Infant Precursors of Executive Function in Down Syndrome

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Abstract

Background. Though early features of infant cognition are predictive of executive function (EF) in typically developing (TD) children, there is little information regarding the developmental origins of EF in neurogenetic conditions, such as Down syndrome (DS). *Methods.* The current study compared the performance of infants with and without DS on four dimensions that are hypothesized EF precursors: attention shifting, sustained attention, processing speed, and action planning. The relationship between these EF precursors at Time 1 and EF performance at Time 2 (6 months later) was also examined in the DS group. Participants were 58 infants with DS, *M* chronological age = 11.32 months, *SD* = 3.50; *M* developmental age = 7.93 months, *SD* = 2.79, and 40 TD infants, *M* chronological age = 8.14, *SD* = 3.25; *M* developmental age = 8.18 months, *SD* = 3.51. *Results.* Results showed that infants with DS shifted their attention more slowly, looked at objects for longer durations, and demonstrated a longer latency to contact objects when compared to TD infants at Time 1. Attention shifting at Time 1 significantly predicted EF performance at Time 2 in the DS group. *Conclusions.* This study provides evidence that an early atypical presentation of EF precursors is detectable during infancy in DS and is predictive of subsequent EF performance. These findings contribute to the identification of areas of early cognitive risk in DS and can inform future interventions in this population.

Infant Precursors of Executive Function in Down Syndrome

Background

Down syndrome (DS) is the most common chromosomal cause of intellectual disability and affects approximately 1 in every 691 live births in the United States per year (Parker et al., 2010). Individuals with DS are predisposed to a specific phenotypic profile that includes relative competencies in visual processing, receptive language, and nonverbal social functioning, and relative challenges in motor skills, expressive language, and auditory processing (Daunhauer & Fidler, 2011). In addition to general cognitive delays present throughout the lifespan in DS, there is growing evidence of specific challenges in the 'executive functions' (EFs) required for goal-directed behavior (Carney, Brown, Henry, 2013; Daunhauer et al., 2017; Lanfranchi, Jerman, Dal Pont, Alberti, & Vianello, 2010; Pennington et al., 2003; Rowe, Lavender, & Turk, 2006). At present, little is known about the developmental origins of EF challenges in DS. This study aims to advance our understanding of early disruptions in cognitive development, and specifically EF precursors, in DS to inform future targeted early intervention.

Executive Function

'Executive function' is a term that refers to the cognitive skills required to attend to and complete goal-directed behavior. Most EF models include (but are not limited to) the subdomains of working memory, inhibition, cognitive flexibility, and planning (Miyake, Friedman, Emerson, Witzki, & Howerter, 2000; Müller & Kerns, 2015). In children with DS, EF is predictive of adaptive outcomes and academic achievement, and in adulthood, aspects of EF predict employment status (Daunhauer et al., 2017; Daunhauer, Will, Schworer, & Fidler, 2020; Tomaszewski et al., 2018; Will, Fidler, Daunhauer, & Gerlach-McDonald, 2017). Because of the profound impact of EF on school performance and achievement, there is a need to better understand the precursors of EF in their earliest presentations so that initial disruptions in cognitive development can be identified, and potentially targeted via intervention.

Infant Precursors of EF in DS

Advances in early developmental science may serve as an important guide for research on the mechanisms underlying the emergence of EF challenges in DS. In recent work, researchers have identified hypothesized precursors of EF in typically developing (TD) children that can be measured during infancy, including sustained attention, attention shifting, and processing speed (Hendry, Jones, & Charman, 2016). Performance in each of these areas during infancy is predictive of later EF performance in TD school-aged children and adolescents (Garon, Smith, & Bryson, 2014; Kochanska, Murray, & Harlan, 2000; Rose, Feldman, & Jankowski, 2012; Rothbart, Sheese, Rueda, & Posner, 2011). These findings can serve as a guide for examining infant precursors of dysregulated EF in DS and may answer clinically important questions regarding the emergence of EF vulnerabilities in young children with DS.

Attention shifting. There is mounting evidence that attention regulation in the form of flexible engagement with a stimulus and subsequent disengagement is an important precursor to EF in TD infants (Hendry et al., 2016). By approximately 4 months, TD infants develop the ability to shift attention from one stimulus to another (Johnson, Posner, & Rothbart, 1991). Prior to 4 months, however, infants have more difficulty with disengaging from stimuli, and this lack of gaze shifting is referred to as "sticky fixation" (Atkinson, Hood, Wattam-Bell, & Braddick, 1992; Johnson et al., 1991; Kulke, Atkinson, Braddick, 2017). Faster disengagement during infancy when peripheral stimuli are presented is predictive of self-regulatory behavior (McConnell & Bryson, 2005) and shifting rates at 5 months predict EF performance at 3, 4, and 6 years of age in TD children (Blankenship et al., 2019). Attention shifting and concurrent overall cognitive skill acquisition are correlated in infants with DS, but a greater examination of the predictive power of this dimension has not yet been examined longitudinally (Fidler, Schworer, Will, Patel, & Daunhauer, 2019).

Sustained attention. As infants develop greater overall control of attention, the ability to focus attention and inhibit distraction, i.e. sustained attention, progresses rapidly and is thought to serve as a precursor for EF (Blankenship et al., 2019; Devine, Ribner, & Hughes, 2019; Hendry et al., 2016; Johansson et al., 2015; Kochanska et al., 2000). Sustained attention is often measured via infant directed attention toward objects during free play activities (Gaertner, Spinrad, & Eisenberg, 2008; Johansson et al., 2015; Kannass, Oakes, & Shaddy, 2006). Infant sustained attention at 4 and 5 months is associated with toddler self-regulatory behavior (Johansson et al., 2015; Kochanska et al., 2000) and is predictive of EF performance at 1, 3, 4, and 6 years of age (Blankenship et al., 2019; Devine et al., 2019). Infants and toddlers with DS focus attention for shorter periods and direct less attention to objects during play than developmentally equated TD infants and toddlers (Brown et al., 2003; Krakow & Kopp, 1982; Krakow & Kopp, 1983; Legerstee & Weintraub, 1997). Sustained attention difficulties during this early developmental period in DS may have important downstream implications, but there is no longitudinal work of this nature as yet.

Processing speed. Another hypothesized EF precursor, processing speed, refers to the time that it takes to encode and complete a cognitive task (Canfield et al., 1997). During infancy, processing speed can be measured through habituation tasks, which measure the amount of time that infants spend encoding an object (Colombo & Mitchell, 2009; Stoecker, Colombo, Frick & Ryther, 1998). Processing speed increases between 2 and 6 months in TD infants (Colombo & Mitchell, 2009), and faster processing speed at 5 months is associated with stronger EF performances at 2, 3, and 4 years in TD children (Cuevas & Bell, 2014). Previous research has demonstrated delays in the development of habituation in DS, with infants acquiring this skill at approximately 8 months (Lewis & Brooks-Gunn, 1984). Further information is needed to characterize the trajectory of early processing speed in infants with DS and the relationship between processing speed and EF in this population.

Action planning. The literature reviewed thus far highlights previously investigated infant precursors of later EF (i.e., attention regulation and processing speed). In addition to examining these EF precursors, it may be equally informative to identify and characterize the earliest forms of goal-directed behavior and planning in infancy. Foundational goal-directed actions can be measured in the form of early volitional acts on objects, and in particular, by examining infant reaching behavior (Bridgett et al., 2011; Elsner & Hommel, 2001). Active engagement with objects, including reaching, is important for developmental skill acquisition during infancy and has been linked to later achievement during childhood and adolescence (Bornstein et al., 2006; Bornstein et al., 2013). In TD infants, appropriate and efficient action planning at 14-18 months has also been connected to caregiver report of greater infant inhibitory control (Kaur, Detherage, & Needham, 2020). Infants with DS reach and grasp less frequently than TD infants matched on chronological age (de Campos et al., 2013) and toddlers with DS demonstrate challenges with planning during object retrieval tasks (Fidler et al., 2005). Taken together, these findings provide an initial look at the early challenges with goal-directed regulatory behavior in DS and warrant further investigation into potential connections to later EF skill.

Early Measurement of Executive Function

Early EF presentation in young TD children is commonly measured with the A-not-B task, which involves the early use of cognitive flexibility, inhibition, and working memory (Blankenship et al., 2019; Bernier, Carlson, Deschenes, & Matte-Gagne, 2012; Carlson, 2005; Diamond, 1985; Johansson et al., 2016; Kochanska et al., 2000; Miller & Marcovitch, 2015). The A-not-B task is a location search task that requires a child to shift the location of their search across trials. Infants with TD as young as 8 months begin to pass the A-not-B task without error (Diamond, 1985), but little is known regarding the norms for performance on this task in infants with DS. There is evidence that, by the preschool years, young children with DS perform comparably to developmentally-equated counterparts without DS (Roberts & Richmond, 2015). Additional research on predictors of early A-not-B performance in DS will provide information regarding the developmental origins of performance on this task, and possibly shed light on the potential sources of early within-group variability on the dimension of EF.

The Current Study

In this study, the hypothesized precursors of EF were examined in infants with DS and TD infants, with the goal of identifying early disruptions in cognition that may be linked to later, more pronounced executive dysfunction. Infants with DS and TD infants were compared on four EF precursors: attention shifting, sustained attention, processing speed, and action planning at Time 1. Next, the longitudinal associations between EF precursors at Time 1 and EF performance at Time 2 were assessed in the DS group. Findings from this study contribute to the growing scientific knowledge base regarding cognitive precursors of later EF skills and can facilitate the identification of cognitive risk and key targets for early intervention in young children with DS.

Methods

Participants

Participants were 58 infants with DS and 40 TD infants. At Time 1, participants in the DS group were 5-17 months old, *M* chronological age (CA) = 11.32 months, *SD* = 3.50, and the TD participants were 3-13 months old, *M* CA = 8.14, *SD* = 3.25. Groups were equated on cognitive status using the Bayley Scales for Infants and Toddler Development, Third Edition (BSID-III; Bayley, 2006), DS group mean developmental age (DA) = 7.93 months, *SD* = 2.79, and TD group mean DA = 8.18 months, *SD* = 3.51. One-way ANOVA results indicated that participants with DS were well equated to the TD group, F (1, 96) = .15, p = .70, $\eta 2 < .01$, and the sample had a variance ratio of .63 (Kover & Atwood 2013; Mervis & Klein-Tasman 2004). A variance ratio of less than one is expected, even in this equated sample, due to the commonly observed pattern of greater variance among children with DS compared to TD children (Karmiloff-Smith et al. 2016). The examination of the *p*-value, effect size, and variance ratio are all recommended for group matching in the field of intellectual and developmental disabilities research (Kover & Atwood 2013; Mervis & Klein-Tasman 2004). Both groups included an approximately equal number of male and female participants (see Table 1). Exclusion criteria included severe hearing loss, serious visual impairment, or concurrent treatment for acute otitis media. Documentation of trisomy 21 was provided by parent report in the group of infants with DS. See Table 1 for full participant demographics.

Time 2: 6-month follow-up. The majority of infants with DS also participated in a 6-month follow-up (n= 40). At Time 2, infants with DS were 11-24 months old, *M* CA = 17.26 months, *SD* = 3.55. The mean cognitive age of the participants with DS at Time 2 was 11.48 months, *SD* = 2.99. Prior to the 6-month follow-up, 23 infants participated in a brief (3-week) parent-mediated reaching intervention, and 14 of those 23 infants were assigned to the treatment condition. Participation in the reaching intervention was controlled for in all longitudinal analyses. Infants who participated in the 6-month follow-up did not significantly differ in performance at Time 1 from infants who did not participate in the second wave of data collection on relevant EF precursor measures (attention shifting t (54) = .83, p = .41; sustained attention t (49.5) = 1.13, p = .27; action planning t (52) = .43, p = .67). For the subset of infants with DS who did not participate in Time 2 (n = 16), eight infants were not re-contacted because of chronological age inclusion criteria in a broader study, five were lost due to attrition, three were not seen due to travel restrictions, one infant did not comply with administration of EF outcome task measured at Time 2, and one was not seen due to illness.

Procedure

There were two recruitment sites for this study. One site recruited all infants with DS and two sites recruited TD infants. Infants with DS were recruited through regional Down syndrome associations, clinics, and support groups in XX and XX regions of the United States and XX Canada. Some TD infants were recruited through campus resources and other local advertisements (n= 20). TD participants at the second site (n = 20) were recruited through birth records from a XX region of the United States and word of mouth.

The examiner obtained informed consent from the caregiver before completing the study tasks. Participants were seated on their caregiver's lap during the administration of each laboratory task and supported around their torso by the hands of their caregiver as necessary. Following the administration of the battery of EF precursor laboratory tasks, infants participated in a developmental assessment. Time for breaks was allotted to reduce any discomfort for infant participants. Data collection procedures for infants with DS participating in Time 2 was identical to procedures at Time 1.

Measures

Developmental abilities. The Bayley Scales of Infant and Toddler Development, Third Edition (BSID-III; Bayley, 2006) is a standard assessment used to measure cognitive, receptive language, expressive language, fine motor, and gross motor developmental domains in children ages 1-42 months. This measure has been standardized with a sample of 1,700 children in the United States and has high internal consistency (.86-.93) and test-retest reliability (.80-.87; (Bayley, 2006). The cognitive domain of the BSID-III was used to equate groups for cognitive developmental status.

EF precursors. Precursors of EF were assessed using four laboratory tasks. Coders were trained to achieve and maintain inter-rater reliability (Cohen's Kappa) for 30% of the sample for each task. All coders were naive to the study hypotheses and a kappa of .70 was set as the minimum criteria for reliability. Coders met with the project leader bi-weekly to address any discrepancies in reliability. All laboratory task stimuli are pictured in Figure 1.

Attention Shifting. This task was administered as per Mullen (1995) and is also described in *(withheld for review),* which reported data on a subsample of participants with DS included in the present study. A red ball and schematic face were held approximately 7-8 inches from the infant's eyes, with the red ball 4 inches to the left of the infant's midline and the schematic face 4 inches to the right of the infant's midline (Mullen, 1995). The examiner shook the red ball to attract the infant's attention. After the infant localized on the red ball, the examiner shook the schematic face. The examiner then alternated between the red ball and the schematic face, shaking each object several times (at least 2 trials on each side; Mullen, 1995). Both attention orienting (Colombo, 2001) and disengagement of attention (Elsabbagh et al., 2013) were captured in this task, which are shown to be valid measurements of attention shifting (Colombo, 2001; Hood & Atkinson, 1993; Kulke, Atkinson, & Braddick, 2017; Stifter & Braungart, 1995). The latency to shift attention was coded and averaged across trials. Average kappa statistics were high, indicating strong inter-rater agreement (Cohen's Kappa = .93; Landis & Koch 1977; Cohen, 1960). The distribution of this variable was found to be positively skewed and a log transformation was used to achieve a normal distribution of scores. Missing data on the attention shifting task was due to administration issues (DS n= 2; TD n= 4).

Sustained Attention. Focused attention was measured in the context of an infant exploration task, as per Needham et al. (2002). This measure is described in (*withheld for review*), which reported findings on a subset of participants with DS included in this study. A red teether with multiple textures was placed at the mid-line in front of the infant (Needham, et al., 2002). The examiner allowed for free exploration of the teether for approximately one minute. Total visual attention to the teether was coded. The amount of time that the infant had the teether in front of them was also calculated to control for trials that varied in time and provided a precise description of the percentage of the total time the infant was visually oriented to the teether during the task (Rose et al., 2012). Average kappa statistics were high indicating strong inter-rater agreement (Cohen's Kappa = .88; Landis & Koch 1977; Cohen, 1960).

Processing Speed. Processing speed was measured with a habituation task (as per Barten & Ronch, 1971; Colombo & Mitchell, 2009). One child-sized spoon was placed in front of the infant in a series of three 30-second trials. Between each trial, the experimenter placed the object underneath the table so that the infant would not know whether the object was the same one as in previous trials. Visual exploration for the first and third trials was coded and difference scores between trial 1 and trial 3 were calculated (Barten & Ronch, 1971). Reverse scoring was also used to allow for scores to be interpreted in the same direction as the other variables (all difference scores were subtracted from 100). Any difference score above 100 indicated that the infant did not habituate to the spoon (longer visual engagement on trial 3), and difference scores below 100 indicated the infant did habituate (longer visual engagement on trial 1). Average kappa statistics were high, reflecting strong inter-rater agreement (Cohen's Kappa = .85; Landis & Koch 1977; Cohen, 1960). Missing data on the processing speed task was due to examiner error (TD n= 3), infant refusal of the task (DS n = 1), or a change in task administration from beginning stages of the project (DS n= 8).

Action Planning. Infant action planning was measured with a reaching task (Barrett et al., 2008). Two balls, each with different properties (varying soft textures) were placed in front of the infant at midline, one at a time, throughout the task. The experimenter presented each ball for free exploration and retrieved the ball after 30 seconds elapsed. The latency to contact each ball was coded and averaged. Average kappa statistics were high, indicating strong inter-rater agreement (Cohen's Kappa = .98; Landis & Koch 1977; Cohen, 1960). The distribution for this variable was found to be positively skewed and was subsequently recoded to achieve a normal distribution of scores. Six categories were generated, ranging from 1 (infants who made contact most quickly) to 6 (infants who made contact the slowest). A latency of 0-.60 s was coded 1, .61-.75 s was coded 2, .76-1.5 s was coded 3, 1.51-3.0 s was coded 4, 3.1-10.0 s was coded 5, and 10.1-30.0 s was coded 6. The scale also included the value 7 for infants who did not make contact with either ball. Missing data on the action planning task was due to examiner errors (DS n= 4; TD n= 1). There were also two infants in the DS group and two infants in the TD group that had missing latencies on the action planning task because they did not make contact with the object.

Early EF performance. EF performance at Time 2 was measured by the A-not-B task (Diamond, 1985). The examiner placed two cloths, side by side (location A and location B), and just out of reach in front of the infant. The examiner then shook a colorful rattle to gain the infant's attention and placed it under location A. The examiner then pushed both cloths toward the infant and encouraged the infant to "find the toy." After the infant pulled either one or both cloths, the trial was repeated twice more, hiding the colorful rattle in location A. On the fourth trial, the location of the toy was switched to location B.

Infant responses on the fourth trial were coded and there were four categories of responses: only location B; both locations, correct; both locations, incorrect; and only location A. First, "only location B" was coded if the infant manually pulled only the location B cloth. There were also instances where the infant pulled both cloths. These observations were separated into a "both locations, correct" category when the infant pulled location B at least 1 second before pulling location A, or a "both locations, incorrect" category when the infant pulled the location A cloth first. If the infant pulled both cloths at the same time, "both locations, incorrect" was coded. The final category of infant response was "only location A," which was coded if the infant manually pulled only the location A cloth. Correct responses included "only location B" and "both locations, correct". Although "only location B" was the more advanced and regulated response, the "both locations, correct" category was considered correct because infants demonstrated emerging self-regulatory skills by pulling the location B cloth first and locating the toy prior to pulling the location A cloth. Incorrect responses included "both locations, incorrect," "only location A," and the absence of a manual search. Coders were naïve to the hypotheses for the study and demonstrated reliable inter-rater agreement (Cohen's Kappa = .88; Landis & Koch 1977; Cohen, 1960) for 30% of the sample.

Analysis Plan

Hypothesis 1. This study aimed to characterize the performance on EF precursor tasks (attention shifting, sustained attention, processing speed, and action planning) in infants with DS and TD infants equated by group on cognitive level at Time 1. Although there is limited empirical work examining these specific dimensions in infants with DS, based on reported EF deficits in older children with DS (Daunhauer et al., 2017; Lee et al., 2011), we hypothesized that all of these EF precursors would be impaired relative to the equated TD group. Specifically, we posited that infants with DS would display slower attentional shifting, shorter durations of sustained attention, slower processing speed, and challenges with action planning. Group differences were analyzed using *t*-tests for normally distributed outcomes and Mann-Whitney U tests for non-normally distributed outcomes. A chi-squared test was also used to compare the percentage of infants who habituated during the processing speed task by group.

Hypothesis 2. The second goal of this study was to examine the longitudinal relationship between proposed EF precursors and subsequent EF performance in DS. It was hypothesized that infant EF precursors would be significant predictors of early EF at Time 2 in young children with DS. Early cognitive and attention skills in TD infants have been connected to EF outcomes in early childhood and adolescence (Cuevas & Bell, 2014; Johansson et al., 2015; Rose et al., 2012) and therefore, we expected to observe a similar pattern of association in DS. Binary-logistic regression analysis was used to test the relationship between EF precursors and early EF outcomes at Time 2.

Results

Research Question 1: Group Differences in EF Precursors

Group comparisons. Systematic performance differences were observed on EF precursor tasks when comparing the DS and TD groups. Infants with DS looked for longer amounts of time during the sustained attention task, t (96) = 3.91, $p < .01$, $d = .80$ (DS group M = 57.96% time looking, SD = 20.61; TD group M = 41.17% time looking, SD = 21.25) and infants with DS shifted their attention more slowly than TD infants, U = 669.5, $p < .01$ (DS group M = 2.89 seconds, SD = 2.09; TD group M = 1.80 seconds, SD = 1.17). Analyses using the transformed attention shifting variable (log transformation described in methods) also yielded group differences, t (90) = 2.90, $p < .01$, $d = .62$. Similar between-group differences were observed on the action planning task, U = 664.0, $p = .01$. Infants with DS demonstrated longer average latencies to contact the objects, M = 4.42 seconds, SD = 6.11, when compared to the TD infants, M = 3.25 seconds, SD = 4.44. The transformed, categorical action planning variable (transformation described in methods) demonstrated the same pattern of group differences, t (63.9) = 2.23, $p = .03$, $d = .48$.

In contrast to the other three measures, there were no significant between-group differences for the processing speed task, t (84) = .54, $p = .59$, $d = .11$. Based on scores from the processing speed measure, performance was categorized into two groups: infants who habituated (scores below 100) and infants who did not habituate (scores above 100). There were no significant group differences in the percentage of infants who habituated during the task, χ_2 (1, 86) = .524, $p = .47$. Fifty-nine percent of the infants in the DS group habituated and 51% of the infants in the TD group habituated. See Table 2 for full descriptive statistics on EF precursor measures. Because no group differences were identified, the processing speed task was subsequently excluded in further longitudinal analyses. Uncertainty related to the accuracy of capturing habituation using this measure contributed to its exclusion from subsequent analyses as well, which is expanded upon further in the Discussion.

Research Question 2: Relationship Between EF Precursors and Early EF Skills in DS

A subset of the sample of infants with DS (n=40) completed a 6-month follow-up assessment, during which the A-not-B task was administered. Of the 40 infants who participated in the Time 2 visit, 50% produced correct A-not-B responses, with half manually searching exclusively in location B and the other half manually searching in location B, followed by searching in location A ("both locations, correct").

To assess the relationship between EF precursors and early EF skills, a binary logistic regression was completed to examine whether group classification of success on the A-not-B task could be predicted by the EF precursor variables (attention shifting, sustained attention, and action planning), controlling for cognitive ability at Time 2 and intervention condition when appropriate. Results of the binary logistic regression indicated that there was a significant association between the independent variables and post switch A-not-B performance, $\chi_2(5)$ = 11.42, p = .04, Nagelkerke R Square = .33, -2 Log likelihood = 44.04. Attention shifting was a significant predictor in the model such that for each unit increase in latency to shift attention (slower attention shifting), infants were 98% less likely to complete the A-not-B task successfully, Wald (1) = 5.46, SE = 1.62, p = .02, Exp (B) = .02, 95% CI : .001- .54. No other variables included in the model were significant predictors of A-not-B performance.

Discussion

This study examined the developmental origins of EF abilities in infants with DS. EF precursors, including attention shifting, sustained attention, processing speed, and action planning, were evaluated in infants with DS and a TD comparison group at Time 1. There were observable group differences in EF precursors, suggesting that specific cognitive delays related to the underpinnings of EF skills are detectable in DS. In the group of infants with DS, longitudinal associations between EF precursors and performance on an early EF task at Time 2 were also characterized. Attention shifting was found to be a significant predictor of early EF performance in the DS group, such that slower shifting of visual attention at Time 1 was associated with less successful manual shifting on the A-not-B task at Time 2. Findings from this study add to the growing literature on early cognition in infants with DS and provide an important first step toward identifying early neuropsychological risk in this population.

EF Precursors and Early EF Skills in DS

The most notable finding from this study was the significant relationship between EF precursors in infants with DS and subsequent EF performance six months later. Average latency to shift attention was predictive of the shifting required for successful performance on the A-not-B task. This association may be evidence of construct continuity, wherein emerging EF is first captured through infant visual attention flexibility and then develops into flexibility of manual search behavior on the A-not-B task. However, there are alternative explanations for the finding as well. For example, it may be that both performances were contingent on the ability to take in perceptual information about multiple spatial locations. Thus, the early ability to attend to the two spatial locations in the infant shifting task may serve as a foundation for a later, more sophisticated ability to represent the two potential locations of the toy in the A-not-B task. Additional examination of this longitudinal relationship may help to further clarify the early nature of these associations.

Attention regulation replication. Another main finding of this study is that patterns of associations previously reported in TD samples were replicated in infants with DS. Cognition and attention in TD infants have been linked to later EF performance during early childhood and adolescence in numerous studies (Cuevas & Bell, 2014; Rose et al., 2012; Rose, Feldman, & Jankowski, 2016; Rothbart et al., 2011). The replication of this association in infants with DS provides evidence that the cognitive systems responsible for early EF skills function similarly in infants with TD and DS, despite the delayed cognitive skill acquisition observed in DS.

Although this is the first study to report longitudinal connections between infant attention shifting and early EF in DS, it is not the first to identify attention regulation as an important developmental skill in this population. A previous study comprised of a subsample of participants in the present study reported a significant relationship between attention shifting and overall cognitive skill acquisition in infants with DS (*citation withheld for review*). The current study extends these findings and reports longitudinal associations between early attention shifting skills and later cognitive flexibility, inhibition, and working memory skills. Taken together, findings from these two studies suggest that infant attention shifting may have significant implications for cognitive development in DS. Efforts should be made to replicate the results with a different sample of infants to verify the reported relationship.

Group Differences

In addition to the reported longitudinal findings, this study also compared infants with DS and TD infants on EF precursor performances at Time 1. A key finding from this comparison was the contrast in early cognitive skills across the two groups. Even after equating groups on overall cognitive level, the infants with DS, on average, demonstrated poorer than anticipated performances in attention shifting, action planning, and sustained attention. Infants with DS demonstrated slower attention shifting latencies when compared to TD infants, which reflects early differences in the development of the attentional system in DS. Although the mean group difference in attention shifting latency was approximately one second, this difference is clinically meaningful and likely to impact infants with DS in a variety of contexts.

Similarly, action planning latencies were slower in the group of infants with DS than the TD comparison group. One straightforward interpretation of these results is that motor delays in infants with DS (de Campos, Rocha, & Savelsbergh, 2010) generate slower latencies. However, due to the combined visual appraisal and motor output required for this action planning task, it may be the case that in addition to motor delays, infants with DS take longer to mentally represent the goal of reaching for the object compared to TD infants. Early delays in action planning could contribute to more pronounced gaps in later planning and EF challenges in DS beyond infancy.

Additionally, infants with DS showed longer sustained attention than TD infants, which may be attributed to the changing nature of attention in infancy. It was hypothesized that infants with DS would sustain attention for shorter durations, so the observed longer durations of looking were unexpected. However, during the first 3 to 6 months of typical development, longer looking time is thought to indicate a lack of attention disengagement skills and slower processing speed (Atkinson et al., 1992; Colombo & Mitchell, 2009; Kulke et al., 2017). With this interpretation, infants with DS may have demonstrated *poorer* attention regulation and processing speed due to the deficits in disengagement of attention and extended time needed to encode the object, which signals that infants with DS experience early disruptions in the development of attention regulation skills.

Intervention Implications for Supporting Early EF

The cross-sectional and longitudinal findings reported in this study have important translational relevance. Identifying early vulnerabilities in EF precursors may facilitate the use of targeted interventions to strengthen these early foundations (Daunhauer et al., 2017). In particular, the link between early attention shifting and later EF performance could be considered part of a potential mechanism to improve intervention in infants with DS. Attention regulation training has been implemented in TD infants as young as 11-months (Wass, Porayska-Pomsta, & Johnson, 2011), and may be feasible for infants with DS. Similarly, action planning interventions that facilitate reaching have been empirically supported for prereaching TD infants (Needham et al. 2002). Investigating whether facilitated reaching activities may benefit EF and cognitive development over time could be informative for early intervention in DS as well.

Limitations

The present study has several limitations that should be considered when interpreting the results. One limitation of the study is that each infant EF precursor construct was assessed with only one laboratory measure. The use of only one measure per construct makes the study more vulnerable to measurements that do not have adequate construct validity. Additionally, for the TD sample, data were collected exclusively at one time point, which restricts the comparisons that can be made between groups longitudinally. Another consideration is that the sample size was modest, which restricted the generalizability of the findings and increases the risk for type II error. Mean CA in the group of infants with DS was also 3.5 months older than the TD comparison group mean.

There are methodological limitations worth noting as well. First, the sustained attention variable was measured solely using eye gaze rather than examining biomarkers, such as heart rate variability. Additionally, the processing speed variable was collected on a fixed time scale (three set trials of 30-seconds) rather than in contingency with infant behavior. This means that rather than calculating a rate of habituation, the differences in visual interest over the 90-second period were captured by comparing the total exploration time between the first and third trials. This may have been problematic because infants may have habituated within the first 30-second trial, which would make the observations on the third trial inconsequential, and subsequent difference scores difficult to interpret. Because of these interpretation issues, the processing speed measure was removed from further analyses.

Future Directions

This study provides important novel information regarding the atypical presentation of EF precursors that are predictive of subsequent EF performance in infants with DS. Future research should explore the association between infant performance and longer-term cognitive outcomes to identify areas of early cognitive risk. Previous studies on TD children follow participants from infancy to age 3 or 4, and some studies even into adolescence (Cuevas & Bell, 2014; Rose et al., 2012; Rose et al., 2016; Rothbart et al., 2011). Therefore, longer-term follow-up assessments are warranted to improve our understanding of how cognitive foundations cascade onto EF skills in early childhood or identify risk for potential comorbidities.

Many intraindividual and environmental variables are also likely related to the early development of EF in young children with DS outside of early cognitive skills. One variable that should be considered in future work is maternal responsiveness, which has been found to be related to the development of EF in young TD children (Bernier, Carlson, & Whipple, 2010; Mahoney & Nam, 2011). A broader look at access to intervention is another area that warrants further examination related to early EF development. It is likely that these variables account for a portion of the variability in early EF performance and should be pursued in future studies.

Conclusions

This study investigated the developmental origins of EF deficits in infants with DS. Group differences in EF precursor performance, including attention shifting, sustained attention, and action planning, were identified between infants with DS and their TD counterparts. In the group of infants with DS, the predictive nature of EF precursors was evaluated at a 6-month follow-up and attention shifting emerged as the single predictor of EF performance. Identifying areas of cognition in infants that are connected to early EF equips service providers with knowledge to support personalized care in this area of known challenge for young children with DS. Early intervention that supports EF foundations has the potential to improve the growth trajectory of EF skills and, ultimately, cognitive and adaptive outcomes in this population.

List of Abbreviations

DS, Down syndrome
TD, typically developing
EF, executive function
CA, chronological age
DA, developmental age

Declarations

Ethics approval and consent to participate. Institutional Review Boards at Colorado State University and Vanderbilt University approved all study procedures. Caregiver's of infant participants provided consent.

Consent for publication. Not applicable

Availability of data and materials. The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests. The authors declare that they have no competing interests.

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Authors' contributions. ES collected data, led the team of behavioral coders, and analyzed and interpreted the data under the direct supervision of DF, with contributions from LD. MP supervised data transformation and data analysis. MK and AN collected data and contributed to editing the final manuscript. All authors read and approved the final manuscript.

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Figures

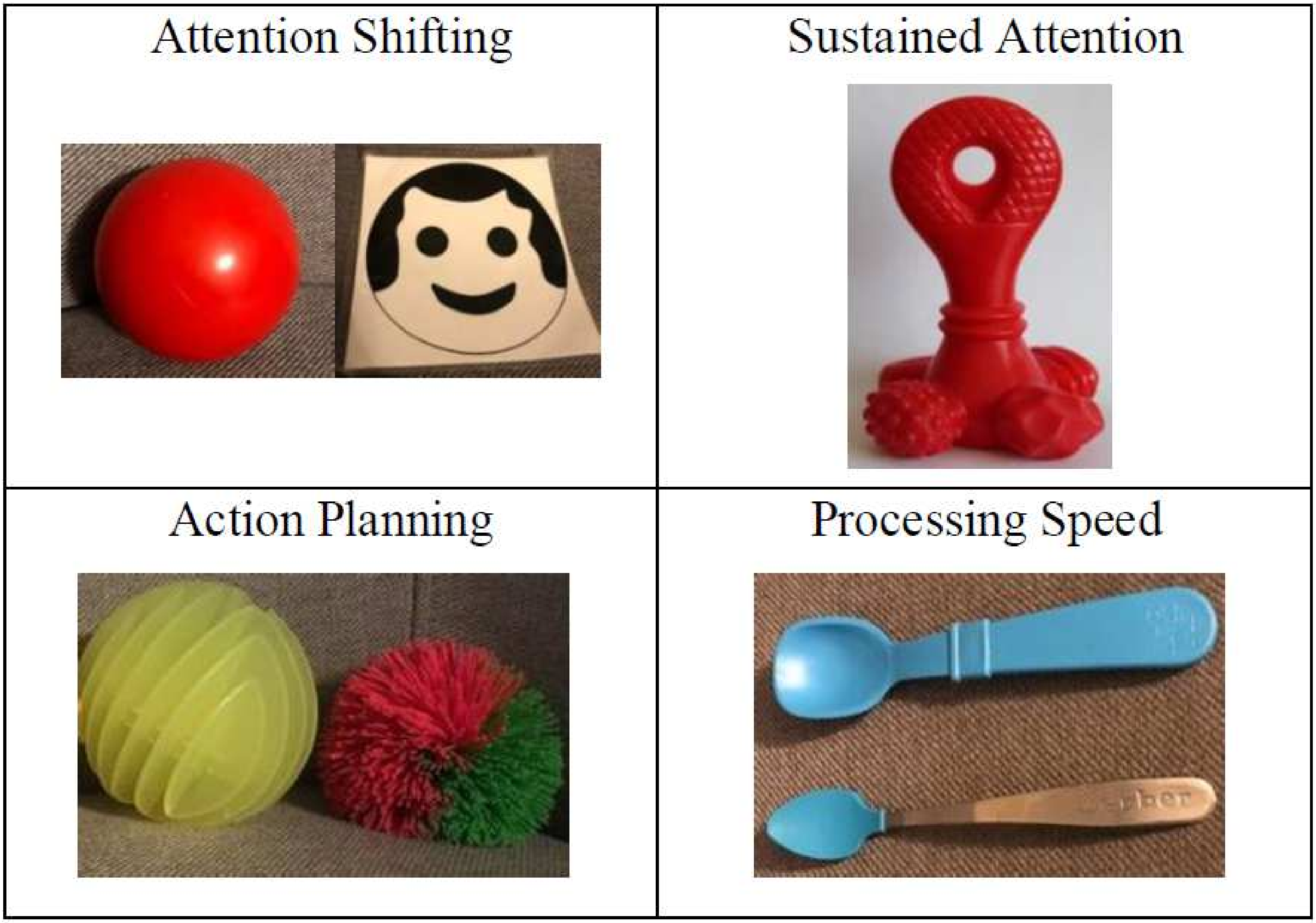

Figure 1

EF precursor laboratory task stimuli

Supplementary Files

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