American Journal on Intellectual and Developmental Disabilities

Parent- and teacher-reported executive functioning and behaviors in children with Down syndrome

--Manuscript Draft--

Manuscript Number:	AJIDD-D-20-00025R2
Article Type:	Research Report
Keywords:	Down syndrome; behavior; executive functioning; children
Corresponding Author:	Anna J Esbensen, PhD Cincinnati Children's Hospital Medical Center Cincinnati, OH UNITED STATES
First Author:	Anna J Esbensen, PhD
Order of Authors:	Anna J Esbensen, PhD
	Emily K Hoffman
	Rebecca C Shaffer
	Lina R Patel
	Lisa M Jacola
Manuscript Region of Origin:	UNITED STATES
Abstract:	The current study evaluates the concurrent relationship between parent ratings of executive functioning and maladaptive behavior among children and adolescents with Down syndrome and then repeats this evaluation using teacher reports. Parents and teachers of 63 school-age children with Down syndrome rated the child's executive functioning (Behavior Rating Inventory of Executive Function) and behaviors (Achenbach Child Behavior Checklist). For parent and teacher ratings, elevated behavior dysregulation predicted higher levels of rule-breaking, aggressive, and externalizing behavior. For teacher ratings, elevated behavior dysregulation also predicted higher levels of inattention problems. Among both parent and teacher ratings, greater metacognitive difficulties predicted challenges with attention. Understanding the relationship between these constructs has important implications for targets of intervention and developing preventative strategies.

Running head: EXECUTIVE FUNCTION AND BEHAVIOR IN DOWN SYNDROME

Relationship between parent- and teacher-reported executive functioning and maladaptive behaviors in children with Down syndrome

Abstract

The current study evaluates the concurrent relationship between parent ratings of executive functioning and maladaptive behavior among children and adolescents with Down syndrome and then repeats this evaluation using teacher reports. Parents and teachers of 63 school-age children with Down syndrome rated the child's executive functioning (Behavior Rating Inventory of Executive Function) and behaviors (Achenbach Child Behavior Checklist). For parent and teacher ratings, elevated behavior dysregulation predicted higher levels of rule-breaking, aggressive, and externalizing behavior. For teacher ratings, elevated behavior dysregulation also predicted higher levels of inattention problems. Among both parent and teacher ratings, greater metacognitive difficulties predicted challenges with attention. Understanding the relationship between these constructs has important implications for targets of intervention and developing preventative strategies.

Keywords: Down syndrome, behavior, executive functioning, children

Relationship between parent- and teacher-reported executive functioning and maladaptive behaviors in children with Down syndrome

Down syndrome is the most common chromosomal cause of intellectual disability, impacting 1 in 691 live births (Parker et al., 2010). It is now widely understood that Down syndrome not only predisposes individuals to a distinct phenotype across the lifespan, but also to a range of outcomes across many different domains of development, including social-emotional functioning, behavior and self-regulation, motor development, and language acquisition (Antonarakis et al., 2020; Silverman, 2007). Despite an expected behavioral phenotype, there is also great heterogeneity within individuals with Down syndrome. Although Down syndrome was identified over 150 years ago, there is still much to be learned in understanding this heterogeneity and the interrelationship between these different domains within the distinct Down syndrome phenotype (Down, 1887).

One domain that underlies heterogeneity in social-emotional functioning and self-regulation is executive functioning. Executive functioning includes higher order cognitive processes that are necessary for engaging in goal-directed behavior including sustained attention, behavior and emotional regulation, problem solving, organization, and planning (Goldstein & Naglieri, 2014). Individuals with Down syndrome exhibit challenges in multiple areas of executive function in comparison to their typically developing peers, including the ability to curb impulses, to shift flexibly between tasks, and to manipulate information with working memory (Camp, Karmiloff-Smith, Thomas, & Farran, 2016; Daunhauer et al., 2014; Daunhauer, Gerlach-McDonald, Will, & Fidler, 2017; Esbensen et al., 2019; Lee et al., 2011). These findings are present from infancy to adolescence in Down syndrome, and across performance measures and parent- and teacher-reports.

In individuals with Down syndrome, challenges with joint attention, which provides the foundation for higher order skill development, are evident during infancy. Infants with Down syndrome spend less time engaging in simultaneous appraisal of the environment and social interaction seeking than their typically developing peers, and respond less often to maternal prompts to shift attention between toys compared to infants matched for cognitive and motor development (Landry & Chapieski, 1989). This discrepancy in response pattern is not seen in the infants' responses to maternal prompts that did not involve shift of attention, such as encouragement to play with the same toy, demonstrating early difficulty for infants with Down syndrome with responses that require shifting of attention (Landry & Chapieski, 1989). Challenges with sustained attention continue to be present among toddlers and preschoolers with Down syndrome, evidenced by significantly shorter total duration of sustained attention, when compared to mental-age matched peers and children with Williams syndrome (Brown et al., 2003).

Studies of working memory, planning, sustained attention, and problem-solving demonstrate that children and adolescents with Down syndrome continue to have challenges with these areas of executive functioning in performance-based tasks. Children and adolescents with Down syndrome perform worse and demonstrate slower development of working memory than age-matched typically developing peers (Lanfranchi, Jerman, & Vianello, 2009; Vicari, Carlesimo, & Caltagirone, 1995). Poorer performance is also demonstrated on measures of set shifting, planning and problem solving, inhibition, perseveration, and sustained attention among adolescents with Down syndrome compared to typically developing children matched for mental age, yet stable in age-related performance (Camp et al., 2016; Lanfranchi, Jerman, Dal Pont, Alberti, & Vianello, 2010; Pennington, Moon, Edgin, Stedron, & Nadel, 2003). Conversely,

others demonstrate no significant differences on a composite score that reflected performance across a variety of executive function tasks (Pennington et al., 2003).

Parent-report measures of executive functioning corroborate these findings on performance-based tasks, and illustrate a pattern of declining skills in middle childhood, with recovery of skills in adulthood (Loveall, Conners, Tungate, Hahn, & Osso, 2017). Children with Down syndrome present with these areas of challenge of executive functioning on parent-report measures (Lee et al., 2011), as well as on teacher-report measures (Daunhauer et al., 2014; Lanfranchi et al., 2010; Memisevic & Sinanovic, 2014), with corroboration of areas of challenge including working memory and self-monitoring (Esbensen et al., 2019). Further, clinically significant rates of executive dysfunction are reported to be very common in children with Down syndrome, with over 40% of children reported to have concerns with executive functioning on parent-report and over 70% reported to have concerns on teacher-report (Esbensen et al., 2019). The converging evidence of challenges with executive functioning across infancy to adolescence in Down syndrome across performance-based tasks and informant-reports reflect the ecological validity of this deficit.

Another domain contributing to heterogeneity within individuals with Down syndrome is maladaptive behaviors. Maladaptive behaviors, including noncompliance, inattention, hyperactivity, and impulsivity, are commonly reported in 18-43% of children with Down syndrome (Capone, Goyal, Ares, & Lannigan, 2006; Cornish, Steele, Monteiro, Karmiloff-Smith, & Scerif, 2012; Corrice & Glidden, 2009; Dykens & Kasari, 1997; Dykens et al., 2015; Patel, Wolter-Warmerdam, Leifer, & Hickey, 2018; Visootsak & Sherman, 2007). The rates of maladaptive behavior in children with Down syndrome are higher than that reported in typically developing children, even after controlling for the developmental level of the child (Capone et

al., 2006; Coe et al., 1999; Cuskelly & Dadds, 1992; Foley et al., 2015; Gath & Gumley, 1986; Glenn & Cunningham, 2007; Nicham et al., 2003; Patel et al., 2018; Pitcairn & Wishart, 1994; Pueschel, Bernier, & Pezzullo, 1991; van Gameren-Oosterom et al., 2011). Between 6-8% of children with Down syndrome are diagnosed with ADHD, and 16-44% are reported to have difficulties with inattention (Dykens, Shah, Sagun, Beck, & King, 2002; Esbensen, 2018; Jacola, Hickey, Howe, Esbensen, & Shear, 2014). Between 10-15% of children are reported to have a diagnosis of oppositional defiant or conduct disorder, with 71% of children presenting to a specialty clinic, demonstrating concerns for aggression, and 77% for concerns with noncompliance or rule-breaking behaviors (Gath & Gumley, 1986; Patel et al., 2018). Preliminary findings in studies analyzing both children and adolescents with Down syndrome point to higher prevalence rates in males and a decline in externalizing behaviors during adolescence (Dykens et al., 2002; Maatta, Tervo-Maatta, Taanila, Kaski, & Iivanainen, 2006; Nicham et al., 2003; van Gameren-Oosterom et al., 2013). A recent review of a clinic sample of children with Down syndrome suggests that over 70% of children present with concerns of wandering (Patel et al., 2018).

To understand heterogeneity in executive functioning and maladaptive behavior with Down syndrome, there is a body of evidence to support an association between challenges with executive functioning and maladaptive behavior in children and adolescents in the general population. Executive functioning theoretically and conceptually underlies the child's ability to inhibit an aggressive response, identify the problem, goals, and potential solutions, evaluate potential solutions, make and try the best plan, and then to evaluate that plan (Shure & Spivack, 1982; Spivack & Shure, 1974). Thus, challenges with inhibitory control, shifting, planning, working memory, and task-monitoring are all areas of executive function that are theoretically

associated with elevated rates of inappropriate responses and maladaptive behaviors. Among typically developing children, areas of executive functioning are empirically demonstrated to impact behavior, maladjustment, social skills, daily living skills, relationships with teachers and peers, academic achievement, and academic engagement (Brock, Rimm-Kaufman, Nathanson, & Grimm, 2009; Eisenberg, Valiente, & Eggum, 2010; Riggs, Blair, & Greenberg, 2003). Challenges in inhibitory control are more common in inattentive and overactive children, and are associated with more delinquent behaviors (Gorenstein, Mammato, & Sandy, 1989; White et al., 1994). Challenges in inhibitory control and planning ability are both related to greater aggressive behaviors among typically developing boys (Ellis, Weiss, & Lochman, 2009). Among early-grade children, inhibitory control is predictive of more externalizing behaviors (Nigg, Quamma, Greenberg, & Kusche, 1999). Effortful control is also related to concurrent and future general externalizing behaviors in typically developing children (Lengua, 2003).

The relationship between executive function and behavior has also been studied in the broader population of individuals with intellectual disability and among adults with Down syndrome. Among adolescents with 22q deletion syndrome, there is evidence of a relationship between impairments in executive and maladaptive behavior (Rockers et al., 2009). Among adults with Down syndrome, there is evidence of an association between performance on tasks of executive function and behavioral and personality changes during adulthood, potentially related to the early onset of dementia (Adams & Oliver, 2010). Separate from maladaptive behavior, recent studies in adolescents with Down syndrome have demonstrated an association between parent and teacher ratings of executive function and adaptive behavior skills (Sabat, Arango, Tassé, & Tenorio, 2020). The direction of findings did not differ between rater groups; however,

differential relationships were found between core executive function skills and specific domains of adaptive skills.

While the relationship between executive functioning and maladaptive behavior has been extensively explored in typically developing children, the relationship between these constructs is not yet fully understood in children with Down syndrome. Understanding areas of deficit in executive functioning in children with Down syndrome and any inter-relatedness with inattention and maladaptive behaviors has important implications for understanding heterogeneity within individuals with Down syndrome, and for intervention development and management of these symptoms and behaviors. To best understand and generalize any relationship between executive functioning and maladaptive behavior, one must consider the environment and raters in study design. Considering the environment and different raters is especially important given that teachers tend to report higher rates of concern in both executive functioning and maladaptive behavior than parental reports (Esbensen et al., 2019; Esbensen et al., 2018). Given the greater challenges present in some areas of executive functioning among children with Down syndrome compared to typically developing peers, in addition to increased maladaptive behaviors, we focus on specific subdomains of executive functioning. Specifically, we target indices of behavioral regulation and metacognitive skills, and specific symptoms and behaviors. For behaviors, we focus on inattention and externalizing behaviors such as aggression and rule-breaking, given their elevated rates of concern in children with Down syndrome.

Current Study

This study aimed to evaluate the concurrent relationship between parent-reports of executive functioning and parent-reports of maladaptive behavior among children with Down syndrome. We further aimed to corroborate any concurrent relationship among parent-reports

with teacher-reports of executive functioning and teacher-reports of inattention and maladaptive behavior. To support evaluation of both aims, first we described the rates of parent- and teacher-reported challenges with executive functioning and maladaptive behavior present in school-age children with Down syndrome. Relatedly, we examined the inter-correlations between the constructs of executive functioning and maladaptive behavior, to better understand the constructs in a population with an intellectual disability. Second, we examined the relationship between constructs that comprise executive function (i.e., Behavior Regulation Index [BRI] and Metacognitive Index [MI]) and maladaptive behaviors using regression analyses separately for parents and teachers, controlling for the impact of age at assessment and cognitive ability. These initial regression analyses were conducted to help refine secondary subscale analyses. Third, based on significant findings of BRI and MI, we conducted secondary analyses to examine the relationship between specific subscales of the BRI or MI and maladaptive behaviors using regression analysis, again controlling for age and cognitive ability. We hypothesize that the relationship between impaired executive functioning and challenges with inattention and maladaptive behavior among children with Down syndrome will be replicated across both parent- and teacher-reports.

Method

Participants

As part of several larger community-based studies on behavior and cognition, rating forms were completed by parents and teachers of 63 children with Down syndrome. Demographics for children with Down syndrome are presented in Table 1. Respondents for caregiver forms were primarily mothers (96.8%).

Procedure

Inclusion criteria included the age of the child (ages 6-18 years) and a diagnosis of trisomy 21 Down syndrome. Families were recruited through a pediatric medical center, a Down syndrome specialty clinic, and through newsletters distributed by the local Down syndrome association. Children were recruited for multiple studies on cognitive and behavioral aspects of Down syndrome. Parents provided information on the child's demographics and completed rating scales of the child's executive functioning, maladaptive behaviors, and daily living skills while the child completed the KBIT-2. Teachers also completed rating scales of the child's executive functioning and maladaptive behaviors within 2 weeks of parents completing rating forms. All study activities were approved and overseen by the Institutional Review Board at the medical center and conform to recognized standards of the US Federal Policy for the Protection of Human Subjects.

Measures

Cognition and Adaptive Behavior. The KBIT-2 is a brief measure of cognitive ability appropriate for individuals aged 4-90 years and yields a full-scale standard IQ score (Kaufman, 2004). The Scales of Independent Behavior-Revised (SIB-R) rates children's adaptive daily living skills and yields a standard score in four domains (motor skills, social interaction/communication skills, personal living skills, and community living skills) and an overall Broad Independence score (Bruininks, Woodcock, Weatherman, & Hill, 1996). Both the KBIT-II and SIB-R are recommended for use in children with Down syndrome (Edgin et al., 2010).

Executive Functioning. The Behavior Rating Inventory of Executive Function (BRIEF 5-18) Parent Form is a rating scale of everyday skills measuring executive functioning completed by parents (Gioia, 2000). The companion BRIEF Teacher Form is completed by teachers. The

BRIEF Parent and Teacher Forms each include 86 items that provide omnibus indices of a Behavior Regulation Index (BRI) which includes subscales of Inhibit, Shift, and Emotional Control, and a Metacognitive Index (MI) which includes subscales of Initiate, Working Memory, Plan/Organize, Organizing Materials, and Monitoring. Items are rated on a 3-point Likert-type scale of (1) Never, (2) Sometimes, and (3) Often, based on problems demonstrated over the last six months. Scores are age and gender standardized, with a mean of 50 and a standard deviation of 10. Higher scores indicate more problems, with scores ≥ 1.5 standard deviations above the mean (t-score above 65) reflecting clinically significant elevations. The BRIEF Parent and Teacher Forms demonstrate excellent internal consistency, good interrater agreement, and good convergent validity with neuropsychological measures for some subscales when used with children with Down syndrome (Edgin et al., 2010; Esbensen et al., 2019).

Attention and Maladaptive Behavior. The Achenbach Child Behavior Checklist (CBCL) for children ages 6-18 years obtains parent ratings of 112 problem behaviors demonstrated by their child over the past six months, in addition to descriptions of their child's strengths and challenges (Achenbach & Rescorla, 2001). The Teacher Report Form (TRF) obtains similar ratings on problem behaviors from teachers. Both the CBCL and TRF provide T-scores for Internalizing Problems, Externalizing Problems, and a Total Problems score. In addition, eight subscales are also assessed on the CBCL, including Anxious/Depressed, Withdrawn/Depressed, Somatic Complaints, Social Problems, Thought Problems, Attention Problems, Rule-Breaking Behavior, and Aggressive Behavior. Scores are age and gender standardized, with a mean of 50 and a standard deviation of 10. Higher scores indicate more problems, with scores ≥ 1.5 standard deviations above the mean considered clinically significant. For the purposes of the current analyses and based on the areas of concern identified in the

research literature, we are restricting our analyses to the following subscales: Attention Problems, Externalizing Problems, and its two subscales of Rule Breaking Behavior and Aggressive Behavior. These subscales were selected as they best map onto clinical presentations that are concerning in Down syndrome, such as ADHD (Ekstein, Glick, Weill, Kay, & Berger, 2011), as well as to the pattern of behaviors related to executive functioning in typically developing children. Items are rated on a 3-point scale from (0) Not True to (2) Very True. Internal consistency and one-week test-retest reliability ranges from good to excellent for each of the domains with typically developing children (Achenbach & Rescorla, 2001). Internal consistency is moderate to high for all composite and syndrome scales with children with intellectual and developmental disabilities (Jacola et al., 2014). The CBCL subscales selected for analysis demonstrate fair to excellent internal consistency, good interrater agreement with teacher reports on the TRF, and good convergent validity with the Aberrant Behavior Checklist and Nisonger Child Behavior Rating Form when used with children with Down syndrome (Esbensen et al., 2018).

Data Analysis

Descriptive statistics and correlational analyses were completed for measures of executive functioning and maladaptive behavior, with missing items deleted listwise in all analyses. Hierarchical linear regressions were used to test whether parent-report indices of the BRIEF BRI and MI predicted parent-reports of maladaptive behavior. Separate regressions were run for parent-reported Attention Problems, Rule-Breaking Behavior, Aggressive Behavior, and Externalizing Behavior on the CBCL. Age and IQ (raw scores as standard scores are skewed) of the child were entered as covariates to control for any differences in the presence of challenges

with executive functioning, given past concerns for differences continuing to be present after normative data conversions (Esbensen et al., 2019).

These initial analyses were used to refine if specific subscales of the BRIEF should be examined in more detail in secondary analyses. If the parent-report BRI significantly predicted a parent-report behavioral outcome, then a subsequent hierarchical linear regression was run with the subscales that comprise the BRI (Inhibit, Shift, and Emotional Control) predicting the outcome measure on the CBCL. If the parent-report MI significantly predicted a parent-report behavioral outcome, then a subsequent hierarchical linear regression was run with the subscales that comprise the MI (Initiate, Working Memory, Plan/Organize, Organization of Materials, and Monitor) predicting the outcome measure on the CBCL.

To replicate any findings from parent-reports with teacher-reports, hierarchical linear regressions were again used to test whether teacher-report indices of the BRIEF BRI and MI predicted teacher-reports of maladaptive behavior from the TRF. Separate regressions were run for teacher-reported Attention Problems, Rule-Breaking Behavior, Aggressive Behavior, and Externalizing Behavior on the TRF. The same analysis structure that was described above for parent-reports was replicated with teacher-reports. The secondary analyses, with subscales that comprise the BRIEF Teacher Form BRI and MI, were based on the relationships between the teacher ratings on the BRIEF Teacher Form and TRF.

Possible increases in Type I error rates due to multiple analyses were addressed by using false discovery rate (FDR) controlling procedures (Benjamini & Hochberg, 1995). The FDR procedure provides a *q*-value, similar to a *p*-value but accounts for the number of analyses conducted in a family of analyses. The current study reports both *p*- and *q*-values and utilized the standard of $< .05$ for the minimum level at which an individual test may be called significant.

Q-values were calculated for each predictor, across the set of four regression equations. For example, comparing the p-values for BRI across the four regression equations predicting the outcomes of inattention, rule-breaking behaviors, aggression, and externalizing behaviors to obtain q-values.

Results

Descriptive data for measures of parent- and teacher-reports of executive functioning and behavior are presented in Table 2. Scores above the clinical cut-off for behavior regulation were reported by 28% of parents and 59% of teachers, whereas scores above the clinical cut-off for metacognition were reported by 33% of parents and 72% of teachers. More than a third of parents reported specific clinical concerns above the clinical cut-off with working memory, and monitoring. In contrast, more than a third of teachers reported concerns above the clinical cut-off for *all* areas of executive functioning. The most frequently rated areas of concerns above the clinical cut-off noted by teachers include working memory, initiation, and monitoring.

Common behavioral concerns above the clinical cut-off reported by parents on the CBCL were for Attention Problems (33%) and Aggressive Behavior (18%). A similarly high rate of concern above the clinical cut-off was noted by teachers for these behaviors (Attention Problems 27%; Aggressive Behavior 31%). In contrast, Rule-Breaking Behavior was noted to be above the clinical cut-off by only 3% of parents and 10% of teachers.

Inter-correlations between measures of parent-reports of executive functioning and behaviors are presented in Table 3, and inter-correlations between teacher-reports of executive functioning and behaviors are presented in Table 4. Despite a moderate bivariate correlation between individual subscales on the BRIEF (all p-values were > .05, correlation table not

presented), multivariate collinearity was found not to be a concern in subsequent regression analyses, with VIF < 4 and tolerance > .2.

Parent-reports of executive functioning predicting parent-reports of behavior problems

Table 5 summarizes results of regressions in which parent-report BRIEF BRI and MI were entered as predictors of parent-reported behaviors as measured by selected CBCL subscales (Attention Problems, Rule-Breaking Behavior, Aggressive Behavior, and Externalizing Problems). Neither age nor IQ were significantly related to any of the CBCL subscales in Step 1 after controlling for FDR. However, in Step 2 age was related to worse symptoms of externalizing behavior (β = -.20, p = .012, q = .048). Collectively, omnibus parent-report measures of executive functioning (BRI, MI) accounted for 37-67% of the variance in parent-reported behavior measures. Higher parent-reported BRI was related to higher reports on parent-report subscales of Rule-Breaking Behavior (β = .58, p < .001, q < .001), Aggressive Behavior (β = .75, p < .001, q < .001), and Externalizing Problems (β = .72, p < .001, q < .001), thus additional secondary analyses were conducted evaluating the effect of individual BRI subscales on these three CBCL subscales. Higher parent-reported MI was only related to higher parent-reported Attention Problems (β = .56, p < .001, q < .001), thus additional secondary analyses were conducted evaluating the effect of individual MI subscales on Attention Problems.

In secondary analyses, again neither age nor IQ were related to the outcome measures in Step 1. In Step 2, age was significantly related to worse symptoms of aggressive behavior (β = -.20, p = .010, q = .020), and externalizing problems (β = -.25, p = .002, q = .008). In Step 2 of these secondary analysis, the individual BRIEF subscales accounted for an additional 36-62% of the variance in predicting parent-reported Attention Problems, Rule-Breaking Behavior, Aggressive Behavior, and Externalizing Problems, after controlling for age and IQ. Higher

parent-reported concerns on the BRIEF Working Memory subscale were related to elevated parent-reported Attention Problems (β = .58, p < .001). Higher parent-reported concerns on the BRIEF Inhibit subscale were related to elevated parent-reported Aggressive Behavior (β = .26, p = .006, q = .009) and Externalizing Problems (β = .28, p = .002, q = .006). Higher parent-reported concerns on the BRIEF Shift subscale were related to elevated parent-reported Rule-Breaking Behavior (β = .45, p = .001, q = .003), Aggressive Behavior (β = .30, p = .003, q = .003), and Externalizing Problems (β = .32, p = .002, q = .003). Higher parent-report concerns on the BRIEF subscale of Emotional Control were related to elevated parent-reported Aggressive Behavior (β = .38, p < .001, q = .001), and Externalizing Problems (β = .34, p = .001, q = .001). The other parent-report BRIEF subscales (Initiate, Plan/Organize, Organization of Materials, and Monitor) did not contribute statistically significantly to the models or were not entered into the secondary models (see Table 5).

Teacher-reports of executive functioning predicting teacher-reports of behavior problems

Table 6 summarizes results of regressions in which teacher-report BRIEF BRI and MI were entered as predictors of teacher-reported daytime behaviors as measured by selected TRF subscales (Attention Problems, Rule-Breaking Behavior, Aggressive Behavior, and Externalizing Problems). Neither age nor IQ were significantly related to any of the TRF subscales in Step 1 after controlling for FDR. However, in Step 2 older age (β = -.28, p = .004, q = .016) and higher IQ scores (β = -.32, p = .001, q = .004) were related to worse symptoms of teacher-reported concerns for inattention. Collectively, omnibus teacher-report measures of executive functioning accounted for about one-third to half of the variance in teacher-reported behavior measures of Attention Problems, Rule-Breaking Behavior, Aggressive Behavior, and Externalizing Problems (R^2 change = .31-.53). Higher teacher-reported BRI was related to all selected TRF subscales,

including higher reports on teacher-reported Attention Problems (β = .34, p = .005, q = .005), Rule-Breaking Behavior (β = .48, p = .002, q = .002), Aggressive Behavior (β = .77, p < .001, q < .001), and Externalizing Problems (β = .66, p < .001, q < .001). Higher teacher-reported MI was only related to higher teacher-reported Attention Problems (β = .44, p = .001, q = .004). Thus, additional analyses were conducted evaluating the effect of individual BRI and MI subscales on Attention Problems, and of individual BRI subscales on Rule-Breaking Behavior, Aggressive Behavior, and Externalizing Problems.

In subsequent secondary analyses, neither age nor IQ were related to the TRF outcome measures in Step 1. However, in Step 2 older age (β = -.32, p = .003, q = .012) and higher IQ scores (β = -.27, p = .006, q = .024) were again related to worse symptoms of inattention. In Step 2 of these secondary analyses, the individual BRIEF subscales accounted for an additional 38-56% of the variance in predicting teacher-reported Attention Problems, Rule-Breaking Behavior, Aggressive Behavior, and Externalizing Problems. Higher teacher-reported concerns on the BRIEF Working Memory subscale were related to elevated parent-reported Attention Problems (β = .35, p = .016). Higher teacher-report concerns on the BRIEF Inhibit subscale were related to elevated teacher-reported Rule-Breaking Behavior (β = .58, p < .001, q < .001), Aggressive Behaviors (β = .31, p = .016, q = .021), and Externalizing Problems (β = .39, p = .006, q = .012). Despite teacher-report BRIEF subscale of Emotional Control being related to teacher-reported Aggressive Behavior (β = .35, p = .014, q = .056) and accounting for a significant portion of the variance, this beta-weight did not retain statistical significance when using FDR controls. The other teacher-report BRIEF subscales did not contribute statistically significantly to the secondary models.

Discussion

The current study examined the magnitude of concerns with executive functioning, inattention, and maladaptive behaviors in school-age children with Down syndrome, as measured by parent- or teacher-reports. The average level of difficulty with specific areas of executive functioning was consistent with previously published rates of difficulty when using the BRIEF parent-report (Esbensen, 2018; Lee, Pennington, & Keenan, 2010; Loveall et al., 2017) and teacher-report in children with Down syndrome recruited from the community (Esbensen, 2018; Memisevic & Sinanovic, 2014); yet slightly lower than rates reported in a sample recruited from a clinical setting (Esbensen et al., 2019). Further, the frequency of concerns with inattention and maladaptive behaviors were only slightly lower than previously reported rates of concerns when using the CBCL (Esbensen et al., 2018). Thus, the present findings corroborate the pattern of areas of challenge in executive functioning, inattention, and maladaptive behavior for children with Down syndrome. More areas of executive functioning above the clinical cut-off were reported by teachers than parents. Given that the academic environment (more frequent transitions, need to stay seated, more frequent task demands) places greater demands on executive functioning, it is not unusual that greater challenges with executive functioning were noted by teachers than by parents.

The current study further examined our hypothesis of a significant relationship being present between executive functioning and behavior problems among school-age children with Down syndrome, as measured by parent- or teacher-reports. Specifically, parent- and teacher-reports of behavioral dysregulation were related to parent- and teacher-reports of externalizing behavior problems (including rule-breaking and aggressive behaviors), and of teacher-reported concerns for inattention. Parent- and teacher-reported concerns with metacognition were also related to parent- and teacher-reports of concerns for inattention. The effect size of these

relationships were large, accounting for over a third to almost two-thirds of the variance in behavior problems (Cohen, 1988). Thus, the present findings among children with Down syndrome not only support the previous literature of a relationship between some areas of executive functioning with externalizing behaviors and inattention in the general population of children (Dennis, Brotman, Huang, & Gouley, 2007; Eisenberg et al., 2001; Lengua, 2003; Pritchard, Kalback, McCurdy, & Capone, 2015), but also demonstrate the substantial relationship between some areas of executive functioning and the comorbid presentation of specific challenging behaviors in children with Down syndrome. These findings suggest an opportunity to support executive functioning and to potentially have a cascading impact on specific behavioral challenges that affect daily functioning of children with Down syndrome both at home and at school.

Inhibitory control played a strong role in cross-sectionally predicting externalizing behavior problems at home and at school. Inhibitory control was related to rule-breaking behavior at school, and to aggression and the omnibus measure of externalizing behavior problems at both home and school. The ability to shift between tasks was related to rule-breaking behavior, aggression, and externalizing behaviors at home, but not at school. Emotional control was related to aggressive behavior, and externalizing behavior at home, yet did not retain statistical significance after applying FDR control to being related to aggressive behavior at school despite accounting for a large portion of the variance. Thus, treatment targets aimed at supporting the behavioral regulation of inhibitory, shifting, and emotional control may be helpful for children with Down syndrome identified as having behavioral concerns and challenges with behavioral regulation (Flook et al., 2010). For example, strategies such as mindfulness-based interventions teach children to bring their awareness to the present moment

and increase focus on their current experience. This strategy then slows the child down and helps with decision making, theoretically decreasing impulsivity and increasing emotional control. Research has demonstrated the strength of mindfulness strategies in general psychiatry (Kumar, Feldman, & Hayes, 2008; Vollestad, Nielsen, & Nielsen, 2012) and more recently in children with autism spectrum disorder or developmental disabilities (Flook et al., 2010; Shaffer et al., 2019) for reducing behavioral concerns. Thus, mindfulness programs or treatment targets aimed at teaching relaxation, strategies to self-calm, or to ask for a break when dysregulated, may be helpful for children with Down syndrome who struggle with impulsivity and challenges with emotional control. In addition, difficulties with sleep often lead to behavioral difficulties and decreased emotional and inhibitory control. If a child is struggling with sleep, interventions aimed at improving sleep are noted to improve executive functioning in the general population. Others have noted the link between sleep and executive functioning in children with Down syndrome (Cremone-Caira, Root, Harvey, McDermott, & Spencer, 2019). Addressing sleep concerns might be a way to rule out sleep impacting executive functioning.

Other components of executive function were not found to meet level of statistical significance for being related to behavioral concerns in the current analysis. Working memory, the ability to initiate tasks, and monitoring are common areas of difficulty in children with Down syndrome, impacting 38-56% of children based on parental report and 52-75% of children based on teacher report (Esbensen et al., 2019; Lanfranchi et al., 2010; Lanfranchi et al., 2009). Yet these aspects of executive functioning were not statistically related to externalizing behavioral concerns. Working memory was related to inattention in parental reports, but this finding was not supported in analyses with teacher reports. In contrast, initiating on tasks was related to inattention in teacher reports, but this finding was not supported in analyses with parent reports.

Monitoring was not predictive of any area of executive functioning in either parent or teacher reports. These non-significant findings suggest that treatments targeting executive functioning difficulties more broadly or targeting certain specific areas of challenge (working memory, initiation, monitoring), while helpful for other purposes such as academics or language and communication, may not necessarily have cascading impacts on behavioral concerns. Thus, there is a need to target those areas of executive functioning, such as inhibitory control, shifting, and emotional control, which are related to behavioral dysregulation.

The direction of effect cannot be understood from these cross-sectional analyses. For example, while difficulties with the ability to shift may contribute to the development of symptoms of oppositional behaviors, the reverse could also be true. Children with Down syndrome may be fixated on their schedules or hyper-focused on a task and thus be oppositional surrounding transitions. Similarly, oppositional behaviors may contribute to difficulties with following adult directed tasks, where oppositional behaviors interfere with the ability to attend to instructions or prompts, and thus also with the ability to shift between tasks. Thus, difficulties with shifting may appear to others as non-compliance or rule breaking. Longitudinal studies are necessary to evaluate the direction of effect between executive functioning and behavioral concerns in children with Down syndrome, and to evaluate which construct is best targeted in treatments and which contributes to downstream effects.

Older age was cross-sectionally related to teacher-reports of fewer concerns with inattention, and with parent-reports of fewer concerns with aggressive behaviors and omnibus externalizing behaviors. Although preliminary, these findings are intriguing as teacher-reports indicate trends of improvements in attention with older age, yet others have previously reported cross-sectional patterns of stability with attention (Dykens et al., 2002). Our finding of

improvement in aggression in older ages is consistent with prior findings of improvements in adolescents, yet potentially masks a peak of previously reported concerns with aggression and externalizing behavior among children ages 10-13 years with Down syndrome (Dykens et al., 2002). These current and past cross-sectional findings further demonstrate the need for longitudinal studies to evaluate the natural development of maladaptive behaviors to clarify these disparate cross-sectional findings.

Some limitations should be noted. The analysis plan was based on mono-method data, and direct assessment of executive functioning with the child was not available for all children. Large effect sizes could be argued to be due to item/construct overlap, such as between emotional control on the BRIEF and aggression on the CBCL/TRF. We conducted an item comparison between the two measures. Two items on CBCL/TRF aggressive behavior subscale (mood changes, tantrums) overlap with items on the BRIEF emotional control subscale, which may inflate effect sizes. Yet no items on CBCL/TRF rule-breaking overlap with items on the BRIEF. Although some items appear to overlap between BRIEF inhibit and working memory and CBCL/TRF attention problems, these item overlaps did not contribute to significant findings on analyses with teacher data evaluating the impact on inattention, or to significant findings between BRI/inhibitory control on inattention, thus minimizing potential concerns for item overlap impacting findings. Further, low intercorrelations between constructs (see Tables 3 and 4) and evidence of divergent validity between the BRIEF and CBCL further minimize concerns for item/construct overlap (Gioia, 2000). Despite these limitations, the current study has many strengths. The inclusion of both parent- and teacher-report measures, and of samples recruited from the community and in the clinic, ensured that data was collected across multiple environments and from children with clinical and non-clinical concerns, resulting in a more

representative sample. In addition, use of FDR to control for Type I error combined with the large magnitude of the effect size for the regression models, reflects the large contribution of executive functioning in predicting concurrent behavioral concerns.

Our study corroborates the previously reported rates of difficulties in executive functioning in children with Down syndrome, and findings from the general population regarding this link between some areas of executive functioning and specific behavioral concerns. Children with Down syndrome present with difficulties in many areas of executive functioning, which was demonstrated to be related to a large portion of the variance in explaining inattention and externalizing behaviors at home and school. Thus, when designing behavioral interventions, treatments targeting areas of executive functioning may be appropriate, or in need of evaluation among children with Down syndrome (Kirk, Gray, Ellis, Taffe, & Cornish, 2017). Future research is needed to understand the bidirectional relationship between these constructs.

References

Achenbach, T. M., & Rescorla, L. (2001). *ASEBA School-Age Forms & Profiles*: Aseba.

Adams, D., & Oliver, C. (2010). The relationship between acquired impairments of executive function and behaviour change in adults with Down syndrome. *Journal of Intellectual Disability Research, 54*(5), 393-405.

Antonarakis, S. E., Skotko, B. G., Rafii, M. S., Strydom, A., Pape, S. E., Bianchi, D. W., . . . Reeves, R. H. (2020). Down syndrome. *Nature Reviews Disease Primers, 6*(1), 1-20.

Benjamini, Y., & Hochberg, Y. (1995). Controlling the false discovery rate: a practical and powerful approach to multiple testing. *Journal of the Royal Statistical Society: Series B, 57*(1), 289-300.

Brock, L. L., Rimm-Kaufman, S. E., Nathanson, L., & Grimm, K. J. (2009). The contributions of 'hot'and 'cool'executive function to children's academic achievement, learning-related behaviors, and engagement in kindergarten. *Early Childhood Research Quarterly, 24*(3), 337-349.

Brown, J. H., Johnson, M. H., Paterson, S. J., Gilmore, R., Longhi, E., & Karmiloff-Smith, A. (2003). Spatial representation and attention in toddlers with Williams syndrome and Down syndrome. *Neuropsychologia, 41*(8), 1037-1046.

Bruininks, R. H., Woodcock, R., Weatherman, R., & Hill, B. (1996). *SIB-R: Scales of Independent Behavior-Revised*. Itasca, IL: Riverside.

Camp, J. S., Karmiloff-Smith, A., Thomas, M. S., & Farran, E. K. (2016). Cross-syndrome comparison of real-world executive functioning and problem solving using a new problem-solving questionnaire. *Research in developmental disabilities, 59*, 80-92.

Capone, G., Goyal, P., Ares, W., & Lannigan, E. (2006). Neurobehavioral disorders in children, adolescents, and young adults with Down syndrome. *American Journal of Medical Genetics Part C: Seminars in Medical Genetics, 142*(3), 158-172.

Coe, D. A., Matson, J. L., Russell, D. W., Slifer, K. J., Capone, G. T., Baglio, C., & Stallings, S. (1999). Behavior problems of children with Down syndrome and life events. *Journal of Autism and Developmental Disorders, 29*(2), 149-156.

Cohen, J. (1988). The effect size index: d. *Statistical power analysis for the behavioral sciences, 2*, 284-288.

Cornish, K., Steele, A., Monteiro, C. R. C., Karmiloff-Smith, A., & Scerif, G. (2012). Attention deficits predict phenotypic outcomes in syndrome-specific and domain-specific ways. *Frontiers in psychology, 3*, 227.

Corrice, A. M., & Glidden, L. M. (2009). The Down syndrome advantage: fact or fiction? *American journal on intellectual and developmental disabilities, 114*(4), 254-268.

Cremone-Caira, A., Root, H., Harvey, E. A., McDermott, J. M., & Spencer, R. M. (2019). Effects of Sleep Extension on Inhibitory Control in Children With ADHD: A Pilot Study. *Journal of Attention Disorders*.

Cuskelly, M., & Dadds, M. (1992). Behavioural problems in children with Down's syndrome and their siblings. *Journal of Child Psychology and Psychiatry, 33*, 749-761.

Daunhauer, L. A., Fidler, D. J., Hahn, L., Will, E., Lee, N. R., & Hepburn, S. (2014). Profiles of everyday executive functioning in young children with Down syndrome. *American journal on intellectual and developmental disabilities, 119*(4), 303-318.

Daunhauer, L. A., Gerlach-McDonald, B., Will, E., & Fidler, D. (2017). Performance and ratings based measures of executive function in school-aged children with Down syndrome. *Developmental Neuropsychology, 42*(6), 351-368.

Dennis, T. A., Brotman, L. M., Huang, K.-Y., & Gouley, K. K. (2007). Effortful control, social competence, and adjustment problems in children at risk for psychopathology. *Journal of Clinical Child and Adolescent Psychology, 36*(3), 442-454.

Down, J. L. (1887). *On Some of the Mental Affections of Childhood and Youth*. London: Churchill.

Dykens, E., & Kasari, C. (1997). Maladaptive behavior in children with Prader-Willi syndrome, Down syndrome, and nonspecific mental retardation. *American Journal on Mental Retardation, 102*(3), 228-237.

Dykens, E., Shah, B., Davis, B., Baker, C., Fife, T., & Fitzpatrick, J. (2015). Psychiatric disorders in adolescents and young adults with Down syndrome and other intellectual disabilities. *Journal of neurodevelopmental disorders, 7*(1), 1-8.

Dykens, E., Shah, B., Sagun, J., Beck, T., & King, B. (2002). Maladaptive behaviour in children and adolescents with Down's syndrome. *Journal of Intellectual Disability Research, 46*, 484-492.

Edgin, J. O., Mason, G. M., Allman, M. J., Capone, G. T., DeLeon, I., Maslen, C., . . . Nadel, L. (2010). Development and validation of the Arizona Cognitive Test Battery for Down syndrome. *Journal of neurodevelopmental disorders, 2*, 149-164.

Eisenberg, N., Cumberland, A., Spinrad, T. L., Fabes, R. A., Shepard, S. A., Reiser, M., . . . Guthrie, I. K. (2001). The relations of regulation and emotionality to children's externalizing and internalizing problem behavior. *Child development, 72*(4), 1112-1134.

Eisenberg, N., Valiente, C., & Eggum, N. D. (2010). Self-regulation and school readiness. *Early Education and Development, 21*(5), 681-698.

Ekstein, S., Glick, B., Weill, M., Kay, B., & Berger, I. (2011). Down syndrome and Attention-Deficit/Hyperactivity Disorder. *Journal of Child Neurology, 26*, 1290-1295.

Ellis, M. L., Weiss, B., & Lochman, J. E. (2009). Executive functions in children: Associations with aggressive behavior and appraisal processing. *Journal of abnormal child psychology, 37*(7), 945-956.

Esbensen, A. J. (2018). *Reliability of parent report measures in children with Down syndrome*. Paper presented at the World Down Syndrome Congress, Glasgow, Scotland.

Esbensen, A. J., Hoffman, E., Shaffer, R., Chen, E., Patel, L., & Jacola, L. M. (2019). Reliability of informant report measure of executive functioning in children with Down syndrome. *American Journal of Intellectual and Developmental Disabilities, 124*, 220-233.

Esbensen, A. J., Hoffman, E. K., Shaffer, R., Chen, E., Patel, L., & Jacola, L. (2018). Reliability of parent report measures of behaviour in children with Down syndrome. *Journal of Intellectual Disability Research, 62*(9), 785-797.

Flook, L., Smalley, S. L., Kitil, M. J., Galla, B. M., Kaiser-Greenland, S., Locke, J., . . . Kasari, C. (2010). Effects of mindful awareness practices on executive functions in elementary school children. *Journal of Applied School Psychology, 26*, 70-95.

Foley, K.-R., Bourke, J., Einfeld, S. L., Tonge, B. J., Jacoby, P., & Leonard, H. (2015). Patterns of depressive symptoms and social relating behaviors differ over time from other behavioral domains for young people with Down syndrome. *Medicine, 94*(19), e710. doi:10.1097/MD.0000000000000710

Gath, A., & Gumley, D. (1986). Behaviour problems in retarded children with special reference to Down's syndrome. *British Journal of Psychiatry, 149*(2), 156-161.

Gioia, G. A. (2000). *Behavior Rating Inventory of Executive Function: Professional Manual*. Odessa, FL: Psychological Assessment Resources, Incorporated.

Glenn, S. M., & Cunningham, C. (2007). Typical or pathological? Routinized and compulsive-like behaviors in children and young people with Down syndrome. *Intellectual and Developmental Disabilities, 45*(4), 246-256.

Goldstein, S., & Naglieri, J. A. (2014). *Handbook of Executive Functioning*. New York, NY: Springer Science+Business Media.

Gorenstein, E. E., Mammato, C. A., & Sandy, J. M. (1989). Performance of inattentive-overactive children on selected measures of prefrontal-type function. *Journal of clinical Psychology, 45*(4), 619-632.

Jacola, L. M., Hickey, F., Howe, S. R., Esbensen, A., & Shear, P. K. (2014). Behavior and adaptive functioning in adolescents with Down syndrome: Specifying targets for intervention. *Journal of Mental Health Research in Intellectual Disabilities, 7*(4), 287-305.

Kaufman, A. (2004). KBIT-2: Kaufman Brief Intelligence Test. Second Edition. In. Upper Saddle River, NJ: Pearson.

Kirk, H., Gray, K., Ellis, K., Taffe, J., & Cornish, K. (2017). Impact of attention training on academic achievement, executive functioning, and behavior: A randomized controlled trial. *American journal on intellectual and developmental disabilities, 122*(2), 97-117.

Kumar, S., Feldman, G., & Hayes, A. (2008). Changes in Mindfulness and Emotion Regulation in an Exposure-Based Cognitive Therapy for Depression. *Cognitive Therapy and Research, 32*(6), 734. doi:10.1007/s10608-008-9190-1

Landry, S. H., & Chapieski, M. L. (1989). Joint attention and infant toy exploration: Effects of Down syndrome and prematurity. *Child development, 60*(1), 103-118.

Lanfranchi, S., Jerman, O., Dal Pont, E., Alberti, A., & Vianello, R. (2010). Executive function in adolescents with Down Syndrome. *Journal of Intellectual Disability Research, 54*, 308-319.

Lanfranchi, S., Jerman, O., & Vianello, R. (2009). Working memory and cognitive skills in individuals with Down syndrome. *Child Neuropsychology, 15*(4), 397-416.

Lee, N. R., Fidler, D. J., Blakeley-Smith, A., Daunhauer, L., Robinson, C., & Hepburn, S. L. (2011). Caregiver report of executive functioning in a population-based sample of young children with Down syndrome. *American journal on intellectual and developmental disabilities, 116*(4), 290-304.

Lee, N. R., Pennington, B. F., & Keenan, J. M. (2010). Verbal short-term memory deficits in Down syndrome: Phonological, semantic, or both? *Journal of neurodevelopmental disorders, 2*(1), 9-25.

Lengua, L. J. (2003). Associations among emotionality, self-regulation, adjustment problems, and positive adjustment in middle childhood. *Journal of Applied Developmental Psychology, 24*(5), 595-618.

Loveall, S., Conners, F., Tungate, A., Hahn, L., & Osso, T. (2017). A cross-sectional analysis of executive function in Down syndrome from 2 to 35 years. *Journal of Intellectual Disability Research, 61*(9), 877-887.

Maatta, T., Tervo-Maatta, T., Taanila, A., Kaski, M., & Iivanainen, M. (2006). Mental health, behaviour and intellectual abilities of people with Down syndrome. *Downs Syndr Res Pract, 11*(1), 37-43.

Memisevic, H., & Sinanovic, O. (2014). Executive function in children with intellectual disability–the effects of sex, level and aetiology of intellectual disability. *Journal of Intellectual Disability Research, 58*(9), 830-837.

Nicham, R., Weitzdorfer, R., Hauser, E., Freidl, M., Schubert, M., Wurst, E., . . . Seidl, R. (2003). Spectrum of cognitive, behavioural and emotional problems in children and young adults with Down syndrome. *Journal of Neural Transmission Supplement, 67*, 173-191.

Nigg, J. T., Quamma, J. P., Greenberg, M. T., & Kusche, C. A. (1999). A two-year longitudinal study of neuropsychological and cognitive performance in relation to behavioral problems and competencies in elementary school children. *Journal of abnormal child psychology, 27*(1), 51-63.

Parker, S. E., Mai, C. T., Canfield, M. A., Richard, R., Wang, Y., Meyer, R. E., . . . Correa, A. (2010). Updated National Birth Prevalence estimates for selected birth defects in the United States, 2004-2006. *Birth Defects Research Part A: Clinical and Molecular Teratology, 88*, 1008-1016.

Patel, L., Wolter-Warmerdam, K., Leifer, N., & Hickey, F. (2018). Behavioral characteristics of individuals with Down syndrome. *Journal of Mental Health Research in Intellectual Disabilities, 11*(3), 221-246.

Pennington, B. F., Moon, J., Edgin, J., Stedron, J., & Nadel, L. (2003). The neuropsychology of Down syndrome: evidence for hippocampal dysfunction. *Child development, 74*(1), 75-93.

Pitcairn, T., & Wishart, J. G. (1994). Reactions of young children with Down's syndrome to an impossible task. *British Journal of Developmental Psychology, 12*(4), 485-489.

Pritchard, A., Kalback, S., McCurdy, M., & Capone, G. T. (2015). Executive functions among youth with Down Syndrome and co-existing neurobehavioural disorders. *Journal of Intellectual Disability Research, 59*(12), 1130-1141.

Pueschel, S. M., Bernier, J., & Pezzullo, J. (1991). Behavioural observations in children with Down's syndrome. *Journal of Intellectual Disability Research, 35*(6), 502-511.

Riggs, N. R., Blair, C. B., & Greenberg, M. T. (2003). Concurrent and 2-year longitudinal relations between executive function and the behavior of 1st and 2nd grade children. *Child Neuropsychology, 9*(4), 267-276.

Rockers, K., Ousley, O., Sutton, T., Schoenberg, E., Coleman, K., Walker, E., & Cubells, J. (2009). Performance on the Modified Card Sorting Test and its relation to psychopathology in adolescents and young adults with 22q11. 2 deletion syndrome. *Journal of Intellectual Disability Research, 53*(7), 665-676.

Sabat, C., Arango, P., Tassé, M. J., & Tenorio, M. (2020). Different abilities needed at home and school: The relation between executive function and adaptive behaviour in adolescents with Down syndrome. *Scientific Reports, 10*(1), 1-10.

Shaffer, R. C., Wink, L. K., Ruberg, J., Pittenger, A., Adams, R., Sorter, M., . . . Erickson, C. A. (2019). Emotion Regulation Intensive Outpatient Programming: Development, Feasibility, and Acceptability. *Journal of Autism and Developmental Disorders, 49*(2), 495-508.

Shure, M. B., & Spivack, G. (1982). Interpersonal problem-solving in young children: A cognitive approach to prevention. *American Journal of Community Psychology, 10*(3), 341-356.

Silverman, W. (2007). Down syndrome: Cognitive phenotype. *Mental retardation and developmental disabilities research reviews, 13*(3), 228-236.

Spivack, G., & Shure, M. B. (1974). *Social adjustment of young children: A cognitive approach to solving real-life problems*. San Francisco, CA: Jossey-Bass.

van Gameren-Oosterom, H. B., Fekkes, M., Buitendijk, S. E., Mohangoo, A. D., Bruil, J., & Van Wouwe, J. P. (2011). Development, problem behavior, and quality of life in a population based sample of eight-year-old children with Down syndrome. *PLoS One, 6*(7), e21879.

van Gameren-Oosterom, H. B., Fekkes, M., Van Wouwe, J. P., Detmar, S. B., Oudesluys-Murphy, A. M., & Verkerk, P. H. (2013). Problem behavior of individuals with Down syndrome in a nationwide cohort assessed in late adolescence. *Journal of Pediatrics, 163*(5), 1396-1401.

Vicari, S., Carlesimo, A., & Caltagirone, C. (1995). Short-term memory in persons with intellectual disabilities and Down's syndrome. *Journal of Intellectual Disability Research, 39*, 307-321.

Visootsak, J., & Sherman, S. (2007). Neuropsychiatric and behavioral aspects of trisomy 21. *Current psychiatry reports, 9*(2), 135-140.

Vollestad, J., Nielsen, M. B., & Nielsen, G. H. (2012). Mindfulness- and acceptance-based interventions for anxiety disorders: a systematic review and meta-analysis. *Br J Clin Psychol, 51*(3), 239-260. doi:10.1111/j.2044-8260.2011.02024.x

White, J. L., Moffitt, T. E., Caspi, A., Bartusch, D. J., Needles, D. J., & Stouthamer-Loeber, M. (1994). Measuring impulsivity and examining its relationship to delinquency. *Journal of Abnormal Psychology, 103*(2), 192-205.

Table 1.

Demographics of child participants (n=63).

	Mean (SD)	**Range**
Age (years)	11.63 (3.48)	6-18
KBIT-2	45.67 (8.36)	40-73
SIB-R	48.67 (20.62)	3-82

	Percentage
Gender (male)	61.9%
Race (Caucasian)	85.7%
Comorbid Mental Health Condition	
ADHD	22.2%
Anxiety	11.1%
Disruptive Behavior Disorder	11.1%
Depression	2.0%
Comorbid Medical Conditions	
Vision Problem	63.5%
Sleep Disorder	35.5%
Heart Defect	34.9%
Thyroid Problem	26.9%
Recurrent Otitis Media	25.4%
Gastro-Intestinal Concerns	23.8%
Low Birth Weight	22.2%
Hearing Problem	21.6%
Feeding Difficulties	12.7%
Recurrent Pneumonia	4.9%
Seizures	3.2%

Table 2.

Descriptive statistics for measures of executive functioning and behavior (n=63).

	Parent			Teacher		
	Mean (SD)	Range	Above clinical threshold	Mean (SD)	Range	Above clinical threshold
BRIEF						
Behavioral Regulatory Index	57.3 (10.4)	39-87	28%	69.0 (15.7)	43-112	59%
Inhibit	59.2 (11.9)	42-91	26%	69.3 (15.8)	44-112	57%
Shift	60.0 (11.3)	40-88	31%	67.8 (17.5)	43-126	52%
Emotional Control	51.0 (9.8)	36-77	8%	63.2 (14.8)	44-88	48%
Metacognition Index	60.8 (9.0)	39-86	33%	72.8 (13.9)	44-110	72%
Initiate	56.4 (7.8)	35-72	18%	71.8 (13.0)	41-101	67%
Working Memory	63.5 (9.8)	38-84	48%	74.7 (14.0)	50-111	72%
Plan/Organize	59.6 (11.7)	38-95	31%	66.2 (14.7)	40-101	46%
Organization of Materials	51.0 (9.3)	34-72	10%	65.6 (19.7)	42-129	43%
Monitor	63.5 (10.9)	34-72	51%	72.6 (14.0)	41-102	72%
CBCL/TRF						
Attention Problems	61.3 (7.9)	50-87	33%	60.5 (6.8)	50-83	27%
Rule-Breaking Behavior	55.2 (4.9)	50-66	3%	56.6 (5.9)	50-70	10%
Aggressive Behavior	56.5 (7.8)	50-82	18%	59.9 (6.1)	50-69	31%
Externalizing Behavior	53.3 (9.7)	34-74	16%	58.7 (7.4)	41-71	29%

All t-scores are age and gender standardized, with a mean of 50 and a standard distribution of 10. Higher scores indicate more concerns. Note: Clinical threshold for BRIEF and CBCL/TRF is T=65.

Table 3.
Correlations between parent-reports of BRIEF and CBCL subscales (n=61).

	Attention	Rule-Breaking	Aggressive	Externalizing
BRI	.50**	.58**	.80**	.80**
Inhibit	.44**	.41**	.61**	.62**
Shift	.46**	.57**	.67**	.67**
Emotional Control	.34**	.48**	.73**	.71**
MI	.68**	.41**	.57**	.58**
Initiate	.45**	.22	.38**	.37**
Working Memory	.72**	.24	.51*	.48**
Plan/Organize	.39**	.40**	.36*	.42**
Organization of Materials	.50**	.35**	.45**	.50**
Monitor	.46**	.30*	.42**	.42**

* $p < .05$, ** $p < .01$

Table 4.
Correlations between teacher-reports of BRIEF and TRF subscales (n=58).

	Attention	Rule-Breaking	Aggressive	Externalizing
BRI	.51**	.36**	.55**	.50**
Inhibit	.61**	.62**	.65**	.63**
Shift	.44*	.40**	.56**	.51**
Emotional Control	.58**	.48**	.68**	.58**
MI	.58**	.39**	.66**	39**
Initiate	.51**	.15	.25	.25
Working Memory	.57**	.23	.28*	.29*
Plan/Organize	.34**	.35**	.21	.26
Organization of Materials	.38**	.46**	.21	.29*
Monitor	.56**	.37**	.37**	.42*

* $p < .05$, ** $p < .01$

Table 5.
Predicting parent-report CBCL subscales from parent-report BRIEF subscales (n=61).

	Attention (β)	Rule-Breaking (β)	Aggressive (β)	Externalizing (β)
Step 1				
Age	-.25	-.17	-.24	-.28*
KBIT-2 raw score	-.05	.12	-.02	-.01
R^2 change	*.06*	*.05*	*.06*	*.08*
Step 2				
Age	-.13	-.12	-.16*	-.20$^{*, +}$
KBIT-2 raw score	-.08	.13	-.02	-.01
BRI	.17	.58$^{***, +++}$	.75$^{***, +++}$	.72$^{***, +++}$
MI	.56$^{***, +++}$	.05	.11	.13
R^2 change	*.44****	*.37****	*.67****	*.64****
R^2	*.50*	*.42*	*.72*	*.72*
Secondary Analysis				
Step 1				
Age	-.25	-.22	-.28*	-.32*
KBIT-2 raw score	-.05	.13	-.03	-.01
R^2 change	*.06*	*.08*	*.08*	*.10**
Step 2				
Age	-.12	-.18	-.20$^{**, +}$	-.25$^{**, ++}$
KBIT-2 raw score	-.10	.16	-.01	.01
Inhibit	-	.13	.26$^{**, ++}$	.28$^{**, ++}$
Shift	-	.45$^{***, ++}$	.30$^{**, ++}$	.32$^{**, ++}$
Emotional Control	-	.11	.38$^{***, +++}$	.34$^{***, +++}$
Initiate	-.09	-	-	-
Working Memory	.58***	-	-	-
Plan/Organize	.15	-	-	-
Organization of Materials	.15	-	-	-
Monitor	.11	-	-	-
R^2 change	*.53****	*.36****	*.62****	*.61****
R^2	*.60*	*.43*	*.70*	*.71*

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

Table 6.
Predicting teacher-report TRF subscales from teacher-report BRIEF subscales (n=58).

	Attention (β)	Rule-Breaking (β)	Aggressive (β)	Externalizing (β)
Step 1				
Age	-.17	-.12	-.15	-.13
KBIT-2 raw score	-.31*	.00	-.11	-.06
R^2 change	*.11**	*.02*	*.03*	*.02*
Step 2				
Age	-.28$^{**, +}$	-.15	-.13	-.13
KBIT-2 raw score	-.32$^{***, ++}$	.03	-.04	-.00
BRI	.34$^{**, ++}$	.48$^{**, ++}$	.77$^{***, +++}$	.66$^{***, +++}$
MI	.44$^{***, ++}$	.11	-.07	.01
R^2 change	*.48****	*.31****	*.53****	*.45***
R^2	*.59*	*.33*	*.56*	*.47*
Secondary Analysis				
Step 1				
Age	-.19	-.12	-.17	-.14
KBIT-2 raw score	-.31	.00	-.11	-.06
R^2 change	*.12**	*.01*	*.04*	*.02*
Step 2				
Age	-.32$^{**, +}$	-.08	-.17	-.13
KBIT-2 raw score	-.27$^{**, +}$	.06	-.06	-.01
Inhibit	.09	.58$^{***, +++}$	.31$^{*, +}$	.39$^{**, +}$
Shift	-.04	.12	.17	.13
Emotional Control	.33*	-.05	.35*	.23
Initiate	.35*	-	-	-
Working Memory	.11	-	-	-
Plan/Organize	-.10	-	-	-
Organization of Materials	.19	-	-	-
Monitor	.09	-	-	-
R^2 change	*.56****	*.38****	*.52****	*.45***
R^2	*.68*	*.40*	*.56*	*.47*

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

August 11, 2020

Subject: AJIDD-D-20-00025

Dear Dr Lecavalier,

Thank you for the review of our manuscript entitled "Relationship between parent- and teacher-reported executive functioning and maladaptive behaviors in children with Down syndrome." We very much appreciate the reviewers' helpful comments about our manuscript, and recommendations for reorganization, added literature, and clarification. We have revised the manuscript as requested. We have addressed the individual comments of the reviewers, as detailed below. We have made additions to the manuscript in green font.

Reviewer 1:

"I have only one main concern. The study aims at exploring the relationship between executive function and maladaptive behaviour both from parents and teachers point of view. However, while parents report were collected for 67 children, teacher reports were available only for 37 children. The groups are different and for this reason, we cannot be sure that similarities and differences are due to parents/teachers different point of view, but can be due to the fact that the groups are different. For this reason, it is not possible to make comparisons between parent and teacher assessment of the variables considered. Of course, the data of this study are still interesting, and I agree with the authors that it would be a shame not considering 30 children for teacher's unavailability. However, I would prefer to consider parents and teacher as two separate studies. One with the 67 children that considers only parents reports the second that compare the parents and teacher reports for the 37 children that have both (or, alternatively, study two can report only data on teacher reports). In any case I would like to see reported the descriptive statistics for both groups, both for demographics and for IQ. If the authors choose to focus study one on parents and study two on teachers, of course comparisons are not allowed and in this case the difference in numerosity between the two samples should be acknowledge as a limit.

- As we have continued to collect data, we now have more children available for analysis and have opted to re-run analyses on children for whom we have both parent and teacher reports. While we lose access to the over 100 parental reports available in our dataset, this updated dataset reduces the reviewer's concern by analyzing only children for whom we have both parent and teacher reports. This decision resulted in a new sample size of 63 children. The descriptive statistics are for the full sample of 63 children. We are pleased that this re-analysis had minimal impact on overall findings, and strengthened corroboration of findings with teacher reports.
- We have marked in green font throughout where changes to data were made, with the exception of the tables which have all been rerun.

"Minor point: why the regression analysis was run on 66 and 36 children instead of 67 and 37? Please explain."

- The reason for the difference was that regression equations were run with listwise deletion. Thus, if one item was missing on a measure, a subscale could not be calculated, and thus that child was omitted from the entire analysis.

- The impact of listwise deletion continues with our current sample of 63 children. Because of missing items on different subscale or indices, the sample size for the regression equations are reduced to 61 for parent reports and 58 for teacher reports.

Reviewer 2:

"I encourage the authors to consider including these recent articles in their discussion of how the current study's results fit within the literature, either in the literature review or discussion section:

- o Sabat et al., 2020, https://doi.org/10.1038/s41598-020-58409-5
- o Pritchard et al., 2018, https://doi.org/10.1111/jir.12217

- We have added the Sabat et al 2020 citation to the Introduction (page 7-8).
- We have added the Pritchard et al 2015 (the link was not to a 2018 manuscript) to the Discussion (page 19). We could not find a 2018 manuscript in a review of the literature.

"Pg.3, "It is now widely understood that Down syndrome not only predisposes individuals to a distinct phenotype across the lifespan, but also to a range of outcomes across many different domains…" should include some more updated references."

- We have added a more current citation to this sentence (page 3).

"The summary of executive function challenges documented across various assessment methods (performance-based, parent and teacher report) is appreciated. However, the message appears as if executive function is categorically impaired in individuals with DS. Can the authors include some (brief) discussion of relative strengths and weaknesses within executive function? This seems particularly relevant given the nature of your results."

- Given that the literature/studies have not compared strengths and weaknesses in different areas of executive functioning, we feel it would be premature to review relative strengths and weaknesses in executive functioning within DS.
- We have added to the Introduction some comment on areas of challenge that are commonly reported across parents and teachers.

"The literature review does not present a compelling rationale for the aims of the current study, nor are the aims clearly articulated. The introduction section could be tightened up to more clearly focus on the information most relevant to the current aims. It was difficult to connect the literature review to the study aims. Reading the first part of the paragraph spanning pg. 8-9, it seems that the focus will be on comparing executive function and specific maladaptive behaviors (which also follow logically from the literature review). Then on pg. 9, "We further aimed to corroborate any concurrent relationship among parent-reports with teacher-reports of executive functioning and teacher-reports of inattention and maladaptive behavior." This came as a surprise. As written, it is a bit difficult to find the study's aims in this section. There also seems to be a disconnect between the literature review and the second aim. Subheadings throughout (including a 'Current Study' section) could improve organization and help the authors more clearly set it up to justify the aims.

- We have made edits throughout the Introduction to tie the literature more clearly to our aims.
- We have added commentary on the importance of generalizing findings across settings to page 8, to support our aims to document a relationship between executive functioning and maladaptive behavior in both parent- and teacher-reported data.

- We have added a subheading to the Introduction of "Current Study" as requested.

"Minor consideration: The literature review is a bit disjointed. Using the present tense throughout (unless discussing a specific finding from a specific study) would increase readability. For example, the paragraph spanning pages 6-7 switches between present and past tense.

- We have corrected use of tense specifically on pages 6-7, but also throughout the manuscript.

"The last part on pg. 8 is the analytical plan. I would prefer to see this at the end of the methods or beginning of the results."

- To support organization, we included aims at the end of the Introduction. We feel a description of the research plan and hypotheses are needed here to guide the reader through the Methods. We have a detailed analysis plan in Data Analysis. To address reviewer concerns, we have been clearer with our hypotheses at the end of the Introduction (page 9).

"The current organization of the method section makes it difficult to follow. I believe most of the necessary information is there, but in its present form it is hard to determine whether this is the case."

- We have moved Participant information to a Table, made edits to the measures to better clarify indices and subscales of the BRIEF, and included information on the SIB-R.

"The description of participants (pg. 9) would be much easier to follow in a table."

- We have moved the description of participants to the new Table 1 (page 28).

"I'm struggling to follow the authors' reasoning for focusing on certain subscales of the CBCL. It says the decision was "based on the areas of concern identified in the research literature", but this was not clear in the literature review."

- The literature review on pages 4-6 emphasizes concerns for inattention, aggression, and non-compliance, which informed our selection of these subscales on the CBCL. We have broadened our use of non-compliance / rule-breaking behaviors on page 6, and removed the citation on page 8 that may have contributed to the confusion.

"Were assumption tests performed prior to data analysis? For example, I imagine that KBIT IQ scores may not have been normally distributed due to floor effects. To this end, did the authors consider using KBIT raw scores instead as a covariate (especially since age is also a covariate)?"

- The KBIT IQ data are positively skewed (skew 1.92), whereas the raw scores are not. We have replaced the KBIT IQ scores with raw scores as the covariate in the regression analyses (pages 13, 32-33). Please note that this change had minimal impact on our findings.

"Pg. 13, Could the authors clarify the meaning of "The analyses for each specific research question were used as the grouping for which the qvalues were calculated."?"

- We have revised the text regarding how FDR q-values were calculated to reflect that they were compared across each predictor in the four regression equations (page 14).

“In the regression tables, please define what the numerical values for each variable represent. Are they Beta values? If so, please remove them from the text.”

- The regression tables do include beta-weights. We have indicated this information in the headers of the tables (pages 32-33). To best provide exact p- and q-values, we would like to retain presentation of the beta-weights for the significant findings in the text.

“Please indicate the direction of effects (negative/positive). Also, interpretation of directionality is particularly challenging with measures that are counterintuitive (i.e., higher scores indicate more impairment), so please add a clarification somewhere. This is an example of where certain information gets lost in the method, so try to put it in a more central position or repeat in the results.”

- We have indicated the direction of effects throughout the Results (pages 15-17).

“Be cautious about mentioning "trends" with non-significant p-values, especially given the number of comparisons (e.g., top of pg. 17). This comes across as over-interpretation and I would recommend deleting it.”

- Thank you for catching this error. We have removed mention of all trends.

“Clarification question - Were the current study's findings across subdomains of executive function consistent with the literature? It's difficult to tell from the sentence on pg. 17 "The average level of difficulty with specific areas of executive functioning…" which seems to contradict itself.”

- We have clarified that the current rates are consistent with community samples, yet lower than rates reported in a clinical sample (page 18).

“The authors mention some particularly elevated (symptomatic) components of executive function that are NOT tied to maladaptive behaviors. While the point that interventions targeting these executive functions may not improve maladaptive behaviors is well taken, the authors should acknowledge that these are still areas of concern as reported by parents and teachers. It's quite possible that they affect other important areas of function like academics or language/communication.”

- We have broadened our “for other purposes” to more specifically mention the possible impact of these areas of executive functioning on academics or language and communication (page 21).

“The idea that the relation between executive function problems and maladaptive behaviors could be bidirectional is also well articulated in the discussion. Then, could it also be that targeting behaviors may be another potential route for interventions (rather than focusing solely on executive functions)?”

- We have added the need to evaluate where to target treatments, on executive functioning or on maladaptive behavior to the Discussion (page 21).