THESIS

RELATIONSHIP BETWEEN EARLY EXECUTIVE FUNCTION, COMORBIDITIES, AND MOTOR SKILLS IN INFANTS WITH DOWN SYNDROME

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ABSTRACT

RELATIONSHIP BETWEEN EARLY EXECUTIVE FUNCTION, COMORBIDITIES, AND MOTOR SKILLS IN INFANTS WITH DOWN SYNDROME

Over the last decade, there has been increased research on executive function including working memory, inhibition, shifting, and planning in Down syndrome, yet there are still unanswered questions. The extant research demonstrates that Down syndrome is associated with deficits in executive function, motor skills, and a higher probability of exhibiting comorbid diagnoses. Shifting in infancy is associated with infant motor skills and later school outcomes such as memory in typical development. Questions remain regarding how these factors interact in infants with Down syndrome. The current study examined the associations between shifting performance, co-occurring conditions (congenital heart defects [CHD] and prematurity), and motor skills in infants with Down syndrome. Participants were 51 infants with Down syndrome, mean infant chronological age (CA)=15.9 months; SD=3.95; mean infant developmental age=10.73, SD=0.36, Overall, 41.2% of the infant participants were born prematurely (n=21), and 45.1% had CHD (n=23). The results indicate no statistically significant association between co-occurring conditions (CHD and prematurity) and shifting abilities. Additionally, associations between motor skills and shifting performance were not statistically significant. Future research should include a larger sample size and a longitudinal design to better understand the nature of these relationships.

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Introduction

Intellectual disability is diagnosed when individuals have significant deficits in cognitive functioning and adaptive behavior that occur before the age of 18 (Definition of Intellectual Disability, 2019). One of the most common neurogenetic causes of intellectual disability is Down syndrome, which occurs in approximately 1 in 707 live births (Mai et al., 2019). It is important to note that the incidence of Down syndrome has increased over time (Shin et al., 2010). In most cases, the cause of Down syndrome is due to the presence of an additional chromosome 21 (trisomy 21; Plaiasu, 2017). In addition to the presence of intellectual disability in most individuals, this neurodevelopmental syndrome is associated with dysmorphic facial features (Patterson & Costa, 2005), health challenges such as congenital heart defects (Freeman et al., 2008), and deficits in developmental outcomes (Daunhauer & Fidler, 2011). Therefore, Down syndrome can cause lifelong challenges and influence everyday activities.

The Down syndrome Behavioral Phenotype

A behavioral phenotype refers to the specific behavioral characteristics associated with a genetic disorder such as Down syndrome (Hodapp, 2004). These behavioral characteristics fall under various domains, such as health, cognitive, language, motor, and social abilities (Chapman & Hesketh, 2000). Although a genetic challenge increases an individuals' probability of demonstrating behavioral phenotypic characteristics, not all individuals with the disorder will demonstrate those specific behavioral traits. Therefore, behavioral phenotype only increases the likelihood of exhibiting specific behavioral outcomes (Hodapp, 2004). The probability of exhibiting these characteristics can be higher if the individual has a co-occurring diagnosis (Mahle et al., 2006; Reuner et al., 2015). Research on the behavioral phenotype associated with

Down syndrome informs us that individuals born with this neurodevelopmental disorder are more likely to have relative strengths in areas of core social-relatedness, visual-spatial processing, and relative deficits in cognitive, motor, expressive language, auditory processing, and aspects of social-emotional abilities (Chapman & Hesketh, 2000). However, not every individual with Down syndrome exhibits these phenotypic outcomes.

When considering outcomes and potential novel targets for intervention and prevention for this population, it is critical to consider that the phenotypic profile associated with Down syndrome has early constraints on neurodevelopment present at birth (Edgin, 2003). Previous research on infants with Down syndrome in the 70s and 80s utilized older methodological approaches limiting their generalizability (d'Abrera et al., 2013). However, recently, a small amount of research with new methodological approaches has characterized development in infancy in Down syndrome. Furthermore, because few early assessments have been standardized for this population, interpreting research findings in Down syndrome has been complicated. For example, some assessments may not have been sensitive to phenotypic features associated with Down syndrome; therefore, they may not have detected developmental changes following an intervention (Edgin, 2003). To address these issues, in this literature review, I will examine the early manifestations of the Down syndrome behavioral phenotype in infancy with a focus on cognitive outcomes to highlight specific gaps of knowledge.

Health and Comorbidities

In terms of health outcomes in infancy, the behavioral phenotype associated with Down syndrome predisposes individuals to comorbidities observable from birth (Martin et al., 2018). For example, a significant percentage of infants with Down syndrome are reported to have been hospitalized in the neonatal intensive care unit (NICU) shortly after birth (Martin et al., 2018).

This is partially due to the considerable number of infants with Down syndrome born prematurely or with a heart defect. Infants with Down syndrome have a higher probability of being born prematurely than typically developing infants (Aoki et al., 2018). When compared to typically developing infants born prematurely, infants with Down syndrome have a higher probability of exhibiting cognitive delays and impoverished attention later in life (Aoki et al., 2018; Reuner et al., 2015). There is a paucity of data regarding the effects of prematurity in infants with Down syndrome. The little evidence that does exist suggests that infants with Down syndrome who were born prematurely were found to have increased difficulty with executive function (Fidler et al., 2019b). Therefore, prematurity can add another level of challenge to those associated with Down syndrome.

An additional health complication associated with the behavioral phenotype associated with Down syndrome in infancy is congenital heart problems (Martin et al., 2018). A congenital heart defect (CHD) is an issue with the heart's configuration that causes a range of symptoms, including abnormal heartbeat or having increased difficulty breathing (Martin et al., 2018). In typically developing children, CHD is often associated with deficits in neural processes and structure and deficits in attention, executive function, and motor development (Mahle et al., 2006). Around 40 to 50 percent of infants with Down syndrome are diagnosed with a substantial CHD (Freeman et al., 2008).

A specific type of CHD, atrioventricular septal defects (AVSD), which results in holes between chambers in the heart that can lead to congestive heart failure, is one of the most common congenital heart defects diagnosed in Down syndrome (Loffredo et al., 2001; Visootsak et al., 2011). The findings related to AVSD and outcomes in Down syndrome are nuanced and bear attention. Infants with Down syndrome and AVSD have exhibited increased

neurodevelopmental deficits, especially with motor, cognitive, and language acquisition compared to those without AVSD (Visootsak et al., 2011). Both Alsaied and colleagues (2016) and Visootsak and colleagues (2011) reported that children with CHD presented with more developmental challenges in early development. However, research indicates that when these children, who all received surgical repairs in the first year of life, reached school age, the children with Down syndrome who had CHD had no significant differences in neurodevelopmental outcomes when compared with children with Down syndrome that did not have CHD. The interpretation of findings is limited by the cross-sectional retrospective design (Alsaied et al., 2016).

Taken as a whole, there are a variety of health challenges associated with infancy in Down syndrome. Specific impairments are associated with comorbidities as a result of prematurity or CHD. Importantly, as indicated by CHD research, there is evidence that early treatment can improve later outcomes, particularly outcomes related to cognition. Therefore, additional research on the presence of these comorbidities in Down syndrome is required to understand outcomes for this population better.

Exploration in Infancy

During the first year of life, infants typically learn and gain skills by exploring objects around them (Fidler et al., 2019). Exploration facilitates learning (de Campos et al., 2012) and is associated with later cognitive skills (de Campos et al., 2012). Object exploration is one type of exploration that provides infants with information about the object's physical properties (Lockman, 2000). Infants can use this information to guide decisions and plans about acting on objects (Lockman, 2000). Therefore, infants who cannot explore may have decreased opportunities to process and learn information (de Campos et al., 2012).

Several factors influence exploratory behaviors, including cognitive and motor abilities (de Campos et al., 2012). Infants use sensory and motor skills as a foundation for exploration (de Campos et al., 2013). Motor skills needed for exploratory behaviors can include reaching and grasping (de Campos et al., 2013). Infants with Down syndrome at four months of age demonstrate delays in reaching and grasping (de Campos et al., 2010) and delays in motor functioning have been observed to be below the 10th percentile (Tudella et al., 2011). At nine months, the average motor performance drops to below the 5th percentile (Tudella et al., 2011). This delay in reaching and grasping objects can disrupt typical exploration, affecting development in other areas (de Campos et al., 2013).

On average, infants with Down syndrome enact fewer exploratory behaviors than typically developing infants due to the preference to observe objects instead of reaching for them (MacTurk et al., 1985). These findings suggest that when comparing infants with Down syndrome and typically developing infants, infants with Down syndrome need an increased amount of time to visually process an object before grasping for it, even after starting to reach for the object (de Campos et al., 2013; MacTurk et al., 1985). Along with increased time to process visual information, the muscle weakness typical of Down syndrome could contribute to delays in reaching and grasping behaviors (Tudella et al., 2011). Furthermore, recent research using latent profile analysis indicates that infants with Down syndrome who have more active as opposed to passive exploratory styles also had more advanced developmental outcomes (Fidler et al., 2019a).

Based on the Dynamic Systems Theory of motor development, all developmental domains are constructed from multiple interactions with the person, environment, and task (Thelen et al., 1987). Therefore, Dynamic Systems Theory is a useful framework given that

motor abilities will interact continuously with other domains such as cognition and executive function skills. Importantly, Dynamic Systems Theory would suggest that delays in motor abilities may potentially affect developmental trajectories in other areas such as early executive function skills.

Executive Function and Origins in Infancy

Related to cognitive development, the behavioral phenotype associated with Down syndrome is associated with specific deficits in overall executive function (Daunhauer et al., 2017). Executive function can be defined the thinking skills required for broad goal-directed behaviors categorized into planning, inhibition, working memory, emotional control, and shifting (Carlson, 2005; Hughes, 2011; Pennington & Ozonoff, 1996; Zelazo et al., 1997; Zelazo & Muller, 2011). Executive function has been shown to be a stronger predictor than IQ for behaviors related to school engagement for young students with Down syndrome (Daunhauer et al., 2014). For young students with Down syndrome, working memory and inhibition tasks at the onset of elementary school significantly predicted concurrent academic math achievement better than IQ (Will et al., 2017) and significantly predicted academic achievement two years later (Daunhauer et al., 2020).

The early development of working memory and inhibition has been linked to the progression of attention shifting in infants (Fidler et al., 2019b). Working memory has been hypothesized to overlap with the timing of development for attention shifting in Down syndrome (Alvarez & Emory, 2006). This relationship is also observable in the associations between working memory deficits and attentional shifting in adults with Down syndrome (Salthouse, 2005; Salthouse, 2011). Furthermore, even in typically developing infants, improvements in working memory tasks are associated with improved attention (Reynolds & Romano, 2016).

In early infancy, attention shifting is the ability for an infant to visually engage with a stimulus and then disengage in favor of focusing attention on another stimulus (Fidler et al., 2019b). Typical developing infants under four months of age usually have not developed the ability to disengage with a stimulus (Fidler et al., 2019b). However, after an infant is four months old, they develop the attention control to demonstrate flexible engagement and disengagement. When infants are increasingly able to disengage, shorter looking times are associated with quicker processing speed (Hood & Atkinson, 1993).

These early shifting abilities are critical, given their associations with later outcomes. In typical development, attention shifting abilities in infancy predict both working memory and cognitive flexibility in late elementary school (Rose et al., 2012). Shifting deficits are evident in many adults with Down syndrome and are associated with challenges in prioritizing and ignoring distractors (Breckenridge et al., 2013; Grieco et al., 2015). Increased latency to shift attention, which connotes slower processing speed, is also associated with less competent cognitive performance in typically developing infants (Elsabbagh et al., 2013).

To date, the research on shifting in Down syndrome has yielded mixed findings. Some research has found evidence of no shifting deficits in individuals with Down syndrome, while others have. For example, Fidler and colleagues (2019b) examined shifting in infants with Down syndrome and typically developing children using a two-object shifting task. Results from this study indicated that infants with Down syndrome had increased latency to shift attention (Fidler et al., 2019b) compared to infants who were typically developing matched for chronological age. Furthermore, increased latency to shift was negatively associated with cognitive performance. These results highlighted the importance of shifting in infancy. While notable for its contributions to understanding the emergence of executive function in Down syndrome, there are

some limitations to this study, such as modest sample size (n= 38) and only one task used to measure shifting (Fidler et al., 2019a)

Another example of mixed findings from previous research is that children with Down syndrome had better performance on shifting, also known as cognitive flexibility, compared to children with autism comparing groups equated for mental age (Dawson et al., 1998). However, when children with Down syndrome were compared to children with Williams syndrome and typically developing children equated by chronological age and IQ, they scored less competently (Edgin, 2003). While examining adults with Down syndrome, similar results are suggested. Adults with Down syndrome had lower performance on shifting tasks than adults with Williams and adults with typical development when equated by mental age (Costanzo et al., 2013).

When considering these mixed findings on shifting in Down syndrome, it is also important to note that various methods are used to assess shifting in individuals with Down syndrome. In later development, a common method used is the rule-switch task (Dimensional Change Card Sort), where participants are asked to match a card to a target. Then the child places the card near the target and completes several trials (Zelazo, 2006). After these trials, the rule is changed. The rule-switch task is typically coded based on the correct response, incorrect response, and self-correction (Daunhauer et al., 2017). In infancy, one method in infant development uses a habituation-dishabituation method with two objects that are held in the infant's visual field (Fidler et al., 2019b). Each object is shaken, one at a time, then the infants' latency to shift their eyes to the new object is measured (Fidler et al., 2019b).

Another method used to measure shifting in children is the A-Not-B task (Miller & Marcovitch, 2015). The A-Not-B task has two locations for an object to be hidden by the examiner. The child will be asked to locate the object after the examiner visibly hides it in

location A. The examiner will continue to hide it under the same location then ask the child to retrieve it for several trials. After several trials, the examiner will then hide the object in location B. Research indicates that typically developing infants pass the A-Not-B task if there is no longer than a 2-second delay after the object is hidden (Diamond, 1985). Over time typically developing children can tolerate increased delays between when the object is hidden and when the infant is able to search for the object (Diamond, 1985). Typically developing children's performance on the A-Not-B task improves during the first three years of life in a linear trajectory (Diamond, 1985). During infancy and childhood, this growth on the A-Not-B task reflects cognitive growth in domains required to complete shifting tasks, such as memory and inhibition.

To date, there are questions that remain regarding how children with Down syndrome perform on the A-Not-B task. When comparing performance on the A-Not-B task with typically developing children matched for mental age, children with Down syndrome earned lower scores, but this difference was not statistically significant (Roberts & Richmond, 2015). However, children with Down syndrome had a lower number of passing responses than typically developing children (Roberts & Richmond, 2015). These results should be interpreted cautiously as the study had a modest sample size and only used one task to measure shifting (Roberts & Richmond, 2015).

Additional research findings suggest that school-age children with Down syndrome have challenges with shifting and overall executive function (Dauhauer et al., 2014; Daunhauer et al., 2017; Will et al., 2017). A potential reason for the discrepancies in research findings related to shifting in Down syndrome could be related to task impurity issues. Task impurity issues refer to the problem related to a task demanding abilities from more than one domain (Daunhauer et al., 2017). This is an issue that many researchers studying executive function acknowledge (Will

et al., 2017). For example, Roberts and Richmond (2015) hypothesized that successful performance on the A-Not-B task involved working memory, inhibition, and shifting.

An additional task impurity issue confounding our understanding of early shifting abilities is that the A-Not-B task, as opposed to the two-object shift task, could also be impacted by infant motor skills. Researchers have found more competent infant performance on the A-Not-B task by measuring young infants' looking in contrast to the reaching responses (Cuevas & Bell, 2013). When infants' reaching abilities are more skilled, performance on the A-Not-B-reaching version is comparable to the looking version (Cuevas & Bell, 2013). These task impurity issues should be considered when using the A-Not-B task.

Summary of Extant Literature on the Emergence of Executive Function

Over the last decade, there has been increased research on executive function in Down syndrome, yet there are still unanswered questions. There is a dearth of information about executive function foundations in infants with Down syndrome (Fidler et al., 2019b). However, recent research demonstrates that executive function delays can be observed starting in infancy and have meaningful associations with cognitive outcomes (Fidler et al., 2019b). It is crucial to understand the origins of these effects. Executive function assessed in infancy can predict the later development of these skills in typically developing children (Rose et al., 2012), and early school-age executive function in children with Down syndrome predicts later academic outcomes (Daunhauer et al., 2020).

Current Study

The extant research demonstrates that Down syndrome is associated with deficits in executive function, motor skills, and a higher probability of exhibiting comorbid diagnoses. Furthermore, research on typically developing infants has highlighted that motor abilities may

affect success in shifting abilities. Based on the Dynamic Systems Theory on motor development, all aspects of development are constructed from multiple interactions with the person, environment, and task (Thelen et al., 1987). Therefore, Dynamic Systems Theory is a useful framework when examining infants with Down syndrome, a neurogenetic disorder associated with motor delays (Ulrich & Ulrich, 1993), given that motor abilities will interact continuously with other domains such as cognition. Dynamic Systems Theory would suggest that delays in motor abilities may potentially affect developmental trajectories in other areas such as shifting. Indeed, questions remain regarding shifting tasks that measure visual gaze as opposed to requiring a manual search (Cuevas & Bell, 2013). However, the association between motor and shifting performance in infants with Down syndrome is unknown, despite high rates of observed delays in motor abilities such as reaching. Given that early executive function predicts later outcomes, a more nuanced understanding of how motor abilities and comorbidities affect performance will help inform targeted early intervention. The proposed study will contribute to the field by increasing knowledge surrounding these associations since questions remain on how these deficits interact and are related to each other. The impact and possibilities of increased challenges due to these interactions are unknown.

This study will address gaps in the field by carefully characterizing shifting in infants with Down syndrome. This project seeks to answer the following questions:

Question 1: How do infants with Down syndrome perform on tasks assessing shifting (A-Not-B and two-object shifting task)?

Question 2: In infants with Down syndrome, what is the magnitude of association between two different measurements of infant shifting (A-Not-B and two-object shifting task)?

Question 3: (3a) How do infants with Down syndrome who were born prematurely perform on shifting tasks?

(3b) Do infants with Down syndrome with a CHD diagnosis demonstrate shifting performance that is different from their peers without a CHD diagnosis?

(3c) What is the magnitude of association between shifting and motor abilities in infants with Down syndrome?

Method

This cross-sectional study is a secondary data analysis of infant performance collected as part of a larger, longitudinal project featuring a brief facilitated reaching intervention (Fidler et al., 2019a).

Participants

For this secondary data analysis, 51 infants with Down syndrome (mean infant chronological age [CA]=15.9 months; SD=3.95, mean infant mental age=10.73, SD=0.36) and their caregivers were included in the project. See Table 1 for participant characteristics.

The infants in the current study engaged in a follow-up assessment six months after participating in a facilitated reaching intervention. The intervention condition in the larger study involved caregivers supporting their infants' interest in objects by placing mittens with soft, looped Velcro on the infants' hands and drawing their attention to toys affixed with complementary hooked Velcro. The mittens and adapted toys facilitated the infants' ability to grasp and explore objects before developing efficient independent grasping (Fidler et al., 2021). The alternative treatment condition involved caregivers engaging their infants' interest in objects visually and providing the opportunity to explore without mittens or toys affixed with Velcro (Fidler et al., 2021). Both conditions were administered for 5 to 10 minutes daily for 2-3 weeks.

The inclusion criteria for the larger project included parent-report of their infant receiving a Down syndrome diagnosis and not yet independently reaching. Exclusion criteria for the larger project included having challenges beyond those associated with Down syndrome, such as severe visual impairment, extreme hearing loss, or acute otitis media treatment. For this secondary analysis, inclusion criteria included the infant having a developmental age of 7-19 months, and

the infant's engagement in the targeted shifting tasks (A-Not-B task or two-object shifting task), as well as a developmental assessment. A 12-month developmental age range was selected to allow for the emergence of shifting skills given the high degree of variability associated in the Down syndrome phenotype, particularly in tasks involving early reaching and exploration (Fidler et al., 2019; Hauck et al., 2021). Additionally, a starting mental age of 7 months was chosen based on previous research indicating when typically developing infants perform A-Not-B tasks with reaching (Cuevas & Bell, 2010).

Procedure

Colorado State University's Institutional Review Board approved this study. In the original project, convenience sampling was used to recruit participants. Participant recruitment was conducted through social media posts and mailings to parent support groups and regional Down syndrome clinics and service providers in the south, Midwest, and mountain west of the U.S. Families who indicated an interest in the study were screened and given more information over the phone. After caregivers provided written consent, infants engaged in 15-minutes of video-recorded assessment tasks while the infant was sitting on the caregiver's lap or in a highchair. Then the researcher conducted an approximately 30-minute standardized developmental assessment. Infants engaged in this assessment while sitting in the lap of a caregiver, seated on the floor, or lying down. An advanced doctoral student conducted these assessments during the concluding parts of the visit. Caregivers also completed a child development and family history survey.

Measures

Developmental Status

All participants in this study completed the Bayley Scales of Infant Development 3rd edition (BSID-III; Bayley, 2006). The BSID-III measures cognition, fine motor, and gross motor skills, and language in 1 to 42-month-olds using standardized playful activities and observations (Bayley, 2006). Approximately 10% of the standardization sample included children with intellectual and developmental disabilities such as Down syndrome, cerebral palsy, and specific language impairment.

The BSID-III exhibits high internal consistency (.86-.87) and test-retest reliability (.80-.87; Bayley, 2006). Additionally, the BSID-III exhibits high concurrent validity between the Wechsler Preschool and Primary Scale of Intelligence Third Edition (WPPSI-III; .71-.83; Bayley, 2006), the Peabody Developmental Motor-Scale 2 (79%; Connolly et al., 2012), and Preschool Language Scale Fourth Edition (.51-.71; Bayley, 2006). Additionally, the BSID-III exhibits strong predictive validity for infants born prematurely on the WPPSI-III cognitive score at age 4. (Bode et al., 2014).

Foundations of Early Executive Function Performance

The A-Not-B task is a classic measure assessing the foundations of executive function in infants (Diamond, 1985). For this task, two washcloths were placed side by side, locations A and B, in front of the participant. The washcloths were placed just out of the infant's reach. The examiner shook a vibrant rattle to gain the attention of the infant. Then the examiner placed the rattle under a washcloth labeled location A. The washcloths were pushed towards the infant by the examiner. The examiner told the infant to "find the toy." Once the infant pulled either both or

one cloth, the trial was repeated two additional times, hiding the rattle under location A. On the fourth trial, the rattle was switched to be hidden under a washcloth labeled location B.

On the fourth trial, the infant's responses were coded based on four categories, "only location B", "only location A", "both locations, incorrect", and "both locations, correct". The first responses coded were "only location B" if the infant pulled only location B washcloth manually. When the infant pulled both washcloths manually, this was coded as "both locations, correct" if the infant pulled the location B washcloth 1 second before pulling location A washcloth. When the infant pulled location A washcloth first, this was coded as "both locations, incorrect". The same was coded when the infant pulled both washcloths at the same time. When the infant pulled the only location A washcloth, this was coded as "only location A". Correct response categories included "both locations, correct" and "only location B". While incorrect responses included the remaining two categories, "only location A" and "both locations, incorrect". If there was an absence of manual search during the task, this was coded as an incorrect response. Coders had no knowledge of the study questions or intervention group assignment and exhibited strong inter-rater reliability (Cohen, 1960; Cohen's Kappa = .88; Landis & Koch, 1977).

Two-Object Shifting

Two objects were held in front of the infant's line of sight, a red ball, and a schematic face. The red ball was held 4 inches to the left of the infant's midline, and the schematic face was held 4 inches to the right of the infant's midline (Mullen, 1995). The location of the two objects was in the infant's visual field. First, the examiner shook the red ball to entice the infant's attention. Once the infant gazed at the red ball, the examiner shook the schematic face. The examiner would then alternate between each object by shaking each object several times. A minimum of two trials was conducted for each object. Each trial was coded for the time taken in

seconds once the object, red ball, or schematic face, was being shaken to the infant visually focusing on that object or latency to shift eye gaze. The ocular reaction time was coded using Canfield and colleagues' (1997) method of measuring the latency to shift eye gaze in seconds. This measure was averaged across all the trials for each infant participant. The average kappa reliability was high, suggesting strong inter-rater reliability (Cohen, 1960; Cohen's Kappa = .93).

Child Development and Family History Survey

Caregivers reported information regarding their child's developmental and medical history, including comorbid diagnoses such as prematurity, CHD, history of significant illnesses. Additionally, they reported demographic information, such as age, income, race, and education level.

Data Analytic Plan

For this secondary analysis, the data utilized was drawn from a larger, longitudinal study. For the current study, follow-up assessments conducted six months after a brief, facilitated reaching intervention for infants with Down syndrome were examined. Fidler and colleagues' (2021) findings suggest there was no significant differences between infants in the treatment group and those in the alternative treatment group. However, infants in the treatment group showed shorter latencies in shifting and a higher number of reach attempts at objects than infants in the control group (Fidler et al., 2021). Infants who have completed the intervention versus the alternative treatment could have improved motor skills or perhaps enhanced abilities in other domains not measured.

Therefore, before proceeding, we examined between-group differences on the variables of interest to compare infants who had the intervention and those who participated in an alternative treatment condition. For intervention status, infants who completed the intervention

received the "YES" code were given a nominal representation of "1" and infants who participated in the alternative condition received the "NO" code and were coded as "0". The nominal variables were used to run a Chi-square test for the A-Not-B task, and results indicated that the relation between these variables was not significant, $X^2(1, N=23) =0.006$, p=0.94. A Mann-Whitney U test was used to compare the intervention condition groups on the two-object task. Findings indicated that performance on the two-object shifting task did not statistically differ between infants who participated in the intervention (N=17, M=21.35) and those in the alternative condition (N=18, M=14.83), although the analysis approached significance, U=96, p=0.06, two-tailed. Consequently, because there were no significant performance differences between the infants who completed the reaching intervention and those in the alternative condition, we proceeded with analyses to answer the questions posed for this project.

To answer the question regarding shifting performance in infants with Down syndrome, descriptive statistics were used to characterize the range, median, and mean performance on the shifting tasks by ages and by comorbidities.

To answer the question concerning the magnitude of association between two different measurements of infant shifting (A-Not-B task and two-object shifting task), a point-biserial correlation was used to measure the association. It is hypothesized that the number of correct responses on the A-Not-B task is associated with decreased latency to shift on the two-object shifting task. Both variables were checked for normality of distribution, the two-object shifting task was positively skewed and a log transformation was performed (Feng et al., 2014). The number of correct responses on the A-Not-B task was compared with latency to shift on the two-object shifting task.

For the question regarding whether shifting performance differs for infants with Down syndrome born prematurely in contrast to those born full-term, a Chi-square test was used to analyze A-Not-B performance and a point biserial correlation was used for the two-object shifting task. A dichotomous variable derived from "the presence of prematurity" was used to create groups of infants born prematurely and infants born full term.

To answer the question whether infants with Down syndrome with CHD demonstrate shifting performance that differs from their peers without a CHD diagnosis, a Chi-square test was used was used for the A-Not-B task and Mann-Whitney U test was used for the two-object shifting task. A dichotomous variable derived from "the presence of CHD" was used to create groups of infants with congenital CHD and infants who did not.

For the question testing the magnitude of association between shifting and motor skills in infants with Down syndrome, a point-biserial correlation was calculated to measure the association between the number of correct responses and the total motor score on the BSID-III. The number of correct responses on the A-Not-B task will be compared to the total raw motor skills score. The complete motor skills score is the total of fine and gross motor domains on the BSID-III. It is hypothesized that more developmentally competent performance on the A-Not-B task is associated with total motor skills score.

Results

Overall, 41.2% of the infant participants were born prematurely (n=21), and 45.1% had a CHD (n=23), see Table 1. Other detailed participant characteristics including gender, Down syndrome type, race, and ethnicity, are also included in Table 1. Furthermore, participant developmental age performance on the BSID-III is included in Table 2.

Table 1

Participant and family characteristics

Characteristic	***n***	**%**
Participant	51	
Gender		
Female	25	49%
Male	26	51%
Down syndrome Type		
Trisomy 21	48	94.1%
Mosaicism	1	2.0%
Translocation	2	3.9%
Prematurity	21	41.2%
CHD	23	45.1%
RACE/ETHNICITY AND PARENT EDUCATION LEVELS		
Infant's Race		
White	43	84.3%
Asian	2	3.9%
Black or African American	1	2.0%
More than one race	3	5.9%
Missing	2	3.9%
Infant's Ethnicity		
Hispanic or Non-Hispanic		
Hispanic or Latino	10	19.6%
Non-Hispanic or Latino	37	72,5%
Unknown or not reported	1	2.0%
Missing	3	5.9%
Mother's Race		
White	43	84.3%
Black or African American	1	2.0%
Asian	2	3.9%
More than one race	2	3.9%
Missing	3	5.9%
Mother's Ethnicity		
Hispanic or Non-Hispanic		

Hispanic	10	19.6%
Non-Hispanic	37	72.5%
Unknown or not reported	2	3.9%
Missing	2	3.9%
Mother's Highest Education Level		
Some high school	3	5.9%
High school graduate	4	7.8%
1-3 years of college	13	25.5%
College graduate	15	29.4%
Some graduate or terminal masters	8	15.7%
Professional degree	8	15.7%
Father's Race		
White	44	86.3%
Black or African American	1	2.0%
Asian	2	3.9%
More than one race	2	3.9%
Missing	2	3.9%
Father's Ethnicity		
Hispanic or Non-Hispanic		
Hispanic	9	17.6%
Non-Hispanic	39	76.5%
Unknown or not reported	1	2.0%
Missing	2	3.9%
Father's Highest Education Level		
Some high school	3	5.9%
High school graduate	11	21.6%
1-3 years of college	8	15.7%
College graduate	13	25.5%
Some graduate or terminal masters	9	17.6%
Professional degree	7	13.7%

Question 1 How do infants with Down syndrome perform on tasks assessing shifting?

The majority of the infants (69%) in the current study were able to engage in both shifting tasks. However, only 39/51 or 76% of infants took part in the A-Not-B task. Of the infants who engaged in the A-Not-B task, 49% passed and 51% did not. Performance on the A-Not-B task was broken into developmental age groups that ranged 3 months, see Table 3. When examining the data on performance from 7-10 months developmental age to 11-14 months, infant performance was more successful at 11-14 months, though the infants in the next developmental age band (15-19 months) did not demonstrate this trend. It should be noted that

for this task, the 7-10 month developmental age group had the more participants than the next two age bands which had less participants (n=15 and n=4, respectively).

The majority of infants in the current study were able to engage in the two-object shifting task, 92% or 47/51. A visual inspection of the data for this task indicates that overall, infants presented the slowest shifting responses at 7-10 months and the fastest at 11-14 months. The infants in the 15-19 month developmental age band performed shifting faster than the youngest group and their performance also was slower than the 11-14 month-olds. As with the A-Not-B task, the 7-10 month group had many more participants than the next two age bands which have smaller n's (n=14 and n=4, respectively).

Table 2

Descriptive on BSID domains, A-Not-B task, and two-object shifting task

	Mean (SD)	Minimum	Maximum	Skewness	
				Statistic	Std. Error
Chronological age (in months)	15.90(0.55)	9.66	24.23	0.39	0.33
Bayley-III Cognitive DA (in months)	10.73(2.55)	7.00	19.00	1.562	0.33
Bayley-III Motor Scaled Score*	8.50(3.28)	2.00	16.00	0.38	0.33

*Note: This score reflects combined fine and gross motor

Table 3

Performance on the A-Not-B task and two-object shifting task by developmental age

	Developmental age							
	7-10 months		11-14 months		15-19 months		Combined ages	
Characterist	Mean (SD)	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	n
A-Not-B Task	0.35(.48)	20	0.67(0.48)	15	0.50(0.58)	4	0.49(0.50)	39

Two-object shifting task	1.97(1.33)	29	1.58(1.09)	14	1.66(0.50)	4	1.84(1.21)	47

Table 4

Descriptive on the A-Not-B task and two object shifting task by CHD and prematurity

	n	% correct or Mean (SD)
CHD diagnosis	23	
A-Not-B task	18	44.4%
Two-object shifting task	21	1.71 (0.82)
No CHD diagnosis	28	
A-Not-B task	21	54.5%
Two-object shifting task	26	1.93 (1.46)
Premature	21	
A-Not-B task	16	37.5%
Two-object shifting task	19	2.00 (1.36)
Full term	30	
A-Not-B task	22	58.3%
Two-object shifting task	26	1.66 (1.12)

Question 2 In infants with Down syndrome, what is the magnitude of association between two different measurements of infant shifting (A-Not-B and two-object shifting task)?

A point biserial correlation was used to test the association between the A-Not-B task and two-object shifting task. Findings indicated a nonsignificant negative correlation with a small effect size, ($r_{pb}(34) = -0.11$, p= 0.55).

Question 3(a) How do infants with Down syndrome who were born prematurely perform on shifting tasks?

A Chi-Square test was performed to examine the association between prematurity and performance on the A-Not-B task. Based on the results, the relationship between prematurity status and performance on the A-Not-B task was not statistically significant, $X^2(1, N=39) = 1.37$, p=0.24. A point-biserial correlation was used to test the association between prematurity and the two-object shifting task. Findings indicated a nonsignificant correlation with small effect size,

$r_{pb}(40) = -0.19$, p=0.25 See Table 4 for performance on shifting tasks and prematurity status. As a whole, infants born prematurely did not perform significantly differently from their full-term peers on shifting tasks.

Question 3(b) Do infants with Down syndrome with a CHD diagnosis demonstrate shifting performance that is different from their peers without a CHD diagnosis?

A Chi-square test was performed to examine the association between diagnosis of heart defect and performance on the A-Not-B task. The relationship between these variables was not statistically significant, $X^2(1, N=39) = 0.24$, p=0.62.

A Mann-Whitney U test was used to examine whether infants with CHD performed differently than infants without CHD on the two-object shifting task. Findings indicated no significant performance difference between infants with a diagnosis of heart defect (N=21, M=24.88) and infants without a diagnosis of heart defect (N=26, M=23.29) on the two-object shifting task (U = 254.50, p=0.69, two-tailed). See Table 4 for performance on shifting tasks and CHD status. Therefore, considering these findings together, infants with Down syndrome who had CHD did not perform significantly differently on these shifting tasks compared to infants with no CHD.

Question 3(c) What is the magnitude of association between shifting and motor skills in infants with Down syndrome?

A point biserial correlation was used to test the association between the total (both gross and fine) raw motor score and the A-Not-B task. The correlation results indicated that there was no meaningful association between motor abilities and this task, $r(38) = 0.03$, p=0.88. Additionally, point biserial correlations were used to examine associations among the subdomains of gross and fine motor raw score with performance on the A-Not-B task. The

associations between the gross motor raw score and A-Not-B task indicated that there were no meaningful associations between gross-motor and A-Not-B task performance ($r(38) = 0.09$, p=0.61). Additionally, findings suggest a nonsignificant, positive association between fine motor abilities and A-Not-B task performance with small to medium effect size ($r(38) = 0.20$, p=0.23, see Table 5).

Table 5

Summary of A-Not-B task and motor skills

		Gross Motor Raw Score	Fine Motor Raw Score	A-Not-B Task
Gross Motor Raw Score	Pearson Correlation Sig. (2 tailed)	1		
Fine Motor Raw Score	Pearson Correlation Sig. (2 tailed)	.78** .000	1	
A-Not-B task	Point Biserial Correlation Sig. (2 tailed)	.089 .61	.20 .23	1

** Correlation is significant at the 0.01 level (2-tailed).

Discussion

This secondary data analysis contributes to the literature on (a) the emerging Down syndrome phenotypic profile and (b) assessing early shifting abilities in this population. The current study is the first to compare multiple types of shifting tasks in infants with Down syndrome while examining the associations of co-occurring conditions and motor skills.

Interpreting Question 1: How do infants with Down syndrome perform on tasks assessing shifting (A-Not-B and two-object shifting task)?

More infants were able to engage in the two-object shifting task than the A-Not-B task. When considering assessment tasks for infants with Down syndrome, this difference in engagement is important to consider. It is possible that the demands of the A-Not-B task were misaligned with the infants' ability level, given the range of developmental and chronological ages of the infants in this study. The task demands related to A-Not-B will be discussed in more detail below. Additionally, the traditional version of the A-Not-B task utilized in this study yielded one dichotomous score 1(yes, passes) or 0 (no) based on a motoric response, which limits the ability for this measure to characterize more nuanced variability in performance, such as performance over multiple items or performance based on response time.

In contrast, a visual inspection of the data for the two-object task indicates a trend for infants in the 11-14 month developmental age band to visually respond to shifting faster than the 7-10 month-olds. Additionally, for this task, infants' variability in performance measured by standard deviation decreased between these two age bands, indicating that perhaps the infants in the older age bands demonstrated more stable performance with chronological age. The smaller n's of the age bands limit interpretation. However, these observations of more efficient shifting

with increasing developmental age converge with literature on typically developing infants (Kannass & Oakes, 2008). Taken altogether, the difference in engagement in these two tasks converges with others in suggesting that it is critical to consider measures that are capable of capturing variability in outcomes for infants with Down syndrome (Fidler et al., 2019a). Related to measurement issues, the findings related to the association of these measures are discussed.

Interpreting Question 2: In infants with Down syndrome, what is the magnitude of association between two different measurements of infant shifting (A-Not-B and two-object shifting task)?

When considering the magnitude of association between these two different infant shifting measurements, the results indicate a slight negative correlation that was not significant. The findings might be affected by the different task demands and levels of measurement used for these tasks. Previous research indicates that typically developing infants can visually respond to the A-Not-B task before they can motorically respond with reaching (Cuevas & Bell, 2010). However, the traditional A-Not-B task used in this study measures shifting by having the infants use motor skills to reach for the correct answer resulting in a dichotomous (yes/no) correct measure for this task. Conversely, the two-object shifting task measures shifting by the infants' eye gaze to establish if the infant shifted their attention to the shaking object resulting in latency as the measure for this task. Past literature has suggested that both tasks have been shown to measure shifting (Fidler et al., 2019a; Roberts & Richmond, 2015). However, questions remain regarding how children with Down syndrome perform on the A-Not-B task (Roberts & Richmond, 2015). Previous findings indicate that preschoolers with Down syndrome achieved lower scores than typically developing children matched for mental age, although the scores were not significantly lower (Roberts & Richmond, 2015).

The current findings provide insight into how infants with Down syndrome perform on the A-Not-B task. When comparing the A-Not-B task and the two-object shifting task findings suggest the two tasks measure different aspects or qualities of shifting. These two tasks use different methods and have different levels of challenges, reaching for the A-Not-B task versus measuring the latency to shift eye gaze on the two-object shifting task. A plausible explanation is that the A-Not-B task may involve more synchronization of cognition, especially memory, inhibition, and motor coordination, to reach the hidden object (Marcovitch & Zelazo, 1999; Rose et al., 2012). For the two-object shifting task, the infants simply move their eyes from one object to the other object being shaken. Therefore, the A-Not-B task appears to demand more complex aspects of shifting. Since these shifting tasks were not correlated, the reliability and validity of these measures capturing shifting abilities should be examined. Future studies should develop and pilot tasks that can be reliable and valid measures of shifting abilities in infants with Down syndrome.

Question 3(a) Do infants with Down syndrome born prematurely demonstrate shifting performance that is different from their peers born full term?

Question 3(a) examined the relationship between performance on the targeted shifting tasks in infants with Down syndrome born prematurely and those born full term. For the A-Not-B task, the data indicated the relationship between prematurity status and performance on the A-Not-B task not statistically significant ($p=0.24$). For the two-object shifting task, findings indicated a small negative correlation that was not statistically significant ($p=0.25$).

These results do not align with previous findings that suggest infants with Down syndrome born prematurely have a higher probability of exhibiting difficulty with executive function (Aoki et al., 2018; Reuner et al., 2015). In addition to the potential measurement issues

with these tasks and small group sizes, several confounds could have affected the findings of this study, including parent-report of prematurity and the fact that the measure of prematurity used for this study was dichotomous (premature or full-term). Therefore, attaining medical records for prematurity and other known risk factors related to birth for infants with Down syndrome, such as low birth weight, may improve our understanding of how birth status affects these early abilities.

Another explanation could be that prematurity status impacts shifting abilities, but not enough to be statistically significant. Since this study only examined shifting and no additional executive function skills, there could still be an association between prematurity and other executive function skills. Considering these findings, future research should examine prematurity and additional executive function skills to investigate those associations.

Interpreting Question (3b) Do infants with Down syndrome with a CHD diagnosis demonstrate shifting performance that is different from their peers without a CHD diagnosis?

CHD is another common co-occurring condition in Down syndrome. However, the findings indicated no significant relationship between a CHD diagnosis and infant performance on the two shifting tasks. The past literature has mixed findings, with some indicating that children with CHD had an increased probability of early developmental challenges (Visootsak et al., 2011; Alsaied et al., 2016). However, when the children, whom all received surgical repairs in the first year of life, reached school age, the children with Down syndrome who had CHD had no significant differences in neurodevelopmental outcomes when compared with infants through school-age children with Down syndrome that did not have CHD (n=178; Alsaied et al., 2016). The current study provides some support for Alsaied and colleagues (2016) since the findings

indicate CHD is not significantly associated with shifting abilities. Due to the questions about the measurement of the A-Not-B task and the two-object shifting tasks used for this project, future research is needed to examine the association between CHD and shifting.

Interpreting Question (3c) What is the magnitude of association between shifting and motor abilities in infants with Down syndrome?

Motor skills were also examined to determine their relationship with shifting abilities. The findings indicated a small, positive correlation between total (gross and fine) motor skills and A-Not-B infant performance that was not statistically significant ($p=0.69$). Additional analyses were used to test the association between the A-Not-B task with both gross motor and fine motor separately. While the results were not statistically significant, the positive association between fine motor skills and performance on the A-Not-B task had a small effect size which is worth noting given the small sample size.

There is little literature that examines the association between motor skills and shifting in infants with Down syndrome. Research suggests that infants with Down syndrome exhibit delays in reaching and grasping objects (de Campos et al., 2012). The delays in reaching and grasping objects can cause an interruption in the typical exploration, affecting development in other areas (de Campos et al., 2013). Based on the Dynamic Systems Theory on motor development, all aspects of development are constructed from multiple interactions with the person, environment, and task (Thelen et al., 1987). Therefore, from a Dynamic Systems Theory perspective, delays in motor abilities may potentially affect developmental trajectories in other areas such as shifting. Although infants with Down syndrome have a high risk of demonstrating delays in motor skills, such as reaching and grasping, the current study suggests no statistically significant association between motor skills and the A-Not-B task.

The current finding also relates to previous literature discussing the task impurity issues with scaling executive function measures for younger development (e.g., Daunhauer et al., 2020). The task impurity issue confounding our understanding of early shifting abilities is that the A-Not-B task, as opposed to the two-object shifting task, could be impacted by infant motor skills. Researchers have found more competent infant performance on the A-Not-B task by measuring young infants' looking in contrast to the reaching responses (Cuevas & Bell, 2013). When typically developing infants' reaching abilities were more skilled, performance on the reaching version of A-Not-B was comparable to the looking version (Cuevas & Bell, 2013). Therefore, a possible explanation for the non-statistically significant association between motor skills and the A-Not-B task might be that task impurity, at least in the domain of motor skills, might not affect performance on this task as considerably as we anticipated for infants with Down syndrome. Another explanation could be related to the single dichotomous score derived from this task that limits measurement variability. Further research is needed to examine the association between motor skills and shifting abilities. Future studies should use caution and investigate the A-Not-B task before using it to measure shifting abilities.

Limitations

The current study has several limitations that should be considered when interpreting the results. First, the sample size with this population is relatively large for a group of infants with Down syndrome. However, by statistical power standards, the sample size is modest, and the age range was limited, with most infants being 7 to 10 months chronological age at the time of data collection. Future studies should include a larger sample size to increase statistical power. Additionally, this study did not include a comparison group of children with typical development or another neurogenetic syndrome equated for developmental age, which limited further

comparisons of the variables of interest. More questions could be answered about how motor skills and shifting abilities develop in infants with Down syndrome compared to typically developing infants or another syndrome. For example, with a comparison group of typically developing infants, information can be gained regarding how shifting abilities in infants with Down syndrome differ from a typical trajectory. A comparison group of infants with another type of neurogenetic syndrome can provide information on what abilities might be associated with Down syndrome, specifically in contrast to intellectual disability in general.

Another limitation is the cross-sectional design. A cross-sectional design restricts the extent of conclusions that could be made from the results. Future research should examine the development of motor skills and shifting abilities longitudinally to characterize the progressive growth of these skills over time. Additionally, by conducting a longitudinal study, it will increase the likelihood of identifying the associations between early foundations and later outcomes to clarify outcomes in later childhood associated with infant shifting abilities. The last limitation to the current study is that the participants were from the 6-month visit in a more extensive study (Fidler et al., 2019b). Some participants took part in the facilitated reaching intervention, which could have various potential effects on the current study's results. The reaching intervention facilitated reaching behaviors in the infant (Fidler et al., 2021). Fidler and colleagues' (2021) findings suggest that the infants in the treatment group showed shorter latencies in shifting and a higher number of reach attempts at objects than infants in the control group (Fidler et al., 2021). Therefore, infants who have completed the intervention versus the alternative treatment could have increased motor skills or perhaps enhanced abilities in other domains. The increased motor skills could dynamically affect infant abilities in ways we have not yet measured, particularly regarding motor abilities and performance on the A-Not-B task.

Future Directions

There are several future directions for examining shifting in infants with Down syndrome. There is an issue in the current field regarding the significant need to have accurate measures specifically for the population of individuals with Down syndrome (Esbensen et al., 2017). The current findings suggest infants with Down syndrome demonstrate a great deal of individual variability in shifting. However, more research is needed to elucidate the causes of variability, such as comorbidities and measurement issues. Regarding the measurement issues, another future direction is to examine the A-Not-B task, given that the current findings suggest that it is not associated with motor skills or the two-object shifting task. The A-Not-B task is an important part of Piagetian theory and has been utilized to measure shifting abilities by having the infants reach for the correct response (Fidler et al., 2019a; Roberts & Richmond, 2015). However, it may be limited by the single, dichotomous score and underlying complex interaction of memory, inhibition, and motor skills required to reach for the hidden object. Therefore, the A-Not-B task may not accurately measure the infant's shifting abilities and could be measuring other abilities than shifting. Similarly, the two-object task given the simple, visual response might be a better measure of cognitive processing speed (Fidler et al., 2019b; Rose et al., 2012). Further research is needed to investigate the utility of the A-Not-B task.

An additional direction for future research is to examine the associations between prematurity status and executive function skills. Previous research suggests that infants with Down syndrome born prematurely have a higher probability of exhibiting difficulty with executive function and impoverished attention later in life (Aoki et al., 2018; Fidler et al., 2019b; Reuner et al., 2015). The current findings do not support for the association between prematurity and the two shifting tasks since the results were not significant. Additionally, the current study

only examined shifting and no additional executive function skills. Past literature suggests that infants with Down syndrome born prematurely were found to have increased difficulty with executive function (Fidler et al., 2019b). There could still be an association between prematurity and additional executive function skills. Due to the current study's modest sample size and limited measure of executive function skills; future research should examine prematurity and additional executive function skills to investigate those associations.

Future research should also further examine CHD and shifting. Alsaied and colleagues (2016) illustrated that children with Down syndrome and CHD who received heart surgery early in their life, when they reached school age, showed no significant differences in neurodevelopmental outcomes when compared with children with Down syndrome who did not have CHD. Therefore, future research should examine the difference in shifting tasks' performance between infants with heart surgery and those without. Additionally, the current study did not explore any differences between CHD and AVSD on the two shifting tasks. Alsaied and colleagues (2016) found that when infants with Down syndrome have AVSD, neurodevelopmental deficits are exhibited. Future research should examine the difference between CHD and AVSD on shifting tasks to account for different CHD types and to address the divergent findings in the literature.

Conclusion

This study is unique as it is the first study that has compared multiple types of shifting tasks in infants with Down syndrome while examining the effects of co-occurring conditions and motor skills. Findings suggest that the shifting tasks of interest were not associated. Additionally, the results indicate no significant association between co-occurring conditions (CHD and prematurity) and shifting abilities in infants with Down syndrome. Similarly, no statistically significant association was found between motor skills and shifting performance on the A-Not-B task, though there was a small effect size for an association between fine motor skills and performance on this task. The limitations of this study were the modest sample size and cross-section design. Additionally, some of the participants took part in a brief-reaching intervention that could have affected the results. Future research should include larger sample size and a longitudinal study. Furthermore, future research should examine the A-Not-B task to understand underlying abilities. The associations between shifting, co-occurring conditions, and motor skills should continue to be examined due to increase knowledge surrounding these associations since questions remain on how these abilities interact and are related to each other.

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