Symposium Title: The Intersection of Motor and Other Domains Across ID and Other Neurodevelopmental Disorders

Chair: Audrey Thurm, PhD

Discussant: Cristan Farmer, PhD

Overview: Intellectual Disability (ID) and Autism Spectrum Disorder (ASD) are both neurodevelopmental disorders with diagnostic classifications that do not explicitly include motor delays or impairments as diagnostic criteria. However, motor impairments are frequent and often significant in individuals with both idiopathic and genetically associated ID. In fact, for profound ID, a term Profound Intellectual and Multiple Disabilities (PIMD) is used to indicate that more pervasive impairments characterize many individuals, with motor deficits often prominent. Motor impairments have been studied less in ASD, but recent studies do show some evidence of lower adaptive functioning in the motor domain, compared to same-aged peers. However, very little research has focused on 1) understanding the intersection of how motor impairments, either early on or later in development, relate to neurodevelopmental outcomes, and 2) our ability to measure and accurately assess other important aspects of functioning in individuals with major motor impairments. Moreover, there may be significant confounding effects of cognitive or other areas of functioning (e.g. social-communication) on measurements of motor development.

Here we report on three papers that highlight the ways in which motor delay and impairment, and measurement of functioning in other areas, may show bidirectional effects. In the first paper, the sample includes children with fragile X syndrome, examining both fine and gross motor early trajectories as they relate to language development, finding that fine motor skills, gross motor skills, and to some extent, parent reports of attention shifting, relate to specific aspects of language development by 5 years of age. The second paper focuses more specifically on the gross motor milestone of age of walking as it relates to ID, both in the context of ASD and without. Striking differences were found in the amount of delay in this early marker of gross motor development between these groups, underscoring the early motor delays that are prominent in ID but much less common in ASD in the context of ID. The third paper also examines an ASD sample, finding variability in the early development of both fine and gross motor adaptive functioning between the ages of 3 to 6, and a specific association between the worsening of ASD social-communication symptoms and declines in gross motor adaptive functioning development, compared to same-aged peers. Several of these findings, including this last one, raise questions about our ability to isolate specific constructs, including motor development, in children with various developmental delays. Taken together, these papers provide further evidence for the importance of examining early motor development, even with basic parent report methods, as it relates to the development of specific neurodevelopmental disorder developmental pathways and outcomes.

Paper 1 of 3

Paper Title: The Effect of Motor Abilities on Language Outcomes in Fragile X Syndrome: The Moderating Role of Attention

Authors: Elizabeth Will, PhD2, Jordan Wickstrom, PhD1, Jane Roberts, PhD2

Introduction: Challenges with motor development are common in fragile X syndrome (FXS), emerging in infancy (Hinton et al., 2013) and persisting throughout early development (Bailey et al., 2001; Will et al., 2018). Since it is well-established that motor skills are foundational for communication and language development (Walle & Campos, 2014), impaired motor abilities in addition to cognitive delays, may hinder language and communication in FXS. Furthermore, developmental complexities suggest that attentional abilities may exert additional influence on the role of motor abilities as a mechanism for communication outcomes in FXS (Bruyneel et al., 2019; Kover et al., 2015). Thus, we aimed to identify the role of attention as a moderating factor of motor development on communication outcomes in children with FXS.

Methods: Participants were drawn from a larger prospective longitudinal study and included 51 children with FXS (14 females). Participants had a mean chronological age (CA) of 16 months at initial enrollment and were assessed at regular intervals between

1 The National Institutes of Health
2 The University of South Carolina
6 and 60 months. Measures included the Mullen Scales of Early Learning (MSEL; Mullen, 1995), the Early Childhood Behavior Questionnaire (ECBQ; Putnam et al., 2006), and the Vineland Adaptive Behavior Scales – 2nd Edition Interview (VABS-II; Sparrow et al., 2013). The ECBQ includes an Attention Shifting domain, which was used as a moderator. The VABS-II was our outcome measure of receptive and expressive communication at the last assessment (i.e., typically at 48 or 60 months). First, trajectories of fine and gross motor development were estimated using random slopes and random intercepts models in a multilevel framework. The intercepts and slopes for each of these models were then used as predictors, along with attention shifting, of receptive and expressive communication outcomes. Finally, an interaction term of attention shifting (centered at 24 months) and the motor trajectory parameter (i.e., slope) was included in each model to determine the effect of attention shifting on motor development in predicting communication outcomes.

Results: In the first model, early (i.e., the intercept) gross motor \( b=1.82; p=.004 \), was identified as a significant predictor of receptive communication outcomes, whereas the trajectory parameter and attention shifting were not. There was also no significant interaction between gross motor development and attention shifting on receptive outcomes. Results from the second model indicated that early fine motor \( b=3.43; p<.001 \), the trajectory of fine motor \( b=-378.11; p=.005 \), and attention shifting \( b=6.43; p=.020 \) were all significant predictors of receptive communication outcomes. There was also a significant difference in the effect of fine motor development (i.e., the slope) on receptive communication outcomes as a function of attention shifting \( b=-18.41; p=.003 \). Results from the third model indicated that early gross motor skills \( b=4.72; p=.014 \) were a significant predictor of receptive outcomes, whereas there was no significant effect of gross motor development (i.e., the slope) or attention shifting on receptive communication outcomes. The final model results indicated that early fine motor was also a significant predictor of expressive communication outcomes \( b=6.19; p=.019 \), whereas fine motor development (i.e., the slope) and attention shifting were not.

Discussion: The present study examined whether gross and fine motor development exacts a specific influence on receptive and expressive communication outcomes in children with FXS and considered if and how attentional abilities moderated these associations. Collectively, findings indicated that early fine and gross motor development is an important foundation for both receptive and expressive communication outcomes in children with FXS. Interestingly, motor development over time was only a significant predictor of receptive communication outcomes. Attention shifting was also a significant predictor of receptive communication, as well as a significant moderator on the effect of fine motor on receptive communication outcomes. While early gross motor was a significant predictor of receptive and expressive communication, gross motor development over time did not influence either type of communication outcome. Overall, study findings have implications for targeted intervention efforts, which should aim to address motor impairments in FXS early in development in order to improve communication outcomes. Additionally, these efforts should also consider the role of attentional shifting on the influence of fine motor development on receptive communication outcomes in FXS.

References/Citations:


Paper Title: Late Walking and Intellectual Disability in Autism Spectrum Disorder: Insights from Analysis of a Population-Based Sample

Authors: Alexandra Havdahl, PhD3,4,5 Cristan Farmer, PhD1, Synnve Schjolberg, Cand.Psychol.6, Anne-Siri Øyen, PhD3,4, Pål Surén, PhD6, Ted Reichborn-Kjennerud, PhD6, Per Magnus, PhD3, Michaeline Bresnahan, PhD6,7, Mady Hornig, MD7, Ezra Susser, PhD6,7, W. Ian Lipkin, MD5,8, Catherine Lord, PhD9, Camilla Stoltenberg, PhD4,10 Audrey Thurm, PhD1, Somer Bishop, PhD11

Introduction: Delayed walking (≥18 months) is a common precursor of intellectual disability. Findings suggest that late walking may be less common when intellectual disability occurs in the context of an autism spectrum disorder (ASD). However, previous studies were limited by reliance on samples from ASD clinics and exclusion of children with severe motor deficits. The objective of the current study was to examine, in a population-based sample, if late walking is differentially related to intellectual disability in children with ASD versus children with other childhood-onset psychiatric or neurodevelopmental disorders (CPD). A secondary aim was to examine if a differential relationship is also observed for other markers of early development.

Methods: The Norwegian Mother, Father and Child Cohort Study (MoBa) is a prospective pregnancy cohort study established by the Norwegian Institute of Public Health in 1999, with nationwide recruitment of mothers in association with routine ultrasound examinations (41% participated; Magnus et al., 2016). The cohort includes 114,500 children, 95,200 mothers, and 75,200 fathers. Clinical assessments to identify children with ASD were undertaken in a nested substudy, the Autism Birth Cohort (ABC) Study. Children assessed in the nested ABC Study in 2005-2012 (age 3-11 years), were invited based on questionnaire screening, referral, patient registry linkage and random selection (approximately 50% participation: n=1,033). We applied Cox proportional hazards regression to assess if diagnosis (ASD n=212 versus CPD n=354), nonverbal IQ, and their interaction, were associated with walking age. Secondary analyses replaced walking age with gestational age, birthweight, APGAR scores, and language milestones.

Results: At lower levels of nonverbal IQ, children with ASD were likely to walk earlier than children with CPD (Group x nonverbal IQ interaction, χ²=13.93, p=0.0002). Among those with intellectual disability (nonverbal IQ<=70), on-time walking was observed in 67% (95% CI=54-78%) of children with ASD compared to 15% (95% CI=7-29%) of children with CPD. Although several of the

3 Nic Waals Institute, Lovisenberg Diakonal Hospital
4 Norwegian Institute of Public Health
5 MRC Integrative Epidemiology Unit, University of Bristol
6 New York State Psychiatric Institute, Columbia University Medical Center
7 Department of Epidemiology, Mailman School of Public Health
8 Center for Infection and Immunity, Mailman School of Public Health and Departments of Neurology and Pathology, Vagelos College of Physicians and Surgeons of Columbia University
9 David Geffen School of Medicine, University of California, Los Angeles
10 Department of Global Public Health and Primary Care, University of Bergen, Bergen, Norway
11 10 UCSF Weill Institute for Neurosciences, University of California

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secondary markers differed by diagnostic group and/or nonverbal IQ, there was little evidence of any interaction between diagnostic group and nonverbal IQ.

Discussion: The majority of children with ASD walked on-time, even at very low levels of intellectual ability, while the vast majority of children with intellectual disability but not ASD walked late. The results are consistent with previous findings and fill an important gap left by previous clinic-based studies by providing an epidemiologically-ascertained sample. The study provides support for the hypothesis that intellectual disability, especially in the context of ASD, may be the result of heterogeneous developmental pathways. Late walking may be a useful stratification variable for characterizing these differences in etiological research.

References/Citations:


Paper Title: Characterizing Fine and Gross Motor Skill Developmental Profiles of Children with Autism Spectrum Disorder

Authors: Alexandra Sturm, PhD12, Jordan Wickstrom, PhD1, Teresa Bennett, MD, PhD13,14, Eric Duku, PhD14, Mayada Elsabbagh, PhD15,16, Cristian Farmer, PhD1, Stelios Georgiades, PhD14, Pat Mirenda, PhD17, Isabel M Smith, PhD18,19, Peter Szatmari, MD20,21, Audrey Thurm, PhD22. *Bookmark not defined.*, Wendy J Ungar, PhD21,22, Tracy Vaillancourt, PhD23, Joanne Volden, PhD24, Charlotte Waddell, MD25, Anat Zaidman-Zait, PhD26, Lonnie Zwaigenbaum, PhD24, Somer Bishop, PhD11

Introduction: There is increasing evidence that, despite motor skill being an area of adaptive functioning relatively less impaired than others for many young children with autism spectrum disorder (ASD), various motor delays and impairments are prevalent in this population. A common instrument standardized to assess motor functioning in early childhood is the Vineland Adaptive Behavior Scales. While some studies have examined Vineland-II adaptive behavior trajectories in ASD (Bossu et al., 2019; Farmer et al., 2018; Franchini et al., 2018), subgroups of motor functioning trajectories and their relationship to core ASD symptoms have not been identified.

12 Loyola Marymount University
13 McMaster Children’s Hospital
14 McMaster University
15 Montreal Children’s Hospital
16 McGill University
17 University of British Columbia
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19 IWK Health Centre
20 Centre for Addiction and Mental Health, University of Toronto
21 The Hospital for Sick Children
22 University of Toronto
23 University of Ottawa
24 University of Alberta
25 Simon Fraser University
26 Tel Aviv University
Methods: We examined Vineland-II Fine and Gross Motor domains longitudinally in 421 children (84% male) with ASD who participated in the Pathways Longitudinal Study (Szatmari et al., 2015). Parents completed the Vineland Comprehensive Parent Interview when their children were on average 40.25, 47.91, 54.00, and 79.53 months of age. The purpose of the present study was three-fold in children with ASD: (1) evaluate the stability of comparative gross and fine motor skills, (2) identify trajectories of gross and fine motor skill development, and (3) determine if changes in social communication impact the trajectories of gross and fine motor skills. To accomplish these aims, the number of individuals who fluctuated ≥1 standard deviation between two time points on the Vineland-II for Fine Motor and Gross Motor V scale scores were tabulated. To identify trajectories, the number of individuals who had an increase of ≥1 standard deviation (increasing trajectory group), decrease of ≥1 standard deviation (decreasing trajectory group), and ≤1 standard deviation change (no change group) for Fine and Gross Motor scores between Time 1 (40.25 months) and Time 4 (79.53 months) was tabulated. The average trajectory of change for Fine and Gross Motor scores was also computed using all four time points in a mixed-effects regression model. Finally, a mixed-effects regression model was used to evaluate the impact of change in ADOS Social Affect Calibrated Severity Scores (SA CSS; MT1=7.13, MT2=5.85, MT4=5.34), measured at Time 1, 3, and 4 (time-varying covariate) on change in Gross and Fine Motor scores.

Results: Results revealed that 43% (N=182) of the children with ASD included in the present study exhibited fluctuating Fine Motor scores (+/- 1 SD) between at least one consecutive pair of time points. In addition, 27% (N=112) of the children with ASD exhibited fluctuating Gross Motor scores (+/- 1 SD) between at least one consecutive pair of time points (refer to Figures 1a and 1b). Mixed-effects model analyses revealed no overall significant change in Fine Motor V scale scores from Time 1 to Time 4 (β = -0.014, p = .752), and an overall significant decrease in Gross Motor V scale scores from Time 1 to Time 4 (β = -0.220, p < .001). Trajectory tabulation revealed decreasing trajectory (N=49, 17%), increasing trajectory (N=43, 15%) and no change (N=197, 68%) groups for Fine Motor skills and decreasing trajectory (N=60; 21%), increasing trajectory (N=20, 7%) and no change (N=209; 72%) groups for Gross Motor skills. Mixed-effects regression analyses revealed no significant association between SA CSS and Fine Motor V scale scores (β=-0.013, p = .640), and a significant association between SA CSS and change in Gross Motor v scale scores (β=-0.06, p < .010), such that an increase in ADOS SA CSS scores resulted in a corresponding decrease in Gross Motor V scale scores.

Discussion: This study directly examined fine and gross motor skill trajectories (using Vineland-II scores), and how these trajectories are impacted by social communication (using ADOS SA CSS), in children with ASD. Analyses revealed a general lack of stability of scaled scores over relatively short periods of time. Such lack of stability is important to consider when using cross-sectional data to examine motor profiles of children of different ages, as the same child might end up in different motor skill groupings depending on when the assessment took place. Analyses further suggested that changes in social communication were associated with changes in Gross Motor, but not Fine Motor, scaled scores. Additional planned analyses will directly examine how trajectories of motor functioning are related to intellectual ability. Additionally, we will examine whether attainment and/or measurement of certain types of motor skills is affected by severity of ASD-related impairments. This work has the potential to advance our understanding of developmental cascades in ASD related to attainment of motor skills, as well as inform our understanding of measurement issues in the assessment of motor skills in ASD.

References/Citations:


**Figures 1a and 1b**

*Note:* Plots detail individuals score trajectories for each individual included in the present analyses. The bold horizontal line denotes a v scale score of 15, the average v scale score for each motor domain.