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RESEARCH ARTICLE

Objective measurement of movement variability using wearable sensors predicts ASD outcomes in infants at high likelihood for ASD and ADHD

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Abstract

Early motor delays and differences are common among children with autism spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (ADHD). Yet, little work has shown whether there are early atypical motor signs that differentiate these groups. Quantitative measures of movement variability hold promise for improving the identification of subtle and specific differences in motor function among infants and toddlers at high likelihood for ASD and ADHD. To this end, we created a novel quantitative measure of movement variability (movement curvature) and conducted a preliminary investigation as to whether this measure improves outcome predictions. We used a wearable triaxial accelerometer to evaluate continuous motion-based activity in infants at high and low likelihood for ASD and ADHD at 12, 18, 24, and 36 months of age. At 36 months, participants were categorized into three outcome groups: ASD ($n = 19$), ADHD concerns ($n = 17$), and a comparison group ($n = 82$). We examined group differences in movement curvature and whether movement curvature is predictive of a later ASD or ADHD concerns classification. We found that movement curvature was significantly lower in infants with later ASD diagnosis at 18, 24, and 36 months of age compared to infants with either ADHD concerns or those in the comparison group. Movement curvature was also a significant predictor of ASD at 18, 24, and 36 months (AUC 0.66–0.71; $p = 0.005$–0.039) and when adjusting for high ASD likelihood at 18 and 24 months (AUC 0.90, $p = 0.05$–0.019). These results indicate that lower movement curvature may be a feature of early motor differences in infants with later ASD diagnosis as early as 18 months of age.

Lay Summary

Motor differences are common and often present in early childhood in ASD and ADHD. Here, using a triaxial accelerometer and developmental measures, we developed an objective measure of movement variability and found that lower movement variability predicts an outcome of ASD as early as 18 months of age. Our findings suggest that less variable movement may be a motor difference in infants with later ASD diagnosis.

KEYWORDS
attention-deficit/hyperactivity disorder, autism spectrum disorder, complexity, infants, motor skills, sensors, variability

INTRODUCTION

Autism spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (ADHD) are two prevalent neurodevelopmental disorders (NDDs) that manifest in early childhood. Despite being distinct neurodevelopmental conditions according to current classification systems, ASD and ADHD often cooccur and share similar traits (Johnson et al., 2015; Miller et al., 2018, 2023). Increasingly, efforts have been made to better understand early behaviors that may be shared or differentiate these two conditions to improve early detection and developmental monitoring (Miller et al., 2018). Motor delays and challenges have been frequently reported in ASD and ADHD, both as a prodromal symptom and manifesting through childhood (Athanasiadou et al., 2020; Bhat et al., 2011; Gurevitz et al., 2014). The onset and development of motor skills are clearly visible behaviors that caregivers and clinicians monitor closely in early infancy and throughout childhood to track developmental progress. These motor skills lay an important foundation for how a child engages with their environment and subsequently underlie advances in the development of language and other critical cognitive processes (Campos et al., 2000; Iverson, 2010; Karasik et al., 2012; Piaget, 1952; Walle & Campos, 2014). Conversely, motor delays can impact the development of language, social communication, and spatial perception (Choi et al., 2018; Lebarton & Iverson, 2016; Leonard et al., 2015). Motor challenges such as delayed motor milestones and asymmetric movements have been frequently reported to manifest early in infants at high likelihood for ASD (Bhat et al., 2011; Iverson et al., 2019; Teitelbaum et al., 1998; Wolff et al., 2017). These motor challenges often present as difficulty in coordination, delayed fine and gross motor movements, impaired visuospatial skills, and atypical gait (Bhat, 2020; Fournier et al., 2010). Qualitatively, these motor differences in ASD are often described as clumsy or difficulty generating fluid fundamental motor skills. Similarly in ADHD, motor differences as early as infancy have been described. One retrospective study reported that infants who went on to receive a later diagnosis of ADHD showed delayed gross motor milestones as early as 3 months of age and these delays persisted at 18 months of age (Gurevitz et al., 2014). Studies have also described increased gross motor activity and decreased motor suppression as early motor manifestations of ADHD (Friedman et al., 2007). In the DSM-5, motor deficits such as odd gait and clumsiness are described as being common in ASD and that motor delays often occur in ADHD (American Psychiatric Association, 2013). However, there is a paucity of literature on whether there are motor differences in early childhood that differ between ASD and ADHD.

The range and overlap of motor differences that have been described in these two highly prevalent NDDs may be secondary to which motor domains have been primarily studied (motor milestones in ASD vs. amount of movement in ADHD) and the type of motor assessments used in these studies. Many commonly used standardized assessments of motor function in the first 3 years of life rely heavily on motor milestone achievement and binary classification of motor ability (Wilson, Mccracken, et al., 2018). The use of quantitative and objective tools to measure motor abilities may better identify subtle differences in infants and toddlers at high likelihood for, and diagnosed with, ASD and ADHD. Identification of motor differences that emerge prior to behavioral symptoms of ASD and ADHD and after symptoms are readily visible are both of importance as it can lead to early detection and general developmental monitoring and support. Wearable sensor technology is one method to examine motor skills in infants and toddlers, which can overcome some of the limitations of current standardized motor assessments. Wearable sensors are lightweight and allow for continuous and passive monitoring of participants' motion during different environmental contexts (Hoyt et al., 2019; Wilson et al., 2021). These sensors can easily be placed on an infant's or toddler's body to measure movements during clinical and research assessments of behavior and developmental ability (Hoyt et al., 2019; Reetzke et al., 2022; Smith et al., 2015). Sensors may detect subtle movement differences that are not captured by standardized caregiver report or direct assessment of motor ability. Utilizing quantitative and objective sensor measures may allow for improved detection of motor differences that are shared or differentiate toddlers at high likelihood for ASD and ADHD. A prior study reporting on the current sample used a triaxial accelerometer to measure mean activity and mean intensity of activity in toddlers with ASD and ADHD symptom concerns (Reetzke et al., 2022). The study found that both preschoolers with ASD and ADHD concerns had heightened levels of activity compared with typically developing toddlers by 18 months of age, suggesting that over-activity may be a shared, rather than distinct, motor precursor in infants/toddlers developing ASD and concerns for ADHD (Reetzke et al., 2022). Wearable technology captures large amounts of continuous motion data and allows a platform to explore novel movement metrics from these data. Further derivation of quantitative accelerometer measures that have a hypothesized link to well described ASD behaviors and motor delays may aid in identifying motor differences that (1) present in the prodromal period and serve as an early marker of atypical development, (2) may underlie persistent motor delays in this population, and (3) differentiate diagnoses of ASD and ADHD in early childhood. Furthermore, deep phenotyping of the motor domain in these prevalent NDDs will allow us to construct meaningful measures of motor function that can be evaluated in association with other measures of brain and behavior and improve our

understanding of neurobiological processes of ASD and ADHD.

This study examined differences in movement patterns objectively measured during assessments in the laboratory by a triaxial accelerometer from infants and toddlers 12–36 months of age. This sample was enriched for outcomes of ASD and ADHD concerns, specifically by examining infants with an older sibling with ASD and infants with a first-degree relative with ADHD. Objective motor measurements were examined for the duration of laboratory visits. Using the sensor data, we developed a novel measure that reflects the complexity and variability of movement. Conceptually, this measure is built upon a theoretical framework that healthy neuromotor development is associated with optimal complexity or variability of movement early in life (Hadders-algra, 2008). The ability to use a complex and variable set of movements to achieve specific motor tasks (e.g., walking, running, jumping, and climbing) is important in shaping neuromuscular development, motor learning, coordination, and fundamental motor skills (Harbourne & Stergiou, 2003, 2009). Thus, lower variability and complexity of movement may underlie the inability to develop a rich repertoire of well-coordinated motor behaviors, findings that are often described in ASD. This framework has been previously tested using a measure of motion complexity derived from a longitudinal sensor-based study of infants at high likelihood for ASD. As proof of concept, the motion complexity metric was found to be lower in a small sample of infants who went on to develop ASD compared with those who did not have ASD (Wilson et al., 2021).

In this study, we sought to further validate this theoretical framework by (1) examining a larger sample of infants at high likelihood for ASD, (2) including a comparison group with high likelihood for ADHD, an NDD with a high degree of behavioral overlap and cooccurrence with ASD, (3) constructing a new metric from continuous motion signal data, and (4) testing this novel metric using data from laboratory-based data collection sessions. This metric, which we refer to as curvature, may capture movement characteristics that differentiate infants at high likelihood for ASD from those with high likelihood for ADHD. In line with our previous work, we hypothesized that infants in the ASD outcome group would exhibit lower movement curvature compared with infants in the ADHD concerns and comparison outcome groups across both structured and unstructured contexts. We also hypothesized that lower movement curvature would be predictive of ASD outcomes. We conducted further exploratory analyses to determine the relationship between curvature and measures of developmental ability.

METHODS

The study protocol was approved by the University of California, Davis Institutional Review Board (IRB 1560974, PI: Ozonoff); written informed consent was obtained from parents before participation. Data collection was conducted at the UC Davis MIND Institute in Sacramento, CA between the years of 2013–2019.

Participants

Infants with an older sibling diagnosed with ASD (high likelihood ASD group; $n = 60$), an older sibling or parent diagnosed with ADHD (high likelihood ADHD group; $n = 29$), or no family history of either diagnosis (low likelihood group; $n = 29$) participated in developmental assessment and wore an accelerometer at 12, 18, 24, and 36 months of age as part of a completed longitudinal study.

High likelihood ASD group

Inclusion criteria included status as a younger sibling of a child diagnosed with ASD, with older sibling diagnosis confirmed using the Autism Diagnostic Observation Schedule-Second Edition (ADOS-2) (Lord et al., 2012) and the Social Communication Questionnaire (Rutter et al., 2003). Exclusion criteria included birth prior to 32-weeks gestation and a known genetic disorder in the proband.

High likelihood ADHD group

Inclusion criteria included status as a first-degree relative of someone with ADHD (i.e., older sibling or parent with ADHD). Proband ADHD diagnoses were confirmed with an intake screener (DSM-5 ADHD checklist) and clinician diagnostic reports/documentation of treatment for ADHD. If medical records were unavailable for sibling probands, the study team conducted a diagnostic evaluation (parent and teacher ADHD symptom rating scales, child cognitive testing). When records were unavailable for parent probands, eligibility was based on self-report of prior ADHD diagnosis and a T-score ≥ 65 on the ADHD Index from the Conners Adult ADHD Rating Scale (Conners et al., 1999), rated by partner/spouse. Exclusion criteria consisted of birth before 32-weeks' gestation; ASD in first-, second-, or third-degree relatives; or a known genetic disorder in the proband.

Low likelihood group

Inclusion criteria included status as a younger sibling of a child with typical development. Low likelihood group exclusion criteria included birth before 36 weeks of gestation; developmental, learning, or medical conditions in

any older sibling; and ASD or ADHD in any first-, second-, or third-degree relative.

Participants with a 36-month outcome visit were included in the study. At 36 months, participants from the three likelihood groups were classified into one of three outcome groups by a licensed clinical psychologist based on all available data and observations from the study visit. Participants were classified into the "ADHD Concerns" outcome group if they (a) received an examiner rated clinical best estimate outcome of "ADHD Concerns," and (b) exhibited ≥4 DSM-5 ADHD symptoms within any one symptom domain (i.e., inattentive or hyperactive impulsive) or ≥5 DSM-5 symptoms across both symptom domains (i.e., inattentive and hyperactive-impulsive combined) across reporters (e.g., parent and teacher report on the ADHD rating scale preschool version, examiner observation); at least one of the endorsed symptoms must have been reported on the ADHD rating scale by the parent or teacher to confirm evidence of ADHD symptoms across different environmental settings (Hill et al., 2020). Participants with ASD received a clinician-rated clinical best estimate outcome of "ASD" (met DSM-5 criteria for ASD) and received an ADOS-2-calibrated severity score ≥4 (Lord et al., 2012). The comparison outcome group included all participants who did not meet criteria for ASD or ADHD concerns at the 36-month outcome visit but did include those who may have other developmental concerns (e.g., speech-language delays).

Procedures

Continuous motion-based activity was recorded from the participants' ankles using Empatica E4 multisensor devices (McCarthy et al., 2016) at a sampling rate of 32 Hz across the duration of each visit (mean duration = 138.8 min, standard deviation of duration = 35.6 min) during assessments at 12, 18, 24, and 36 months of age. Variations in visit length were due to administration of the ADOS-2 beginning at 18 months of age and need for breaks for the child during testing.

Measures

Autism symptoms

Evaluation for autism symptoms was completed using the ADOS-2 (Lord et al., 2012), a semi-structured, standardized observation of social communication and repetitive behaviors. It was used to verify inclusion criteria in probands with ASD and determine 36-month outcomes. The total comparison score, social affect comparison score, and restricted and repetitive behavior (RRB) comparison score were used to evaluate the association of curvature and specific ASD related behavioral outcomes. The ADOS-2 was administered at the 18-, 24-, and 36-month visits and represented the semi-structured context.

ADHD symptoms

The Attention-Deficit/Hyperactivity Disorder Rating Scale (ADHD-RS), preschool version (McGoey et al., 2007) was used to assess for symptoms of ADHD. Caregivers completed the preschool version of this measure at the 36-month visit to inform outcome classification and as a continuous measure of preschool ADHD symptoms. Whenever possible, an additional observer who was familiar with the child (e.g., teacher or daycare provider) also completed the ADHD-RS. This constituted 59% of the ADHD Concerns outcome group and 58% of the full sample (across all three outcome groups). The remaining participants did not spend time in a daycare/preschool setting and therefore was no additional rater available.

Developmental abilities

Development was assessed with the Mullen Scales of Early Learning (MSEL) (Mullen, 1995). The MSEL is a standardized measure of developmental abilities for children ages 0–60 months. It is composed of five subscales scores for gross motor, visual reception, fine motor, expressive language, and receptive language. Raw scores, standard scores, and age equivalents can be derived for each subscale. Ratio scores for full-scale developmental quotient (DQ) were calculated for each child and based on division of the age-equivalent score by chronological age and used as a covariate in secondary analyses of the curvature metric.

Accelerometer derived measure

Our proposed motor metric, curvature, was constructed as follows. We first applied a Butterworth high-pass filter (order 4, critical frequency 0.2) to each dimension of the raw accelerometer output in order to reduce the impact of gravity (Reetzke et al., 2022). Next, we computed the L2 norm of the filtered acceleration vector at each time point to obtain a time series of acceleration magnitudes. We then smoothed this series by partitioning it into 14-second segments and calculating the average acceleration within each segment. Though this segment length was selected to roughly optimize the performance of the resulting metric, sensitivity analyses showed that metric performance was robust to a range of segment lengths.

Using the smoothed series, we performed a rolling window analysis as follows. Within each window, we

performed a percentile transformation of the average accelerations. The purpose of this step is to eliminate any distributional differences between windows, so that the metric is focused on the temporal structure of the acceleration series. Next, we computed the curvature of the percentiles (Curvature, 2024).

$$\kappa = \frac{\left|\frac{d^2p}{dt^2}\right|}{\left(1+\frac{dp^2}{dt}\right)^{3/2}},$$

where p is the average acceleration percentile, and t is time. We used first and second finite differences to approximate the first and second derivatives in the calculation above. Finally, we averaged κ over the windows to obtain a summary score for the entire acceleration time series. We used a window size of 100 (corresponding to approximately 23.3 min of data), which was also selected to roughly optimize for metric performance; here, too, sensitivity analyses suggested robustness to a range of window sizes.

The algorithm above was designed to focus exclusively on the local temporal structure of the average accelerations. High movement curvature indicates that accelerations tend to swing rapidly between locally large and locally small accelerations, suggesting a more complex and variable pattern, while low movement curvature indicates more gradual shifts and a less variable pattern. A window with $\kappa = 0$ is a straight line, while a window with $\kappa = 1$ is a maximally oscillating spiral.

Statistical methods

Descriptive statistics were computed for all study variables. Quantitative variables were summarized using means and standard deviations, and categorical variables were summarized using frequencies and percentages. Unadjusted group comparisons of quantitative variables were performed using one-way ANOVA F-tests, and comparisons of categorical variables were performed using chi-squared or Fisher's exact tests as appropriate.

Associations between curvature and quantitative outcomes within the group at high likelihood for ASD were evaluated using Spearman rank order correlation coefficients. Because curvature was captured at multiple ages for the same participant, we constructed a child-level variable as follows. First, we fit a linear mixed effects model to curvature, with a fixed age effect and a random child effect. We then predicted child-specific means at 24 months of age (the midpoint of our observation timeline). Correlations were then evaluated between this predicted child-level mean and 36-month outcomes.

To evaluate the predictive utility of curvature with respect to ASD and ADHD concerns outcomes, we used separate logistic regression models for each age. We fit several models: one containing just curvature at a given age, another adjusting for likelihood group only, a third model adjusting for contemporaneous Mullen full scale DQ score only, and a fourth model adjusting for both covariates. Models were summarized using odds ratios, 95% confidence intervals and p-values, and predictive performance was evaluated using the area under the ROC curve (AUC). To have an adequately powered comparison, our primary logistic regression model compared the ASD outcome group to ADHD concerns and the comparison groups combined. As an additional sensitivity analysis, we conducted a multinomial regression comparing the ASD and comparison groups, ASD to ADHD concerns groups, and the ADHD concerns and comparison groups.

p-values less than 0.1 were considered marginally significant and p-values less than 0.05 were considered statistically significant. The Benjamini–Hochberg step-up procedure was used to control the false discovery rate (FDR) of each analysis at the 10% level. We note which p-values did not remain significant after this correction. All analyses were performed using R v. 4.2.2 (http://www.r-project.org/).

RESULTS

Participant demographics and descriptive variables are presented in Table 1. We sought to evaluate whether the curvature metric was related to and predictive of later ASD diagnosis compared to ADHD concerns or the comparison group outcome classifications.

In unadjusted analyses (Table 2), we found that curvature was significantly associated with ASD at the 18-, 24-, and 36-month time points ($p = 0.039$, 0.005, and 0.038) respectively. Mean curvature was lowest at all three of these time points in children who were diagnosed with ASD (Figure 1). At the 12-month timepoint curvature was not significantly different between the ASD and ADHD concerns outcome groups. Correlation analyses within the high likelihood ASD group identified stronger associations between curvature and ADOS-2 comparison scores ($r = -0.36$, $p = 0.005$), than the association between curvature and Mullen overall DQ ($r = 0.27$, $p = 0.07$).

Regression analyses (Table 2) showed curvature to be a useful predictor of ASD outcome status at 18, 24, and 36 months of age, with odds ratios between 0.06 and 0.14 for each 0.1-increase in curvature (AUC 0.66–0.71; $p = 0.005$–0.039). Though baseline ASD likelihood is, by itself, a very strong predictor of ASD outcome status in this cohort (AUC: 0.79), the 18- and 24-month time points remained significant after adjusting for likelihood group, adding predictive value over and above baseline familial ASD likelihood (combined AUC: 0.90, $p = 0.005$–0.019), while the 36-month time point was marginally significant (combined AUC: 0.87, $p = 0.09$).

TABLE 1 Demographics/participant characteristics.

	ADHD concerns ($n = 17$)	ASD ($n = 19$)	Comparison ($n = 82$)	p-value
Age (months), mean (SD)	36.67 (0.77)	36.20 (0.66)	36.51 (0.97)	0.273
Male sex, n (%)	11 (64.7%)	11 (57.9%)	41 (50.0%)	0.495
Likelihood group, n (%)[c]				
ADHD	11 (64.7%)	0 (0%)	18 (21.9%0	<0.001
ASD	6 (35.2%)	19 (100%)	35 (42.6%)	
Low	0 (0%)	0 (0%)	29 (35.3%)	
Race, n (%)[a]				
Non-White	5 (29.4%)	8 (42.1%)	29 (35.3%)	0.731
White	12 (70.5%)	11 (57.9%)	51 (62.1%)	
Unknown/not reported	0 (0%)	0 (0%)	1 (1.2%)	
Hispanic ethnicity, n (%)				0.309
Hispanic	2 (11.8%)	6 (31.5%)	14 (17%)	
Non-Hispanic	13 (76.5%)	13 (68.4%)	66 (80.4%)	
Unknown/not reported	2 (11.8%)	0 (0%)	2 (2.4%)	
Household income				0.411
$20,000 or less	1	0	2	
$20,001–$60,000	6	5	14	
$60,001–$100,000	3	7	20	
$100,001 or higher	5	7	38	
Unknown/not reported	2	0	8	
ADOS-2, 36 months comparison score, mean, (SD)	1.71 (0.99)	6.79 (2.28)	1.54 (0.85)	<0.001
ADHD rating scale, 36 months total, mean (SD)	20.00 (8.70)	20.24 (9.89)[b]	9.57 (5.80)	<0.001

Abbreviations: ADHD, attention-deficit/hyperactivity disorder; ADOS-2, Autism Diagnostic Observation Schedule-Second Edition; ASD, autism spectrum disorder; SD, standard deviation.
[a]We recognize the approach of "Non-White and White" is not the most comprehensive to capture data on race. We opted for this due to small cell sizes of the formatted table. In the study population the following racial populations and sample sizes were collected: American Indian or Alaskan Native, $n = 1$; Asian, $n = 7$; Black or African American, $n = 1$; More than one Race, $n = 33$.
[b]Missing $n = 2$.
[c]The likelihood groups designate participants recruited based on family history of ASD, ADHD, or no family history of these conditions (low likelihood). Columns designated as ASD, ADHD concerns, and comparison designate outcome that recruited participants receive based on standardized assessments and clinical best estimate at 36 months of age.

TABLE 2 Logistic regression models of ASD versus ADHD concerns/comparison group.

	Unadjusted			Adjusted for recruitment group			Adjusted for Mullen DQ			Fully adjusted		
Model	**OR (95% CI)**	***p***	**AUC**	**OR (95% CI)**	***p***	**AUC**	**OR (95% CI)**	***p***	**AUC**	**OR (95% CI)**	***p***	**AUC**
12 M Curvature (+0.1)	0.99 (0.15, 6.36)	0.992	0.526	0.44 (0.04, 5.25)	0.514	0.870	1.12 (0.14, 9.29)	0.915	0.723	0.58 (0.05, 7.37)	0.676	0.890
18 M Curvature (+0.1)	0.06 (<0.01, 0.87)	0.039	0.678	0.02 (<0.01, 0.54)	0.019	0.903	0.15 (<0.01, 3.77)	0.250	0.885	0.02 (<0.01, 1.44)	**0.074**	0.958
24 M Curvature (+0.1)	0.02 (<0.01, 0.31)	0.005	0.707	<0.01 (<0.01, 0.21)	0.005	0.903	0.10 (<0.01, 2.81)	0.178	0.882	<0.01 (<0.01, 0.73)	0.037	0.960
36 M Curvature (+0.1)	0.14 (0.02, 0.90)	0.038	0.656	0.17 (0.02, 1.28)	0.085	0.865	0.28 (0.03, 2.80)	0.277	0.872	0.39 (0.04, 4.08)	0.431	0.943

Note: Bolded item did not remain significant with 10% FDR control.
Abbreviations: ADHD, attention-deficit/hyperactivity disorder; ASD, autism spectrum disorder; AUC, area under the operating curve; CI, confidence interval; DQ, developmental quotient; FDR, false discovery rate; M, months; OR, odds ratio.

Adjusting for Mullen DQ rendered curvature nonsignificant at all time points; however, estimated odds ratios continued to be large from 18 to 36 months (0.10–0.28). Notably, models adjusting for both likelihood group and Mullen DQ continued to show large odds ratios for curvature from 18 to 36 months (0.01–0.39), with marginal

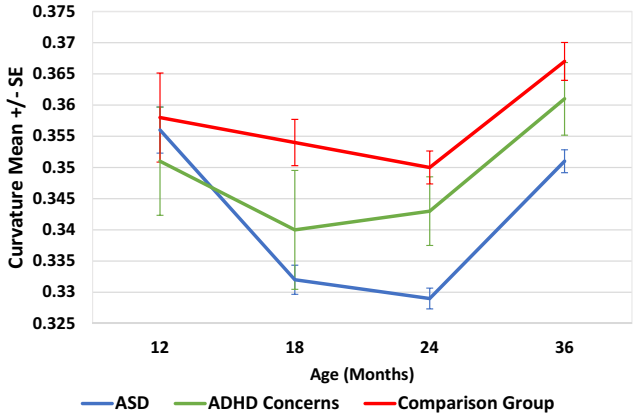

FIGURE 1 Mean curvature at 12, 18, 24, and 36 months of age by outcome group. Error bars denote standard error (SE). ASD, autism spectrum disorder; ADHD, attention-deficit/hyperactivity disorder.

significance at 18 months ($p = 0.07$) and significance at 24 months ($p = 0.037$). We conducted similar analyses for the ADHD concerns outcome group compared to the combined ASD and comparison groups, found curvature was a poor predictor of ADHD concerns outcomes (see Table 1).

Multinomial regression models showed curvature at 18, 24, and 36 months of age to be a useful predictor of ASD outcome status relative to the comparison group, with odds ratios between 0.03 and 0.13 for each 0.1-increase in curvature (AUC 0.66–0.72; $p = 0.005$–0.035). The 18- and 24-month time points remained significant after adjusting for likelihood group (combined AUC: 0.9, $p = 0.007$–0.023). Adjusting for Mullen DQ rendered curvature nonsignificant at all time points, however, similar to the logistic regression results, estimated odds ratios continued to be large from 18 to 36 months (combined odds ratio [OR] of 0.09). Models adjusting for both likelihood group and Mullen DQ showed significance at the 24- month time point ($p = 0.035$). We also evaluated the predictive utility of curvature within just the high likelihood ASD group and found that curvature predicted those who developed ASD at 18 and 24 months of age from those who did not develop ASD (combined AUC: 0.7, $p = 0.007$–0.023).

Multinomial regression comparing the ASD and ADHD concerns groups showed that curvature was not significantly different between groups at any time point in the unadjusted analysis. When adjusting for likelihood group, there was a marginally significant difference in curvature between groups at the 24-time point ($p = 0.082$), but this did not remain significant after FDR correction. Models adjusted for Mullen DQ and for both likelihood group and Mullen DQ were nonsignificant at all time points. Similar analyses contrasting the ADHD concerns and comparison groups found that curvature was a poor predictor for ADHD concerns outcomes in all models. Multinomial regression data are presented in Tables 2a–2c.

DISCUSSION

Motor differences are prevalent in ASD and ADHD, and there has been a paucity of quantitative measures of movement to improve the characterization of these impairments in infancy and early childhood. Here we present the development and evaluation of movement curvature, a novel quantitative measure of movement variability. In our primary analysis, we found that mean movement curvature was lowest in the ASD group (Figure 1), and that movement curvature at 18, 24, and 36 months of age was predictive of 36-month ASD diagnosis. Contrary to our hypothesis, we did not find that mean movement curvature was lower in the ASD group at 12 months, nor was the 12-month movement curvature measure predictive of an ASD diagnosis at 36 months. It could be that differences in movement curvature do not emerge by 12 months of age, but rather later when toddlers have mastered higher level gross motor skills such as walking. However, it is also likely that differences in data acquisition at the 12-month time point compared to the other time points is playing a role in this finding. At 12 months of age, accelerometer acquisition occurred while the infant was participating in an age-appropriate structured testing context (e.g., MSEL and brief experimental tasks), while seated in the lap of a caregiver. Starting at 18 months of age, the accelerometer acquisition occurred during both structured table testing and semi-structured testing as the toddler moved freely throughout the environment (e.g., ADOS administration). Thus, it is possible that the unstructured contexts allowed toddlers to exhibit a larger range of their movement repertoire and improve the evaluation of variability of movement during the measurement time period.

We also found that movement curvature improved prediction of ASD diagnosis after considering whether the child was at high likelihood for ASD, ADHD, or neither, and that it had predictive utility for ASD classification within the high likelihood ASD group. It is important to note that every child who was ultimately diagnosed with ASD was from the high likelihood ASD group. There were no children from the high likelihood ADHD group or the comparison group that ultimately met criteria for ASD at the 36- month outcome assessment. Thus, the high likelihood ASD group was strongly associated with ASD. We found that the addition of movement curvature adds value in outcome prediction by contributing above and beyond our knowledge of likelihood group.

Infants with a sibling with ASD have approximately a 20% higher likelihood of developing ASD compared with the general population (Ozonoff et al., 2011). However, up to 80% of these infants will go on to either have

typical development or have broader developmental delays, including ADHD (Charman et al., 2017; Miller et al., 2016). Furthermore, although clinical symptoms of autism emerge as early as the first year of life, the average age of ASD diagnosis in the United States has remained at 4 years of age for decades (Maenner et al. 2023). The lack of access to developmental specialists and poor follow-up on ASD screening contribute to these diagnostic delays. However, these delays are also secondary to the fact that ASD has a heterogeneous presentation, and there is a paucity of robust, objective predictors of ASD concern in the first 2 years of life. Previous studies have informed our knowledge of early markers of ASD between 12 and 24 months, including reduced gaze to faces, directed vocalizations, social smiles, joint attention, and repetitive behaviors with objects (Cleary et al., 2023; Zwaigenbaum et al., 2015). This body of research has also posited that other early ASD behaviors may include atypical body movements/atypical motor development and dysregulation of temperament (Cleary et al., 2023; Zwaigenbaum et al., 2013). There has been mixed evidence as to whether motor delays are a broad finding in ASD and whether there are atypical movements more specific to ASD. This is in part due to differences in which motor skills have been studied and the methods used to assess these motor domains (Mosconi et al., 2023; Wilson, Enticott, & Rinehart, 2018). We theorized that the inability to produce a more variable array of movements in infancy and early childhood may have more of a mechanistic link to signs of ASD such as poor motor coordination and more constrained, repetitive motor movements (Hadders-algra, 2008; Hadders-Algra, 2018; Wilson et al., 2021). Furthermore, other early behavioral markers of ASD such as joint attention are often dependent on motor ability (e.g., looking, pointing, and showing) and this atypical movement signature could negatively impact these important social behaviors. Atypical motor skills have been described as a potential endophenotype of ASD, constituting a trait that bridges genetic and cellular mechanisms and clinical features (Mosconi et al., 2023). The lack of variable movements may be a more specific motor endophenotype of ASD rather than number of movements produced or delayed motor milestones. Lack of variability could be proxying the behavioral manifestation of atypical genetic or neurobiological traits described in studies of ASD. The emergence of fetal synaptic activity occurs at a similar time the fetus shows more complex and variable movements (Hadders-algra, 2008; Lüchinger et al., 2008). Several studies have highlighted that ASD has atypical synaptic plasticity resulting in imbalances of excitation and inhibition (Brooks-kayal, 2010; Courchesne et al., 2007; Jeste & Geschwind, 2014). It could be that lack of variability in early life movements is related to atypical circuitry in the developing brain. Given our findings, it is possible that objective measurement of underlying movement patterns may aid in improving diagnostic accuracy, especially if combined with measures of other early ASD behavioral markers such as joint attention. In turn, this could help reduce ASD diagnostic delays, which would add value for early detection and access to early interventions.

We also assessed the predictive value of movement curvature after adjusting for Mullen DQ in our ASD model. Controlling for DQ alone resulted in movement curvature becoming a nonsignificant predictor of ASD at each time point. Notably, however, this nonsignificance appears to be primarily due to wider confidence intervals rather than reduced effect sizes. Interestingly, the model adjusting for both Mullen DQ and whether the infant was at high likelihood for ASD, ADHD, or neither found that movement curvature was a marginally significant predictor of ASD at 18 months ($p = 0.07$) and significant at 36 months ($p = 0.04$). In our correlation analyses, we found that, within the high likelihood ASD group, movement curvature exhibited a stronger correlation with the ADOS-2 comparison score than with Mullen DQ. Our interpretation is that while general developmental level likely explains some of the predictive ability of movement curvature, collinearity between the curvature metric and DQ limited our ability to disentangle the effects of each measure. However, further investigation is warranted as atypical motor skills are prevalent in children with broader developmental delays and in children with ASD and intellectual disability (Ramos-Sánchez et al., 2022). It could be that other cognitive factors such as slower processing speed or differences in executive function could lead to the expression of lower variability of movement. Gross and fine motor skills have been associated with working memory and cognitive flexibility and older children with ASD have shown difficulty with tasks requiring simultaneous goal directed and motor behavior (Piek et al., 2008; St John et al., 2016). The sensor data was obtained during an evaluation where the child was often engaged in task-based activities. In a previous study, we found that measurement of infant movement complexity and variability across the whole day in the home environment was lower in a small sample of infants with a later diagnosis of ASD compared with those without a diagnosis of ASD (Wilson et al., 2021). Extending the measurement of movement curvature beyond the testing period and to the home or school environment may allow us to understand whether movement variability differs across multiple ecological contexts.

The previous study examining this unique data set found that accelerometer-derived measures of increased motor activity were a shared motor trait in infants with later ASD diagnosis and ADHD concerns compared with those with typical development (Reetzke et al., 2022). In the current study, we developed the movement curvature metric to test our hypothesis that lower variable movements may specifically be related to a later ASD diagnosis. Our findings suggest that lower

movement curvature by 18 months of age might be a characteristic that is more likely to present in toddlers developing ASD. We did find that movement curvature was significantly associated with the ADOS RRB comparison score, which includes the evaluation of repetitive motor behaviors among other ASD-related behaviors. Although infants developing ASD and ADHD concerns may generate comparable levels of heightened motor activity (Reetzke et al., 2022), the current findings suggest that the evaluation of underlying movement signatures, as exemplified by movement curvature, may be promising to understand motor traits that present more often in infants developing ASD. Although movement curvature was a poor predictor of ADHD concerns when evaluated against the comparison group, we did not find in our sensitivity analysis that movement curvature distinguished those with ASD from those with ADHD concerns by 3 years of age. It may be that lower movement curvature is unique to ASD compared with ADHD, but we were not adequately powered to detect these differences. Although ASD and ADHD are two distinct NDDs, there is a high degree of cooccurrence of these conditions. Cross sectional studies have shown that children with ADHD often exhibit overlapping autism symptoms as measured on the ADOS and a large epidemiological study showed that up to 13% of youth with ADHD were diagnosed with cooccurring ASD (Antshel & Russo, 2019; Hatch et al., 2023). In children with ASD, ADHD is the most common comorbidity, with rates in the 40%–70% range (Antshel & Russo, 2019). It is likely that infants in our ASD outcome group may go on to develop ADHD, and that lower movement curvature may be a shared trait for individuals with these cooccurring NDDs. For these reasons, replication of this work in larger samples and potentially beyond the age of 3 years would be beneficial to understand whether this metric can differentiate these two NDDs.

Limitations

An important limitation of our analysis is that the ASD outcome group consisted of only 19 children and the ADHD concerns group of only 17 children. An evaluation of movement curvature in a larger sample may better illuminate its relationship with ASD, and whether the metric is more specific to ASD as opposed to broader developmental delays and ADHD concerns. The nature of the structured testing at 12 months of age also likely limited the ability to capture a full movement repertoire. Moreover, accelerometer data was obtained from a single limb (ankle). Moving forward, both the addition of quantitative assessment in the home or natural environment and the addition of multiple measurement locations (bilateral wrists and ankles) may allow us to better interpret curvature metrics at an earlier age and between groups.

CONCLUSIONS

Motor delays and differences have been well described in children with ASD and ADHD. Yet, previous studies using quantitative and qualitative measures have not yet identified whether there are motor differences that are distinct to ASD or ADHD, particularly not early in life. Here we use a quantitative technique to develop a measurement of movement curvature and found that this measure may aid in distinguishing motor differences in infants developing ASD from those without an ASD diagnosis. We found that infants with a later ASD diagnosis show lower movement curvature, and that movement curvature predicts later ASD diagnosis reliably by 18 months of age. The measure of movement curvature may specifically shed light on movement differences that present in early life and can perpetuate frequently described motor differences and challenges in ASD that also impact other areas of development such as social communication. These quantitative measures can be easily measured at different time points and monitored whether there is stability over time or change with interventions. These are critical factors when considering early diagnosis and therapeutic interventions for individuals with ASD.

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CONFLICT OF INTEREST STATEMENT

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Child and Adolescent Psychology. All other authors report no biomedical financial interests or potential conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding and senior authors upon reasonable request.

ETHICS STATEMENT

The study protocol was approved by the University of California, Davis Institutional Review Board (IRB 1560974, PI: Ozonoff); written informed consent was obtained from parents before participation.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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