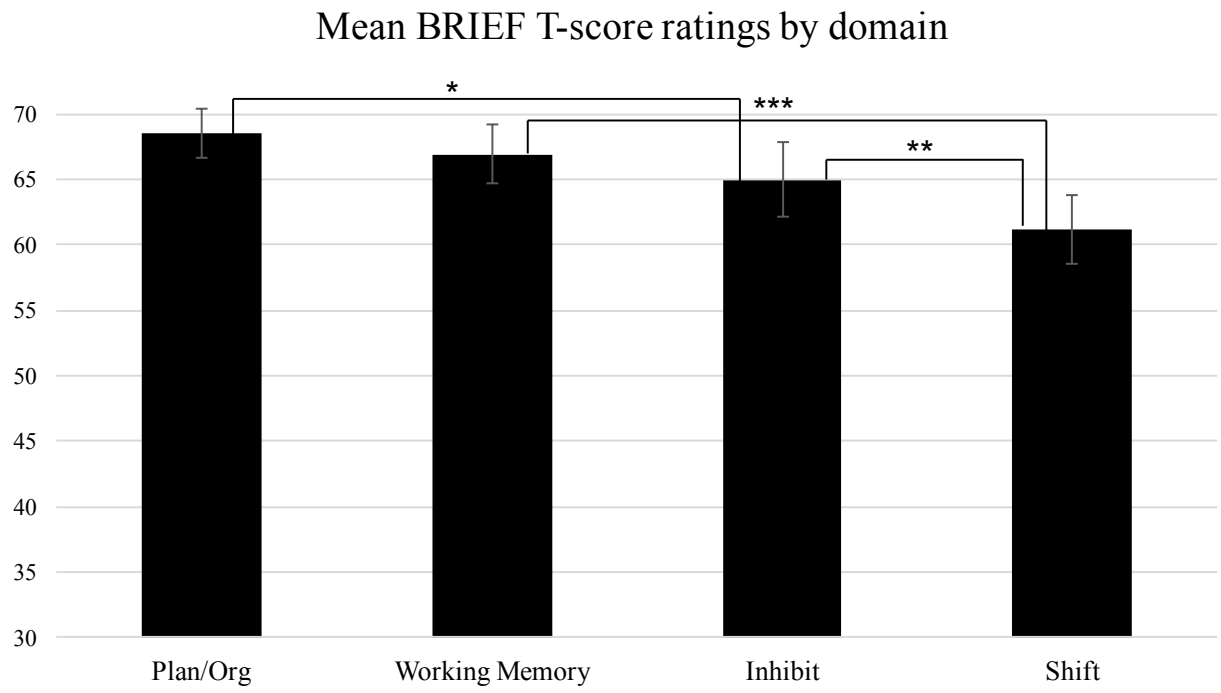
[c]Multiple regression model controlling for the KBIT-2 Nonverbal Standard Score instead of KBIT-2 NV raw score

[d]If removal of additional coefficient specific participants with high standardized DFBETA values (2/sqrt(N)) caused change in significance level, significance level indicated (NS p>.1, †.10<p<.05, *p<.05), along with number of additional participants removed

[e]Kaufman Brief Intelligence Test 2nd edition Nonverbal raw score except in the model predicting GEC using the Standard Score instead (3rd model on top)

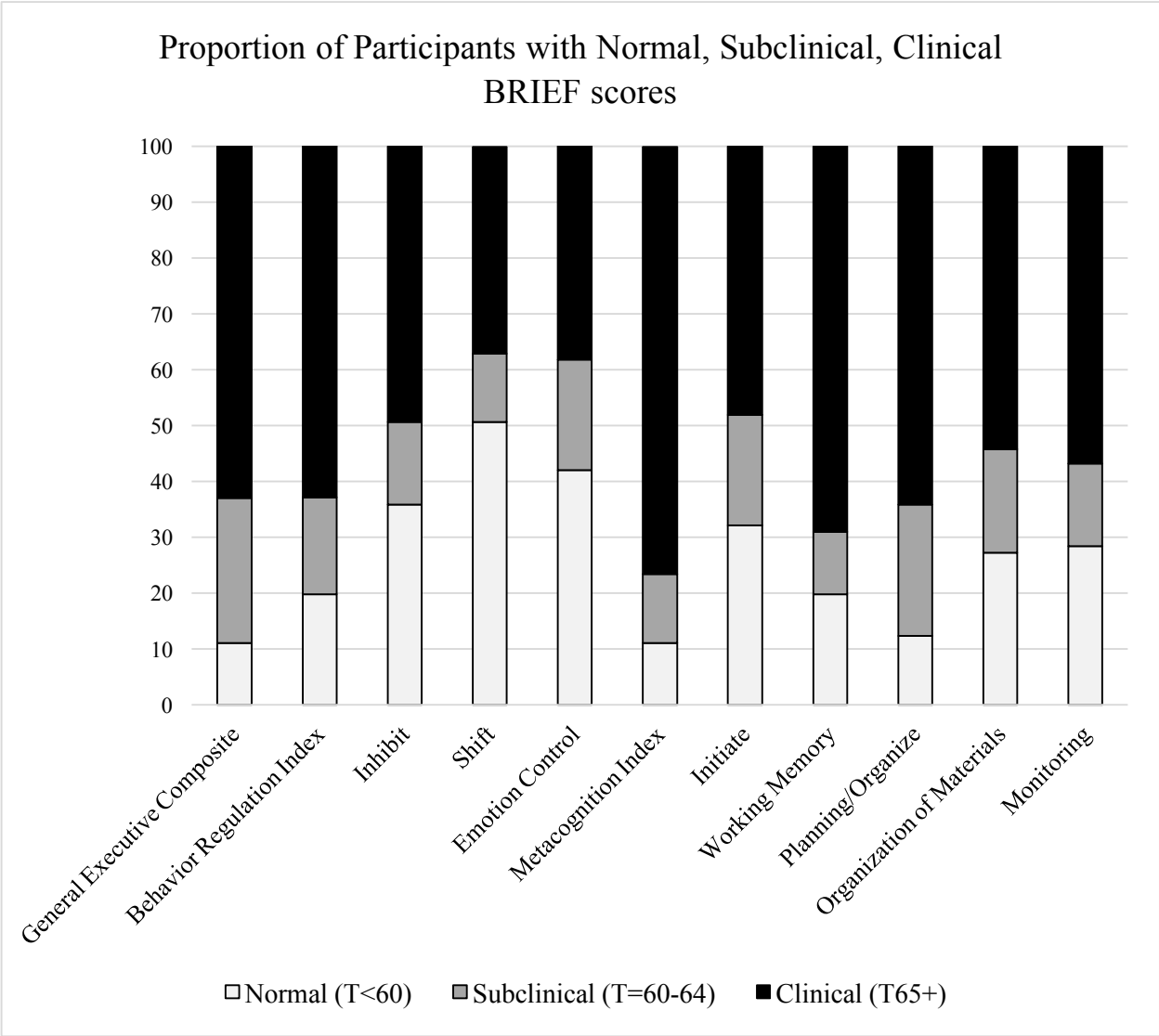
[f]Number of Dimensional Change Card Sort phases passed (1,2 or 3, all participants passed phase 1)

Figure 1



*p<.05, **p<.01, ***p<.001

Figure 2


Proportion of Participants with Normal, Subclinical, Clinical BRIEF scores
100
90
80
70
60
50
40
30
20
10
0
General Executive Composite
Behavior Regulation Index
Inhibit
Shift
Emotion Control
Metacognition Index
Initiate
Working Memory
Planning/Organize
Organization of Materials
Monitoring
Normal (T<60)
Subclinical (T=60-64)
Clinical (T65+)

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