Early Motor Development and Co-occurring Biomedical Conditions in Toddlers with Down Syndrome

Honors Thesis

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Background

Down syndrome (DS) is a neurogenetic condition present in 1:800 live births (Bull, 2020). DS is caused by the presence of a third copy of chromosome 21, known as trisomy 21. Trisomy 21 and the overexpression of genes on chromosome 21 are associated with intellectual disability (ID) and a variety of distinct physical characteristics (Bull, 2020). DS is the most common chromosomal cause of ID, typically presenting with mild to moderate severity (National Institute of Child Health and Human Development, 2023). Individuals with DS are also at a higher risk of developing co-occurring biomedical conditions, including congenital heart defects (CHD), neurological disorders, such as infantile spasms and seizure disorders, and vision problems (Bull, 2020).

Evidence to date suggests that motor skills are a key area of developmental vulnerability in DS (Sacks & Buckley, 2003). Characterizing early motor skill acquisition in infants with DS is critical to better tailor interventions and therapies to optimize outcomes. This study aims to characterize the range of motor skill presentations within a large sample of infants with DS, and the association between motor skills and co-occurring biomedical conditions.

Importance of Motor Skills

Motor skills refer to body movements, which can be categorized into gross and fine motor skills (Sacks & Buckley, 2003). Gross motor skills involve large muscle group coordination, apparent in activities such as walking, sitting, crawling, and running. Gross motor skills facilitate developmental skill acquisition across many early childhood domains. Planning and organizing movement are important for participation in community settings, getting dressed, and ambulating safely within school and home environments. Additionally, gross motor skills are

important for different recreational activities, such as playing on a playground, throwing a ball, and imaginative play with peers. Comparatively, fine motor skills require more precision, most evident when using utensils, cutting with scissors, and writing (Sacks & Buckley, 2003). Hand and finger dexterity is important for environmental exploration, object manipulation, and engaging with different toys, both at home and in school. Fine motor skills are important for accomplishing different activities of daily living (ADLs), such as toileting, teeth brushing, and feeding. Both fine and gross motor skills are important to the daily life of a child, as they learn to engage with their home, school, and community settings.

Motor skill development also impacts achievement in other domains of development. McClelland and Cameron (2019) described how motor skills can affect academic success. They identified that motor skills are critical for early learning, allowing children to navigate and engage in academic settings. They also reported that gross and fine motor skills are important for learning to read and write, as students are required to sit upright and use precise dexterity for these academic tasks. Moreover, they also indicated that gross motor skills are critical for building self-confidence and appropriate social skills (McClelland & Cameron, 2019). This information suggests that motor skills can significantly impact academic performance. Although this study does not discuss early motor development, this information is useful for understanding the impact of motor milestones on classroom learning.

Additional research suggests that very early motor skills play an important role in facilitating broader developmental skill acquisition in critical domains, like cognition (Libertus et al., 2016). A study by Libertus et al. (2016) implemented parent-guided motor training at 3 months of age to determine if it would increase object exploration and attentiveness at 15 months of age. This study found that motor skills did affect both attention and object exploration and

reported a correlation between the developmental domains (Libertus et al., 2016). This supports their claim that motor skills trigger a developmental cascade and affect other domains, suggesting that motor skills can affect cognition, highlighting the importance of early motor development. Similarly, a research paper by Keen (2011) reported that fine motor skills, such as reaching and grasping, reflect cognitive abilities in young children. Keen suggested that infants might use mental imagery and memory to make motor adjustments. She emphasized the importance of object exploration in accomplishing certain tasks, highlighting the importance of gross motor skill development in enabling environmental exploration (Keen, 2011). Evidenced by the current literature, motor skills may serve as a precursor for other developmental domains in the general population of infants and young children, emphasizing the importance of meeting motor milestones. Within this developmental cascade framework, delays in meeting motor milestones may have implications for broader developmental outcomes. Given the critical importance of meeting motor milestones in the general population, there is a need to investigate the nature of early motor delays in DS.

Emergence of Motor Skills

Motor skill delays in children with DS have wide-ranging implications for functioning in school, play, and recreational settings. Understanding the emergence of motor skills in this population will inform more tailored, person-centered interventions and treatments. A study by Winders et al. (2019) contributed to the effort to develop a gross motor schedule for children with DS. A gross motor schedule provides the norms for gross motor development in children with DS, allowing providers to compare the milestone acquisition of an individual patient to their peers. This allows providers to identify which patients are demonstrating more significant delays when compared to other children with DS. The Winders study followed 509 children

longitudinally, ages birth to ten, and reported on 44 gross motor skills of interest. This study found the mean age that children with DS walked independently was 26 months (Winders et al., 2019). A study conducted by the World Health Organization (WHO) assessed 816 typically developing infants and found that the mean age of independent walking was 12.1 months (WHO Multicentre Growth Reference Study Group & de Onis, 2006). The Winders study found that, on average, infants with DS were sitting at 10.3 months, whereas the WHO study found that, on average, neurotypical infants were sitting at 6 months. The studies reported that, on average, infants with DS were crawling at 14.2 months, compared to an average age of 8.5 months in the neurotypical group (Winders et al., 2019; WHO Multicentre Growth Reference Study Group & de Onis, 2006).

In addition to reporting the mean values, the Winders study reported the 5th and 95th percentile values for all skills to display the wide range of scores seen in the population. Children with the greatest degree of delays, or scoring at the 95th percentile, were walking independently at 40 months, sitting at 15 months, and crawling at 23.2 months (Winders et al., 2019). By including individuals with more pronounced developmental delays, the Winders study addressed the heterogeneity commonly seen in DS. The Winders study reported the wide spectrum of motor outcomes, whereas past DS research has primarily focused on group-level findings (Onnivello et al., 2023). The present study is interested in reporting on the heterogeneity seen within a small, critical window in development, similar to the methodology seen in the Winders study.

The information from both studies suggests that the majority of infants with DS are delayed in mastering certain motor skills. The Winders study provided valuable information about gross motor development in a large and diverse sample of children with DS. This provided

fundamental information for better understanding general motor development, while also displaying the high level of variability seen in the population. The Winders study is useful for healthcare providers to broadly compare motor skill acquisition within the DS population. However, there is a lack of specificity within a narrow age range of infants and their motor abilities. As seen in the Libertus, Joh, and Needham (2016) study, early infant motor skills may have ramifications for later outcomes in development. The current study is interested in focusing on a narrower, earlier age range to better understand the different motor presentations in a specific cohort. This, along with the Winders study, will support healthcare professionals in caring for infants with DS.

Measuring Motor Outcomes

Methodology plays an important role in motor skill research because of the need to collect data that accurately represents the child's motor skills. Motor outcomes can be assessed using direct assessment measures, or indirectly, using parent proxy reports. Both approaches have advantages and disadvantages. Proxy report measures provide valuable information that may be unavailable to researchers in a laboratory setting (Miller et al., 2017). This can be due to a variety of factors, such as children being more fearful or less cooperative in research facilities. Parent reports are also more cost effective, allowing for fewer barriers to participation. Additionally, parents can provide insight on their child that would otherwise remain undocumented in traditional assessments. Despite these benefits, there are several challenges associated with parent report measures. Parents and caregivers may interpret a child's behavior and abilities with subjective appraisals. Parents are also accustomed to their child and may unknowingly have biases regarding their child's behaviors. Finally, parents may under report their child's challenges due to the possibility of a developmental delay diagnosis.

In contrast, direct assessment tools provide an objective measurement of the child's developmental skills. Direct testing compares the child's scores to standardized scores, allowing for a comparison to the general population. Additionally, assessments are conducted by trained examiners with backgrounds in child development, providing an objective perspective and less biases. However, children may be less likely to provide a complete picture of their behavioral patterns in an unfamiliar environment. Moreover, developmental assessments are more costly and thus less accessible to the general public (Miller et al., 2017). Overall, parent proxy reports are more cost effective and provide critical information that would otherwise go undocumented; however, they may contain parental biases. In contrast, direct assessments provide an objective measurement with less biases, but they may not accurately describe the child's full skillset, while also being more costly. By using standardized assessments and proxy reports, there is potential for providing a more holistic and accurate account of motor skills. More information is needed about the convergence of these two types of measurement approaches when studying young children in this population. Using both measurements may provide valuable, complementary information, which could contribute to the understanding of motor development in the selected cohort.

Co-occurring Biomedical Conditions

Many factors may contribute to delays in motor development and the variability of motor skills seen in DS, but a key area of interest is co-occurring biomedical conditions. Children with DS are more likely to have CHD, neurological conditions, and vision problems (Bull, 2020). Understanding a potential correlation between biomedical factors and early motor skill acquisition could contribute to the growing body of motor skill research, as well as support future interventionists and providers.

Congenital Heart Defect (CHD)

Between 40 to 63.5% of individuals with DS are born with a CHD (Benhaourech et al., 2016), and CHD is the leading cause of mortality and morbidity during the first two years of life in this population (Benhaourech et al., 2016). The high prevalence of CHD in children with DS poses a question of whether motor skills are affected by CHD. Analyzing a possible correlation between CHD and motor skills may be useful for implementing specific interventions for children with DS and CHD. Additionally, consistent hospitalizations can negatively impact a child's development (Fardell et al., 2023). Fardell et al. (2023) conducted a population-based longitudinal cohort study using the medical and school records of children in different areas to determine how hospitalizations affect children's development. They identified 67,677 hospitalized children with and without chronic conditions and compared their development to 85,174 children without hospitalizations. They found that children with a history of hospitalizations were more likely to be developmentally vulnerable (Fardell et al., 2023). This information indicates a possible correlation between developmental delays and frequency of hospitalization, but more information is needed to better understand if CHD and motor delays are directly correlated.

Neurological Conditions

Infantile spasms are also important to consider when evaluating early individual differences among young children with DS. Infantile spasms are the most common seizure type in the DS population, occurring in 2.5-3.1% of individuals (Daniels et al., 2019). Infantile spasms can lead to future seizure disorders and greater developmental problems. The cause of infantile spasms remains unknown, with literature attributing it to decreased neural density, fewer inhibitory interneurons, or cardiovascular comorbidities (Daniels et al., 2019). Early-life

seizures can have several ramifications, such as problems with fine motor and visuospatial skills (Jensen-Willett et al., 2022). This may be indicative of possible correlations between motor milestone achievements and infantile spasms, but to date, there is little evidence for the association between seizure disorders and motor milestone acquisition in children with DS. More research is needed to address this question to better support intervention strategies for infants with DS and neurological conditions.

Ophthalmic Problems

In addition to CHD and neurological conditions, ophthalmic refractive errors, such as myopia and hyperopia, are the most common eye problems found in individuals with Down syndrome, with studies reporting a prevalence of up to 80% (Sun & Kraus, 2023). A review by Sánchez-González et al. (2022) reported how vision problems affect motor abilities in typically developing children. One of the studies in this review discussed that children with hyperopia, or farsightedness, performed worse than children with normal vision on a motor measure, suggesting that hyperopia may impair motor development. Another group of studies in this review found that children with amblyopia, commonly known as a lazy eye, had postural instability, less precise grip, and difficulties with planning and performing reaching movements (Sánchez-González et al., 2022). This poses a question of whether the presence of eye problems, such as refractive errors, significantly affects motor development in this population.

Visual perception is important for neurotypical infants to carry out different motor skills (Kobaş et al., 2023). This is because in order for infants to grasp and reach for different objects, they need to visualize the object's orientation, location, and appearance (Kobaş et al., 2023). Knowing that motor development is more likely to be delayed in this population, it is critical to evaluate if there is a direct relationship between visual acuity and motor skills in this population.

This information will support clinical interventions in the population, especially for children with visual acuity problems.

Conclusion

The current literature suggests that the emergence of motor skills is broadly delayed in children with DS (Winders et al., 2019). Additionally, current research highlights that motor skills are critical for early development, affecting future cognitive abilities, environmental exploration, and academic performance (Keen, 2011; Libertus, Joh, & Needham, 2016; McClelland & Cameron, 2019). This study aims to describe gross and fine motor skill presentations in a cohort of toddlers with DS. By providing an analysis of the range of motor skills in 1-year-olds with DS, early intervention therapists, developmental researchers, and healthcare providers can better understand which motor milestones can be expected at this age and what services can be utilized. Furthermore, current literature has identified a link between motor development and various biomedical conditions in the general population. This paper will examine how these biomedical factors affect motor skills in a cohort of infants with DS, which may be useful for determining a potential source of within-DS heterogeneity. Findings from this work can inform healthcare professionals regarding conditions that may require closer monitoring.

Methods

Participants

Participants were 117 infants with DS between the ages of 17.38 and 24.74 months, with a mean chronological age (CA) of 20.59 (SD = 1.56). 48.46% of infants were males. Developmental levels were determined using the Bayley Scales of Infants and Toddler

Development, Fourth Edition (Bayley–4). Infants had a mean developmental age of 11.55 months with a standard deviation of 2.7. All infants had a documented Trisomy 21 diagnosis indicated in parental reports.

Table 1: Participant Demographics (n = 117)

Child Characteristics	Mean (SD) or n (%)
Male	57 (48.46%)
CA	20.59 (1.56)
Developmental age	11.55 (2.7)
Participants with CHD	80 (68%)
Participants with Seizure Disorders	9 (8%)
Participants with Vision Problems	30 (26%)

Note: sex, CA, sample statistics, and developmental age values reported.

Procedures

Participants were a part of a large longitudinal study done in Massachusetts, Colorado, and California. Procedures were approved by the institutional review board (IRB) at Colorado State University. Infants participated in several visits at Colorado State University, where the Bayley–4 was administered by trained examiners. Examiners also conducted the Vineland Adaptive Behavior Scales, Third Edition (Vineland–3) caregiver interview. Caregivers provided written consent for the assessments before the first visit. Additionally, trained undergraduate research assistants entered the data from both measures. Graduate research assistants ensured that the data were entered correctly from physical copies.

Measures

Family Demographics and Biomedical History

Parents filled out several questionnaires on REDCap to provide infant demographic and biomedical information. This medical history questionnaire asked about co-occurring and previous conditions and procedures, including congenital heart defects, a history of heart surgery, eye examinations, and a history of seizures.

Bayley Scales of Infants and Toddler Development, Fourth Edition (Bayley-4)

The Bayley–4 is a developmental assessment tool used to diagnose developmental delays in early childhood (Introducing the Bayley–4). Infants in this study completed the five Bayley–4 domains: cognitive, language, motor, social–emotional, and adaptive behavior. The cognitive domain assesses the infant's attention, exploration, and manipulation. The language domain assesses the infant's receptive and expressive communication. The motor domain focuses on fine and gross motor abilities. The social–emotional domain regards an individual's ability to communicate one's needs, as well as emotional regulation skills. Finally, the adaptive behavior domain focuses on relating to others, such as playing and listening (Introducing the Bayley–4). This study only used data from the motor and cognitive domains. The data from the motor domain were used to determine gross and fine motor abilities, and the data from the cognitive domain were used to determine developmental levels. This measure produced an overall motor standard score ($M = 100$, $SD = 15$). These values can be compared to how other children of the same chronological age perform on the same Bayley measure.

Vineland Adaptive Behavior Scales, Third Edition (Vineland–3)

The Vineland Adaptive Behavior Scales, Third Edition (Vineland–3) caregiver interviews were administered to assess several domains: communication, socialization, daily living skills,

motor skills, and maladaptive behaviors (Vineland 3 Publication Summary). The communication domain involves expressive, receptive, and written language abilities. Socialization refers to interpersonal and coping skills. Daily living skills include feeding, bathing, and dressing. Motor skills refer to gross and fine motor, and maladaptive behavior refers to internalizing and externalizing behaviors. The Vineland–3 has a high internal consistency score, test-retest score, and interrater reliability score (Vineland 3 Publication Summary). This measure aims to provide a subjective and comprehensive assessment of developmental milestones. Similar to the Bayley measure, this measure produced an overall motor standard score (M = 100, SD = 15) to determine the infant's overall motor performance.

Data Analysis

Data visualizations and descriptive statistics were generated. Welch t sample tests were then conducted to evaluate mean values across different biomedical conditions. Finally, Pearson's correlations were calculated to assess convergence between the motor measures.

Results

Descriptive Statistics and Data Visualizations

Descriptive statistics and data visualizations for overall motor standard scores in both measures are presented in Tables 2 and 3.

Direct Assessment of Motor Skills

For the Bayley–4 motor domains, the mean standard score value for the sample was over two standard deviations below the normative mean (M = 100, SD = 15). Notably, the range of

overall motor scores was wide, with a minimum score of 45 and a maximum score of 87 (see Figure 1).

Table 2: Descriptive Statistics Overall Bayley–4 Motor Domains

Statistic	Overall Motor Standard Scores
Mean	60.11
SD	9.64
Range	Min = 45, Max = 87

Note: Mean, standard deviation, and range of standard scores provided for the overall motor Bayley–4 domain.

Caregiver Report of Motor Skills

For the Vineland–3 Motor domains, the mean standard score was below three standard deviations from the normative mean (M = 100, SD = 15). The distribution was bimodal and showed high variability with standard scores ranging from 20 to 89 (see Figure 2).

Table 3: Descriptive Statistics Overall Vineland–3 Motor Domains

Statistic	Overall Motor Standard Scores
Mean	54.03
SD	14.59
Range	Min = 20, Max = 89

Note: Mean, standard deviation, and range of standard scores provided for Vineland–3 overall motor domain.

Biomedical Conditions

No differences were found between the Bayley–4 and Vineland–3 motor scores means for CHD (t = 0.82; t = 1.63) and seizure disorders (t = 1.96; t = 1.54). However, a statistically significant difference was observed when comparing the overall motor means for ophthalmic problems across both measures (see Table 4). Infants with vision problems scored significantly lower than infants without vision problems in both the Bayley–4 and the Vineland–3.

Table 4: Ophthalmic Problems and Motor Standard Scores

Statistic	Bayley–4 Overall Motor Standard Scores	Vineland–3 Overall Motor Standard Scores
t value	2.91	3.10
df	56.99	57.13
p value	0.0052	0.0030
M in group 0 (no ophthalmic problems)	61.43	56.25
M in group 1 (ophthalmic problems)	56.10	47.57
CI (95%)	[1.66, 9.00]	[3.07, 14.30]

Note: t scores, degrees of freedom, p value, group means, and confidence intervals provided for both the Bayley–4 and Vineland–3.

Pearson's Correlations Between the Measures

Table 5: Pearson’s Correlations Between the Bayley–4 and Vineland–3

	bayley_gmscaledscore	*bayley_fmscaledscore*	*bayley_motss*	*vabs_motgmv*	*vabs_motfmv*	*vabs_motss*
bayley_gmscaledscore		0.444***	0.770***	0.873***	0.380***	0.719***
bayley_fmscaledscore	0.444***		0.876***	0.361***	0.630***	0.586***
bayley_motss	0.770***	0.876***		0.657***	0.613***	0.741***
vabs_motgmv	0.873***	0.361***	0.657***		0.408***	0.814***
vabs_motfmv	0.380***	0.630***	0.613***	0.408***		0.849***
vabs_motss	0.719***	0.586***	0.741***	0.814***	0.849***	

Computed correlation used pearson-method with listwise-deletion.

Note: Pearson's correlation values provided for Bayley–4 and Vineland–3 across fine motor, gross motor, and overall motor domains. Bayley_gmscaledscore indicates Bayley-4 gross motor scaled score, bayley_fmscaledscore indicates Bayley-4 fine motor scaled score, bayley_motss indicates Bayley-4 overall motor standard score. Moreover, vabs_motgmv means Vineland-3 gross motor scaled score, vabs_motfmv means Vineland-3 fine motor scaled score, and vabs_motss indicates Vineland-3 overall motor standard score.

The measures displayed high convergence, with statistically significant p values across all domains. All three domains, fine, gross, and overall motor, indicated strong correlations, as seen in Table 5.

Discussion

This study aimed to describe gross and fine motor skill presentations within a cohort of 1-year-olds with DS, and to evaluate the association between motor presentations and biomedical factors. On average, participants demonstrated performances that were two standard deviations below the normative mean across overall motor domains in both measures, demonstrating clear delays in early motor development. However, results also showed differences throughout the sample, as seen in the wide range of scores reported, suggesting that different trajectories of

motor skill acquisition may be observed among young children with DS. In addition, ophthalmic problems were associated with differences in gross and fine motor outcomes.

Fine Motor Delays

Infants in the sample displayed a wide range of fine motor delays across both measures. These delays could be attributed to a variety of reasons, one of which is the relationship between hand size and motor delays. Current literature suggests that individuals with DS may have shorter fingers and hands when compared to typically developing peers (Needham et al., 2021). This may contribute to fine motor delays seen in the present study. Fine motor skills are critical for academics and self-care activities, such as handwriting, personal hygiene, and cutting (Needham et al., 2021). A potential avenue for research may be understanding how early fine motor delays affect school-aged children. Additionally, the variability present in the sample raises questions about the need to report the heterogeneity seen in DS. Future research is needed to characterize individual findings in a cohort of infants with DS, and why heterogeneity is prevalent in this population.

Gross Motor Delays

In addition to fine motor delays, participants also displayed gross motor delays in both measures. The presence of gross motor delays for nearly all participants may be related to a number of underlying factors, including the widespread presence of hypotonia and joint laxity in DS (Malak et al., 2015). Ligamentous laxity, defined as increased range of motion in multiple joints when compared to the general population, and hypotonia, defined as low muscle tone that results in floppy muscles, are risk factors for delayed motor milestone achievement (Dasgupta, 2024; Foley & Killeen, 2019; Madhok & Shabbir, 2020). Low muscle tone can result in postural

abnormalities, thus delaying gross motor skills, such as walking (Malak et al., 2015). Early hypotonia may contribute to the gross motor delays seen across the sample. Moreover, ligamentous laxity is related to collagen levels, which are encoded by genes on chromosome 21, implying a possible correlation between DS and joint hypermobility (Foley & Killeen, 2019). The presence and extent of laxity and hypotonia may also contribute to the variability seen in the sample, a gap in the research that should be addressed.

Ophthalmic Problems

A key finding is that differences in motor presentations may be related to the presence or absence of reported ophthalmic conditions. Infants in the present cohort who had a reported ophthalmic problem demonstrated significantly lower motor scores than infants without vision problems. It is notable that this finding was observed despite the use of corrective glasses when needed and tolerated during their visit. Despite having their vision corrected, the group of infants with eye problems still scored significantly lower on motor assessments. This suggests that visual problems are not just about visual acuity, but perhaps a greater neurological disruption that also relates to motor development. A previous study from John et al. (2004) supports this idea, finding that neural abnormalities in the cortex and cerebellum may contribute to the visual problems seen in DS. Eye problems, even when corrected, significantly affected motor skills in the sample, which can have serious implications for development.

Correlations Between Bayley–4 and Vineland–3

The present study used direct assessments and caregiver interviews to gain a comprehensive picture of motor development within the sample. Domains were strongly correlated across both measures, indicating high convergence between the measures. This

suggests that both direct assessment and parent reporting tools provide converging information regarding a participant's motor skills. The r value was strongly correlated (r = 0.741) across the overall motor scores between the measures. Additionally, the r values were strongly correlated (r = 0.630; r = 0.876) across fine and gross motor scores. The information gained from direct assessments seemed to align with caregiver report data, making caregiver reports a potentially more accessible way of obtaining accurate motor development data at this early age, and in this population.

Limitations

This study has several limitations. Infants with DS were recruited from areas with higher socio-economic statuses (SES), thus leading to a possible lack of sample diversity. Additionally, infants were recruited from DS organizations, suggesting that participant families were already involved in support networks and possibly early intervention services to address motor delays.

Conclusion & Future Directions

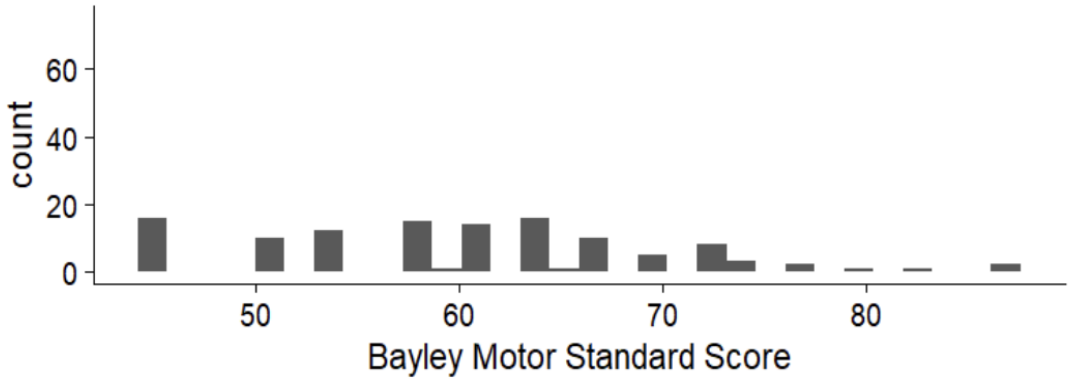
The present study revealed important information about motor delays in early development in children with DS. The cohort of infants with DS exhibited delays in fine and gross motor domains across both measures, which is consistent with current research. Additionally, children with visual impairments were significantly more likely to have lower motor scores, suggesting a relationship between vision and motor development. The present study will assist healthcare professionals and early intervention therapists in improving developmental outcomes in infants with DS, thereby enhancing their quality of life.

Future directions involve repeating this study with a larger sample of infants with ophthalmic problems to address if reduced visual acuity are directly contributing to reduced

motor skills. Additionally, further investigation is needed to determine how cortex and cerebellum abnormalities may contribute to visual deficits. Moreover, future research should investigate if the presence of laxity and hypotonia are directly correlated to the extent of motor delays.

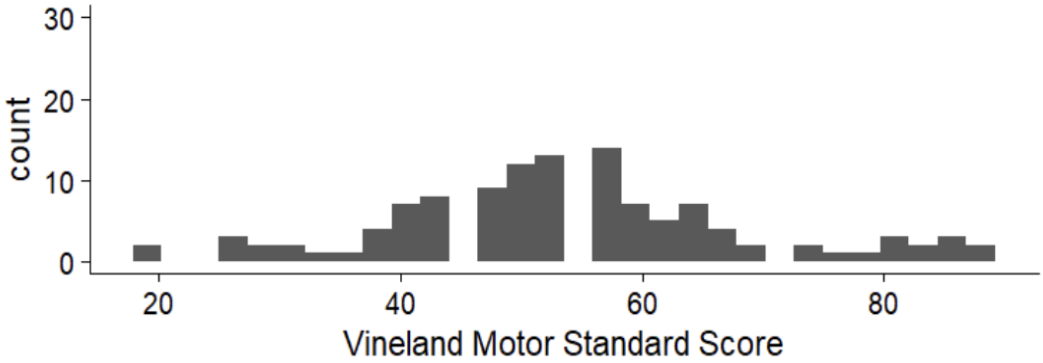
Figures

Figure 1: Bayley Overall Motor Standard Score



Note: figure shows overall motor standard scores from the Bayley–4.

Figure 2: Vineland Overall Motor Standard Score



Note: Vineland–3 bimodal histogram shown above.

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