Associating neuromotor outcomes at 12 months with wearable sensor measures collected during early infancy in rural Guatemala

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Declaration of interest

None

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Abstract

Background: Sensitive measures to predict neuromotor outcomes from data collected early in infancy are lacking. Measures derived from the recordings of infant movement using wearable sensors may be a useful new technique.

Methods: We collected full-day leg movement of 41 infants in rural Guatemala across 3 visits between birth and 6 months of age using wearable sensors. Average leg movement rate and fuzzy entropy, a measure to describe the complexity of signals, of the leg movements' peak acceleration time series and the time series itself were derived. We tested the three measures for the predictability of infants' developmental outcome, Bayley Scales of Infant and Toddler Development III motor, language, or cognitive composite score assessed at 12 months of age. We performed quantile regressions with clustered standard errors, accounting for the multiple visits for each infant.

Results: Fuzzy entropy was associated with the motor composite score at the 0.5 quantiles; this association was not found for the other two measures. Also, no leg movement characteristic was associated with language or cognitive composite scores.

Conclusion: We propose that the entropy of leg movement associated peak accelerations calculated from the wearable sensor data collected for a full-day can be considered as one predictor for infants' motor developmental outcome assessed with Bayley Scales of Infant and Toddler Development III at 12 months of age.

Keyword: Wearable sensor / entropy / infant development / Bayley Scales / movement

Introduction

Timely detection of atypical development in infants in low and middle-income countries (LMICs) is necessary in order to provide optimal developmental support. Many programs in lower resource settings rely on proxy indicators for development such as growth parameters or on indirect measures such as parent-reported developmental concerns. These techniques are indirect measures or not sensitive very early in infancy. As a result, infants needing intervention are often not identified early; consequently, developmental support is not provided or is provided after infants have failed to meet several developmental milestones. Technologies to support earlier identification of atypical development would therefore support earlier intervention and optimal neurodevelopmental outcomes.

Wearable sensors are one possible novel tool to serve this purpose. Prior work in high-income settings has shown that infant limb movement characteristics can be measured using wearable sensors and used to identify atypical development. For example, in a sample of infants from the United States of America, full-day measurement of limb movement could differentiate between infants with typical development, infants at risk for developmental disability who go on to have good developmental outcomes at 24 months, and infants at risk for developmental disability who go on to have poor developmental outcomes at 24 months [1]. The scientific rationale for the use of wearable sensors to monitor development in infants is that the tool can provide detailed and quantitative descriptions of infants' behavior observed in natural settings for a long period, across days and months [2]. Limb movements are one of the earliest outputs of the developing central nervous system. Objectively and thoroughly estimated level of movement control may be useful as a measure to sensitively assess infants' development earlier in life than current developmental assessments.

In addition to movement kinematics characterized by raw sensor recordings, signatures of the time series from sensor recordings has been proposed as another measure to study human movement [3]. Measuring the variability of a time series by calculating *entropy*, such as approximate entropy (ApEn) or sample entropy (SampEn) is one example [4,5]. To clarify, *entropy* in this article refers to the statistical method to measure the complexity of a time series [6], particularly that of a physiological signal such as wearable sensor recording of movement or heart rate. Again in high-resource settings, our group has used the entropy measure to distinguish typically developing infants from infants at risk of developmental disabilities; infants at risk exhibited lower entropy values [7]. The ability to derive multiple measures (ex. movement rate, peak acceleration per movement, or entropy of a recording) makes the wearable sensors even more attractive for early identification of infants' atypical development.

In this study, we attempt to extend these findings from high-resource settings to a lower-resource setting among infants in rural Guatemala. This work builds on our recent work in Guatemala showing that wearable sensors can be used with high fidelity to measure age-related changes in limb movement characteristics in rural Guatemala [8]. The main objective of this article is to investigate the association between measures derived from limb wearable sensor data in early infancy and Bayley Scales of Infant and Toddler Development, Third Edition (BSID-III) composite motor scores at 12 months of age in a rural setting in Guatemala with high rates of poverty, malnutrition, and infant morbidity. We investigate both raw movement characteristics (average movement rate and peak acceleration per leg movement) as well as the entropy of the limb acceleration time series. While the motor composite score of BSID-III was of main interest to relate early motor behaviors to later motor development status, we also checked the associations with the cognitive and the language composite score respectively. The rationale was that both cognitive and linguistic development have been reported to be associated with gross motor skills [9,10]; cognitive, language, and motor development are not independent of one another.

Material and methods

Participants and Recruitment Procedures

Full details of participant recruitment procedures have previously been described as part of our ongoing work to support early childhood interventions in rural Indigenous communities in Guatemala [8]. Forty-one Indigenous Maya infants were recruited in Tecpán, Chimaltenango, Guatemala in collaboration with Maya Health Alliance, a primary healthcare organization with a major clinical center in the study community. Virtually all inhabitants of Tecpán identify as Indigenous. Inclusion criteria included: 1) infant aged 0 to 16 weeks at enrollment; 2) singleton and full-term (> 38 weeks) birth. Exclusion criteria were: 1) acute malnutrition (wasting); 2) presence of a severe medical illness such as congenital heart disease as determined by a Maya Health Alliance clinician. Institutional Review Board approval was obtained from Maya Health Alliance (WK 2019004), the University of Southern California (HS-19-00564), and Children's Hospital Los Angeles (CHLA-20-00201).

Apparatus

Infants wore small, light-weight wearable sensors (Opal Version 2 of APDM Inc., Portland, OR, USA; dimension: 43.7 x 39.7 x 13.7 mm; weight < 25 g) on each ankle. Research staff inserted the sensors into pockets of custom-made legwarmers (Figure 1). The sensors sampled at 20 Hz.

Figure 1
Placement of wearable sensors

Note. Wearable sensors (inside a circle) are inserted into custom-made legwarmers and placed on each ankle of an infant.

Wearable Sensor Procedure

As previously described [8], each infant participated in three visits. Within either the home or clinic setting, at each visit study staff placed sensors on both ankles of the infant in the morning and then asked caregivers to return to typical daily activities. The three visits occurred before 6 months of age; each visit was separated by 1 month (+/- 1 week). At each visit, sensors recorded tri-axial accelerations and angular velocities associated with the infant's leg movement from the morning until bedtime (~10-12 hours). Caregivers could remove sensors shortly if needed, such as for bathing activities. Sensors were removed from the infant at bedtime and were collected on a subsequent day by research staff.

Measurements

Average leg movement rate

Using a movement detection algorithm previously developed and validated [11], we counted leg movements separately for the left and the right leg. The algorithm also estimated the amount of time infants were asleep (aggregation of 5-minute periods where 3 or fewer movements occurred in each period). Each movement count was divided by estimated hours awake to derive leg movement rates per hour awake for the left and the right leg. The average of the two individual limb measures for each infant's visit was used for further analysis. This was a measure representing the overall amount of leg movement of infants when awake and moving. Previous findings reported that the frequency of kicking movement was significantly correlated with walking onset in infants with Down syndrome [12] or infants born preterm with very low birth weight [13]. Further, delayed walking onset has been reported to be associated with a lower level of motor [14], cognitive [15], or language development [16] in infants. This line of thought led us to hypothesize that the leg movement rate may be positively correlated with the neurodevelopmental status of an infant assessed with BSID-III at 12 months, known to be the time some infants start to walk independently or with assistance [17,18]. Consequently, we selected this variable for our study. The averaging of the left and the right leg measures is supported by our previous findings of high correlations between the right and left legs [11,19] with infants similar to our sample (no known or suspected neurological disorders).

Peak acceleration per leg movement

Peak acceleration per leg movement was identified as the maximum acceleration magnitude during a movement [11]. This was a measure representing the intensity with which infants make spontaneous leg movements. A report on infants' peak acceleration of arm reaching movement showed that those with lower peak acceleration values also had lower motor scores of BSID-III [2]. We were interested in observing a similar relationship between the measure from leg movements and BSID-III scores. Thus we decided to study this measure. We used each infant's visit median of peak acceleration per movement time series to represent the overall level of peak acceleration in a visit. The average of the two limb measures was used as well.

Fuzzy entropy of peak acceleration per leg movement

To measure the variability of infant leg movement intensity, we calculated fuzzy entropy [20] of the peak acceleration per movement time series. While sample entropy has been used in studying infant movement and posture control [7,21] we chose fuzzy entropy for two reasons. First, the approach it takes to measure the variability of a time series is similar to that of sample entropy. Briefly, both types of entropy compare vectors or short segments of a time series to their neighbors and measure the overall level of dissimilarity. A low value of sample- or fuzzy entropy would imply that the time series of interest is less variable. Second, the approach aims to address the limitation of sample entropy. Sample entropy adopts a more stringent criterion in determining the similarity of vectors and their neighbors (a binary judgment following a Heaviside function with a threshold). Acknowledging that signals are more ambiguous, fuzzy entropy uses a more relaxed method to determine the similarity (judgment on a gradient scale following a fuzzy function with certain parameter values). There are comparative studies supporting that fuzzy entropy outperforms sample entropy [20,22], and the measure is used in calculating the variability of different types of signals such as electromyography [23,24] or gait velocity [25] time series.

The time series was prepared by concatenating all peak acceleration per leg movement values. We prepared this new time series instead of using the full recording data because the raw time series of a sensor recording has portions that are not movements (e.g. sleeping, being held by parents). This was to understand how a specific characteristic of infant leg movement – peak acceleration – is represented across a full-day recording of infant leg movements. Similar to the average leg movement rate, the average of the two entropy values obtained for each leg was used for further analysis. For steps involved in calculating fuzzy entropy see Appendix A. We used the embedding dimension (m) of 2 and a tolerance (r) of 0.2. Higher entropy values indicated greater variability embedded in the movement peak acceleration time series and can be interpreted as infants making leg movements of diverse peak accelerations throughout the recording.

Bayley Scales of Infant and Toddler Development (BSID-III)

Study psychologists administered the BSID-III at 12 months of age (11 months 15 days – 13 months 15 days), assisted by bilingual Spanish/Kaqchikel interpreters when needed. The psychologists used a previously translated Spanish/Kaqchikel BSID-III version from our team [26]; however, translation wasn't needed since the mother's participants reported they spoke mainly in Spanish to their children. Composite scores for language, cognitive, and motor scales were calculated separately. Each composite score is standardized to age-matched peers. The composite scores are calculated from the reference distributions, which have a mean of 100 and a standard deviation of 15. The standardization is done by comparing the performance of an infant to the reference performance of the age-matched sample of the U.S. infants. These data must be interpreted cautiously given the participant sample is not a sample of U.S. infants. Our analyses were focused on the motor composite scores, because measures derived from wearable sensors are movement-related.

Statistical Analysis

To explore if wearable sensor data derived measures collected early in infancy could be correlated to developmental status as measured by the BSID-III at 12 months of age, we fitted quantile regression models with clustered standard errors. The dependent variable of a model was the BSID-III composite score (motor / language / cognitive). The main independent variable was the average movement rate, peak acceleration per leg movement, or fuzzy entropy value. Change in the main independent variable over time was controlled by including infant age, visit, and independent variable-visit interaction terms. We chose to use quantile regression because of the small sample size and considerable variation in the dependent variable between subjects. A regular regression model like ordinary least squares would have been of limited value, as the model assumption that the response (BSID-III scores) relative to predictors was similarly distributed across the range of observed values was unlikely to hold for BSID-III scores which are often nonlinearly distributed at the extremes. Quantile regression allowed us to relax this restriction and make no assumptions about the behavior of the response variable over its entire distribution while still testing shifts in the distribution around the median. All analyses were done with the **qreg2** function in STATA Version 18 [27]. The Machado Santos Silva test [28] was used to confirm that the model did not violate assumptions around the distributions of the error terms for quantile regression.

Results

Full sociodemographic, clinical, and growth characteristics of this cohort have already been described [8]. In brief, of 41 recruited infants 51% were female and 95% of Indigenous Maya ethnicity. One infant's BSID-III assessment record was not collected, so 40 infants were included in the final analyses. Wearable sensor visits occurred at a median of 63 (IQR 44), 94 (IQR 40), and 129 (IQR 35.5) days from birth. The sample median of the motor composite scores assessed by BSID-III was 85 (IQR 12). The minimum score was 55 and the maximum was 107. The cognitive composite scores had the sample median of 105 (IQR 16.25). The language composite scores had the sample median of 97 (IQR 21.5). The sample median of the average fuzzy entropy of peak accelerations of each following visit was greater than its preceding visit (Table 1).

Table 1

Summary of wearable sensor data derived measures across the visit and BSID-III composite scores.

	Visit 1 (M: 63 days)	Visit 2 (M: 94 days)	Visit 3 (M: 129 days)
Wearable sensor data derived measures			
Fuzzy entropy	1.25 (0.24)	1.40 (0.26)	1.45 (0.22)
Peak acceleration per leg movement (m/s^2)	2.71 (0.37)	2.94 (0.39)	3.03 (0.27)
Average leg movement rate (mov/hour)	930 (464)	1005 (275)	1040 (431)
BSID-III composite scores			
Motor		85 (12)	
Cognitive		105 (16.25)	
Language		97 (21.5)	

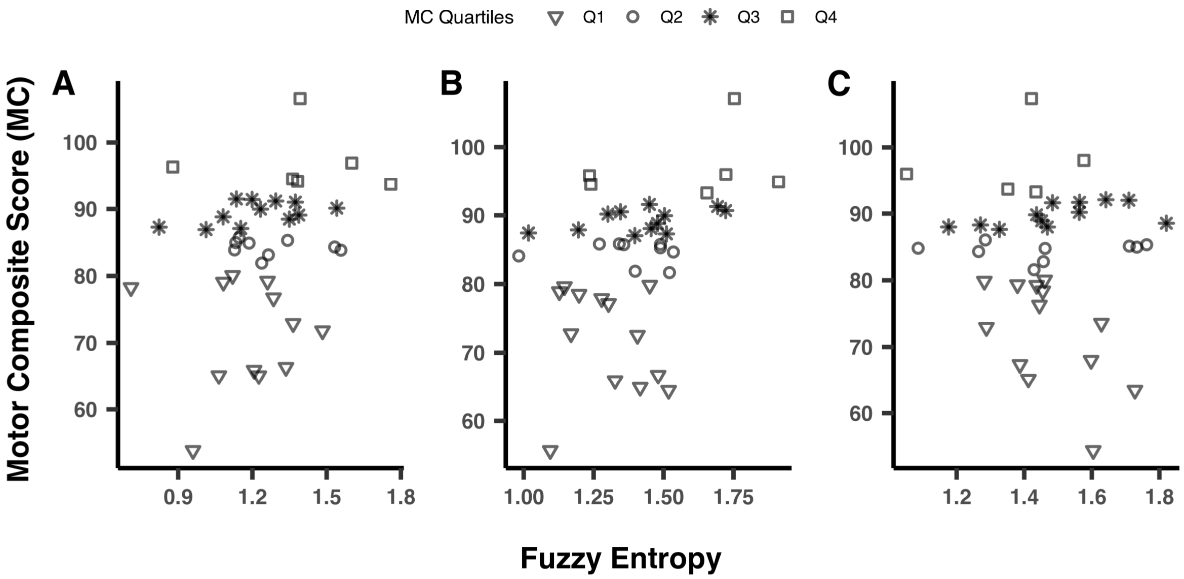
Note. All sensor data derived measures are the average of two limb measurements, and BSID-III scores were obtained at 12 months of age. Medians of the measures at each visit (IQRs in parentheses) are reported. M: Median age of infants in a visit

Association between fuzzy entropy and motor developmental outcomes at 12 months

Associations between BSID-III composite scores and fuzzy entropy were visually inspected using scatterplots of entropy values versus study visit, stratified by BSID-III composite score quartile. Figure 2 shows this relationship for the motor composite score, suggesting a positive association between higher BSID-III scores and fuzzy entropy, especially at the second visit (median age: 94 days from birth). In visit 1, points corresponding to Q1 had the median average fuzzy entropy value of 1.22 (IQR 0.22), while those of Q4 had the median value of 1.39 (IQR 0.18). In visit 2, the distinction between Q1 and Q4 points appear to be maintained (median average fuzzy entropy: Q4 = 1.69 [IQR 0.4] vs. Q1 = 1.30 [IQR 0.25]). This trend is no longer present in visit 3. Q1 points had the median average fuzzy entropy of 1.45 (IQR 0.21) while Q4 points had the median of 1.42 (IQR 0.08). Table B1 reports fuzzy entropy per quartile based on other BSID-III composite scores: language and cognitive.

Figure 2

Scatterplots of infants' fuzzy entropy values and their motor composite score quartiles across the three visits.



Note. Each plot shows the limb-averaged fuzzy entropy values of infants in a visit. A: visit 1, B: visit 2, C: visit 3. Their BSID-III motor composite score quartiles are indicated by different symbols. Q1: infants below the first quartile (n=13), Q2: infants between the first and the second quartiles (n=9), Q3: infants between the second and the third quartiles (n=12), Q4: infants above the third quartile (n=6)

This relationship was further investigated by constructing a median quantile regression model for the composite motor score, adjusting for study visit, age in days at each visit, and the interaction between the changes in fuzzy entropy measures across each study visit (Table 2). In this model, a 1 unit change in limb-averaged fuzzy entropy was associated with a change in median motor composite score of 13.78 (95% CI 0.66-26.91, p=0.04). At visits 1 and 2, most quartiles showed positive associations between the motor composite score and the average fuzzy entropy. At visit 3, the quartile trends were more heterogenous.

Table 2

Summary of the median regression model investigating the association between fuzzy entropy and the motor composite score at 12 months.

Predictors	*Coefficient*	*95% C.I.*	*P*
Limb-averaged fuzzy entropy	13.78	0.66 – 26.91	**0.040**
Study Visit			
Visit 1	--	--	--
Visit 2	-6.29	-32.16 – 19.58	0.631
Visit 3	15.81	-10.68 – 42.30	0.239
Visit:Entropy interaction term			
Visit 1	--	--	--
Visit 2	2.52	-15.72 – 20.76	0.785
Visit 3	-13.76	-33.04 – 5.52	0.160
Age (days)	-8.98e-4	-0.11 – 0.986	0.986
Observations	118		

Note. Standard errors of the coefficients are adjusted for 40 clusters of infants.

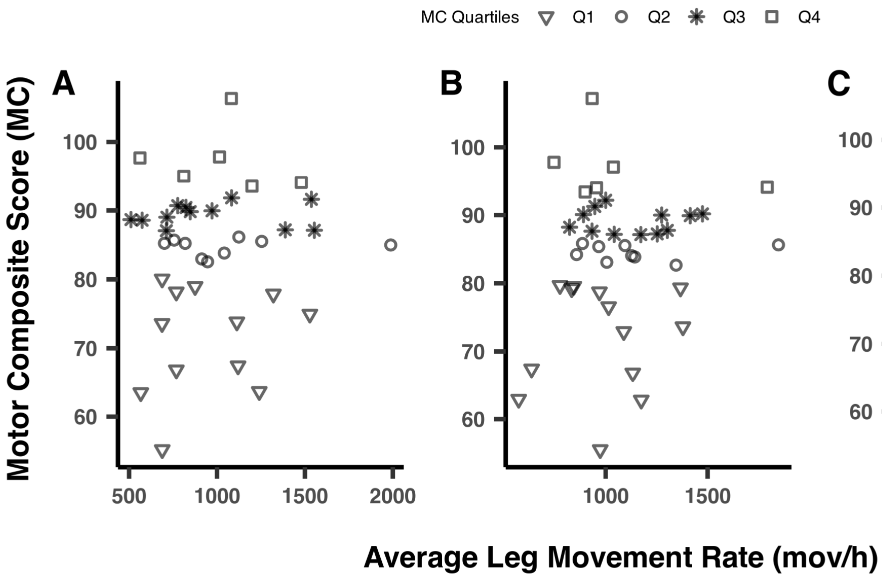
We also checked if fuzzy entropy was associated with other composite scores of BSID-III: language or cognitive. Visual examination (Figure C1 A and B) as well as regression models (Tables D1 and D2) did not support that fuzzy entropy was a significant predictor of either language or cognitive scores of infants.

Average leg movement rate or peak acceleration per movement is not associated with developmental outcomes at 12 months

In contrast to fuzzy entropy, the average leg movement rate did not show a distinguishing relationship with BSID-III motor composite scores. In all three visits, quartiles were not separated by the average leg movement rate (Figure 3). Both lower and higher quartiles were associated with lower and higher movement rates. In visit 1, points corresponding to Q1 had the median average leg movement rate of 822 mov/h (IQR 462), while those of Q4 had the median value of 1048 mov/h (IQR 307). In the following visits, the overlap of the two quartiles was consistently observed (median average leg movement rate at visit 2: Q4 = 944 mov/h [IQR 109] vs. Q1 = 973 mov/h [IQR 300]; at visit 3: Q4 = 951 mov/h [IQR 120] vs. Q1 = 1024 mov/h [IQR 585]). Values of quartiles based on other composite scores are reported in Table B1. The median regression model fitted to infants' motor composite scores using the movement rate, visit, and the interaction of the two reported no significant coefficient after controlling for the age variability (Table D3).

Figure 3

Scatterplots of infants' leg movement rates and their motor composite score quartiles across the three visits.

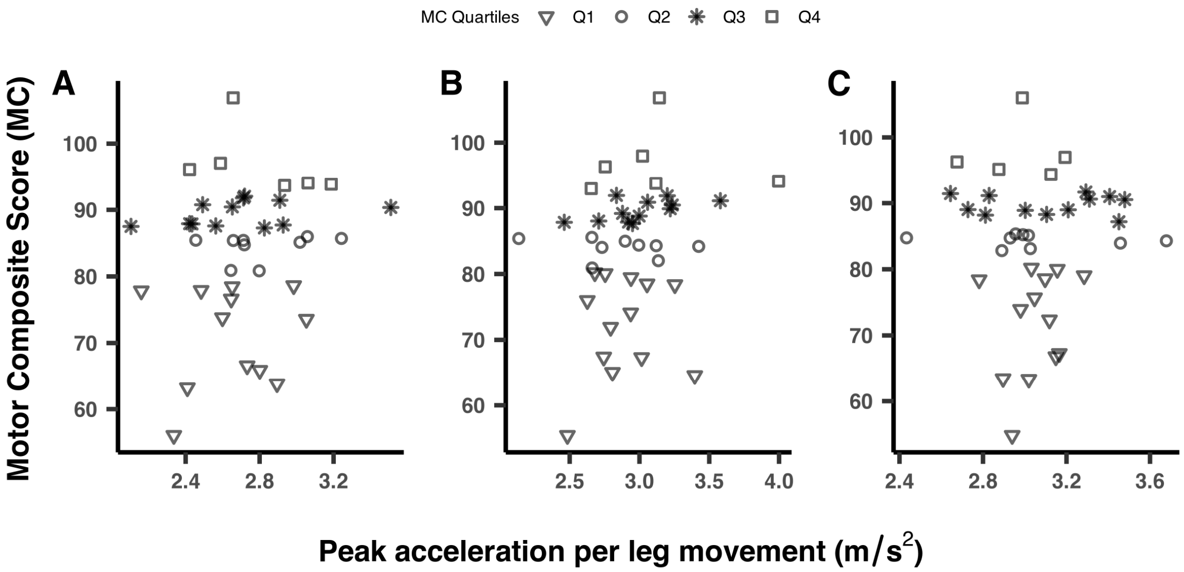


Note. Each plot shows the averaged leg movement rates per hour awake of infants in a visit. A: visit 1, B: visit 2, C: visit 3. Their BSID-III motor composite score quartiles are indicated by different symbols. Q1: infants below the first quartile (n=13), Q2: infants between the first and the second quartiles (n=9), Q3: infants between the second and the third quartiles (n=12), Q4: infants above the third quartile (n=6)

Peak acceleration per leg movement was similar to peak entropy in terms of its association with the motor composite score (Figure 4). At visit 1, the median peak acceleration of Q1 was 2.65 m/s^2 [IQR 0.36] and that of Q4 was 2.80 m/s^2 [IQR 0.43]. This contrast was observed in visit 2: Q1 = 2.81 m/s^2 [IQR 0.27] vs. Q4 = 3.07 m/s^2 [IQR 0.32]. However, the median regression fitted using peak acceleration as one of the predictors for motor composite score reported that it is not a significant predictor (Table D6).

Figure 4

Scatterplots of infants' peak accelerations of leg movements and their motor composite score quartiles across the three visits.



Note. Each plot shows the averaged peak acceleration per leg movements of infants in a visit. Their BSID-III motor composite score quartiles are indicated by different symbols. Q1: infants below the first quartile (n=13), Q2: infants between the first and the second quartiles (n=9), Q3: infants between the second and the third quartiles (n=12), Q4: infants above the third quartile (n=6)

We again checked if BSID-III language or cognitive composite score was associated with either of the two sensor data derived measures. Visual examination (Figure C1 C-F) as well as regression models (Tables D4, D5, D7 and D8) did not support that either the average leg movement rate per hour awake or peak acceleration per leg movement is a significant predictor of either language or cognitive composite score for our sample.

Discussion

Wearable sensor data can predict motor developmental outcomes of infants in rural Guatemala.

In this study, we aimed to associate and tentatively predict the neuromotor outcomes of infants in rural Guatemala at 12 months of age using wearable sensor data collected earlier in infancy. Fuzzy entropy of peak accelerations of leg movements had a significant association with BSID-III motor composite score in the median regression model.

Variability in peak acceleration per movement may be one important factor in motor development.

Understanding from what time series entropy was calculated is a key to interpreting its value appropriately [29]. If behavior is expected to be regular across time (e.g. stride time in adults [30]), high entropy can be interpreted as *deviating from the norm*. In contrast, if behavior is more exploratory and expected to vary over time, high entropy may be a sign of *following the track*. For example, a study on the postural control of infants with developmental delay reported that they showed more rigid and less complex patterns compared to their typically developing peers [31]. Similarly, a higher degree of variability in peak acceleration associated with higher BSID-III motor composite scores in our study may be interpreted as infants *exploring* different movement intensities and learning varying proprioceptive feedback. This afferent sensory information may be critical to the development of the brain areas relevant to the sensorimotor control. Indeed, the developmental status of the brain is associated with the motor development. Infants who showed increased prenatal brain connectivity among regions relevant to motor control also demonstrated higher BSID-III motor scores [32]. Furthermore, continued brain development after birth seems to accompany spontaneous movements and associated sensory input. For example, the somatotopy of the infant brains reflected the spindle bursts of distinctive movements [33,34]. Consequently, it could be implied that less sensory input resulting from less diverse leg movements may delay the development of infants' somatosensory cortex and slow motor skill development. An increase in entropy across visits we observed among some infants of our sample may also be representing their continued exploration, and/or influenced by their physical growth.

Another way to consider this is regarding the role of exploration in learning. It is hypothesized that infants need to explore in order to learn, and repeating the same type of movements does not support learning new motor skills [35–37]. Rather, infants would benefit from "variable enough" spontaneous movements as they may learn spatial and temporal structures in sensorimotor interactions [38]. High variability in the peak acceleration early in life may represent increased exploration. This may be preparing infants with the capacity to learn new motor skills later as reflected by higher motor composite scores on the BSID-III. The finding of a similar study done with infants in the United States [7] also reported that infants at risk of developmental delay showed significantly lower entropy values compared to those of typically developing infants. It was suggested that infants at risk had an insufficient amount of exploration with respect to spontaneous leg movements, resulting in not reaching the level to learn a new motor skill.

The fact that the average leg movement rate did not have a significant coefficient in the fitted median regression model may further emphasize that the nature of movements infants make, as opposed to the quantity alone, has a stronger relationship to motor development trajectories. A visual inspection of the correlation between the fuzzy entropy and the average leg movement rate revealed that there are infants who generated relatively low leg movement rates (below 1000 mov/h) at visit 1 and still scored above-median motor composite scores. While making more movements during hours awake can increase the variability among the movements' peak accelerations, it is also true that achieving high variability does not require a high movement rate.

High variability achieved early in life may be a sign of more advanced motor development trajectories.

We speculate that the timing of achieving high variability in peak accelerations of leg movements may be important in relation to trajectories of motor development. A positive association between fuzzy entropy and motor composite score is supported for visit 1 data. Based on the model estimation and relevant visual of the fits (Figure 2B), the association may be true for visit 2 data as well. At visit 2, the median age of infants was 94 days from birth. The third month is a period with notable changes in the coordination of leg movements. In a study that observed 20 infants [39], 9.4 weeks (SD: 2.76 weeks; range: 6-14 weeks) was the reported mean age of onset for stereotypical leg movements. Relatedly, at the end of the second month, infants' writhing movements are replaced by fidgety movements. This has been assumed to be arising from the calibration of the proprioceptive system [40]. Prechtl [41] viewed this change, along with a set of other changes in smiling, postural control and learning, or vision, as a supporting piece for his argument of the continuum of neural mechanisms from prenatal to postnatal life. In other words, the third month could be the critical time point when infants' repertoire becomes more variable. Specific to leg movements, Thelen [42] reported based on the observation of four infants that the high degree of synchrony in the hip and ankle joints started to decrease by 2 months and even further decreased between 4 and 6 months of age. Again, around 3 months of age, infants shift from predominately in-phase leg movements (e.g., time-synchronized hip and knee flexion or extension) to more variable movements (e.g., hip flexion with extension). If infants typically increase the variability in movement repertoire from 3 months or so, demonstrating a higher amount of variability even before then may be a sign of 'being ahead' in developmental trajectory, resulting in correspondingly higher motor scores at 12 months of age. On the other hand, the opposite may be the case, meaning low entropy of peak acceleration before 3 months of age possibly influenced by malnutrition [43,44] is related to slower developmental trajectories. A better understanding can be achieved by investigating the *optimal* variability [45,46] in the peak acceleration time series by studying a large sample of typically developing infants using wearable sensors.

(No) Relationship between infants' leg movement and BSID-III language / cognitive composite score

We found that the change in infants' leg movement characteristics was not associated with BSID-III language or cognitive composite score. This is opposite to the positive relationship between arm movement characteristics of less than a year-old typically developing infants and their cognitive development [2,47]. Specifically, Shida-Tokeshi and colleagues [2] reported that infants who made more arm reaches had larger increases in language and cognitive scores measured by BSID-III composite scores across multiple visits. Regarding their finding, the authors introduced one argument that infants' motor skills may support the scaffolding of development. Identifying the motor skill(s) benefiting linguistic/cognitive development is at a rudimentary stage. Following this line of thought, our findings suggest that infants' leg movements may not be one of the skills or at least not directly involved in providing the scaffolding. Rather, it could be that the variability of the spontaneous movements of the upper limb, which will later be involved in reaching and object exploration, could be a better marker for linguistic and cognitive development. For example, delays in object exploration demonstrated at 7 months of age in preterm infants were associated with poorer cognitive outcomes at 24 months [48]. It can be speculated that the lack of exploration is associated with less variable arm movements earlier in life. Another possible argument is that making leg movements with varying levels of peak acceleration would promote the general development of the central nervous system [49], enabling earlier onset of postural control or independent gait behavior, both reported to be associated with infant language [50,51] or cognitive development [9]. Nonetheless, the contribution may not be any more notable than that of other influential factors.

Just as the 3 months of age might be a *critical point* for motor development, there may be analogous timepoints for language and cognitive development of infants and our study design did not address this. We only collected motor performance in early infancy and did not have analogous measures for cognitive / language performance in early infancy. Based on our results, we can speculate about a critical period for motor development because we measured movement performance in young infants and related this to later outcomes, but we did not measure cognitive and language performance in young infants in order to relate this to later outcomes.

Limitations

Our finding – a significant association between fuzzy entropy and the developmental outcome – needs to be interpreted with caution. First of all, BSID-III has not been validated in many different languages and cultures, limiting the generalizability of our findings. Second, no local references norms for the BSID-III are available in our population and therefore we scaled scores using the USA reference population. This allowed us to compare standardized scores across time points and between subjects within our sample, but the functional meaning of individual BSID-III scores is unclear. Further work to see if our findings can be replicated in larger samples and with a more diverse population of infants with neurodevelopmental outcomes is needed.

Conclusion

We measured the leg movements of infants between 0 – 6 months in rural Guatemala using wearable sensors. Then we tried to predict their motor developmental outcome estimated at 12 months of age using the measures we collected earlier. We demonstrated that the variability in the peak acceleration per movement time series recorded before 4 months of age can be considered as a predictor of infants' motor developmental outcome. Specifically, the variability was measured with fuzzy entropy value, and the developmental outcome was assessed with BSID-III motor composite scores. This indicates that an early assessment of infants' motor development can be enhanced using measures of wearable sensor data.

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Appendix A

Calculating fuzzy entropy of a time-series

For a time-series $T = \{t(i): 1 \le i \le N\}$, define a vector X_i^m as

$$X_i^m = \{t(i), t(i+1), \ldots, t(i+m-1)\} - t0(i), \qquad i = 1, \ldots, N-m$$

with

$$t0(i) = \frac{1}{m}\sum_{j=0}^{m-1} t(i+j)$$

In other words, X_i^m is a mean subtracted segment of *T*. You then calculate D_{ij}^m, the similarity degree between X_i^m and its neighboring segment X_j^m $(j = 1, \ldots, N-m,\ \ and\ j \ne i)$ defined by a fuzzy function (μ).

$$D_{ij}^m = \mu(d_{ij}^m, r)$$

d_{ij}^m is the maximum absolute difference of the matching scalar values of X_i^m and X_j^m. In our analysis, we set $\mu\left(d_{ij}^m, r\right) = e^{-\left(d_{ij}^m/r\right)^2}$. Each X_i^m will have $N-m-1$ values of D_{ij}^m. Average all those similarity degree values to get

$$\phi_i^m(r) = \frac{1}{N-m-1}\sum_{j=1, j\ne i}^{N-m} D_{ij}^m$$

Then calculate the average of $\varphi_i^m(r)$, $\varphi^m(r) = \frac{1}{N-m}\sum_{i=1}^{N-m}\phi_i^m$ and construct an analogous measure for X_i^{m+1}, $\varphi^{m+1}(r)$.

Finally, estimate Fuzzy Entropy (FuzzyEn) by the following equation:

$$FuzzyEn(m, r, N) = ln\varphi^m(r) - ln\varphi^{m+1}(r)$$

Appendix B

Association between sensor measures and BSID-III composite score quartile

Table B1

Sample median and IQR of variables per BSID-III composite score quartile

		Fuzzy entropy			Peak acceleration per leg movement (m/s^2)			Average leg movement rate (mov/hour)		
Score	Q	Visit 1	Visit 2	Visit 3	Visit 1	Visit 2	Visit 3	Visit 1	Visit 2	Visit 3
Motor composite	1	1.22 (0.22)	1.30 (0.25)	1.45 (0.21)	2.65 (0.36)	2.81 (0.27)	3.05 (0.17)	822 (462)	973 (300)	1024 (585)
	2	1.24 (0.20)	1.40 (0.15)	1.45 (0.43)	2.72 (0.36)	2.90 (0.46)	2.99 (0.10)	947 (305)	1095 (177)	1068 (402)
	3	1.22 (0.23)	1.45 (0.17)	1.48 (0.17)	2.68 (0.37)	2.97 (0.34)	3.16 (0.51)	836 (445)	1107 (339)	1139 (332)
	4	1.39 (0.18)	1.69 (0.40)	1.42 (0.08)	2.80 (0.43)	3.07 (0.32)	2.99 (0.25)	1048 (307)	944 (109)	951 (120)
Language composite	1	1.14 (0.09)	1.45 (0.14)	1.46 (0.22)	2.61 (0.33)	2.89 (0.22)	3.01 (0.19)	794 (377)	1068 (267)	1044 (322)
	2	1.34 (0.21)	1.45 (0.28)	1.51 (0.21)	2.73 (0.28)	2.98 (0.33)	3.14 (0.20)	773 (292)	951 (197)	1243 (390)
	3	1.23 (0.38)	1.29 (0.24)	1.35 (0.18)	2.71 (0.60)	3.00 (0.42)	2.99 (0.29)	1083 (473)	1063 (327)	937 (216)
	4	1.29 (0.09)	1.37 (0.16)	1.47 (0.10)	2.69 (2.70)	2.94 (0.35)	3.17 (0.27)	959 (496)	1191 (395)	1229 (442)
Cognitive composite	1	1.18 (0.14)	1.39 (0.14)	1.52 (0.15)	2.77 (0.37)	2.85 (0.28)	3.01 (0.22)	926 (428)	1034 (264)	1089 (534)
	2	1.24 (0.21)	1.40 (0.32)	1.44 (0.24)	2.65 (0.18)	2.99 (0.41)	3.06 (0.20)	848 (301)	1042 (286)	1046 (244)
	3	1.29 (0.34)	1.38 (0.22)	1.45 (0.21)	2.65 (0.56)	2.85 (0.43)	2.95 (0.38)	1941 (567)	933 (299)	1241 (948)
	4	1.37 (0.20)	1.51 (0.30)	1.42 (0.25)	2.72 (0.39)	3.00 (0.24)	3.11 (0.32)	1014 (418)	1038 (333)	991 (213)

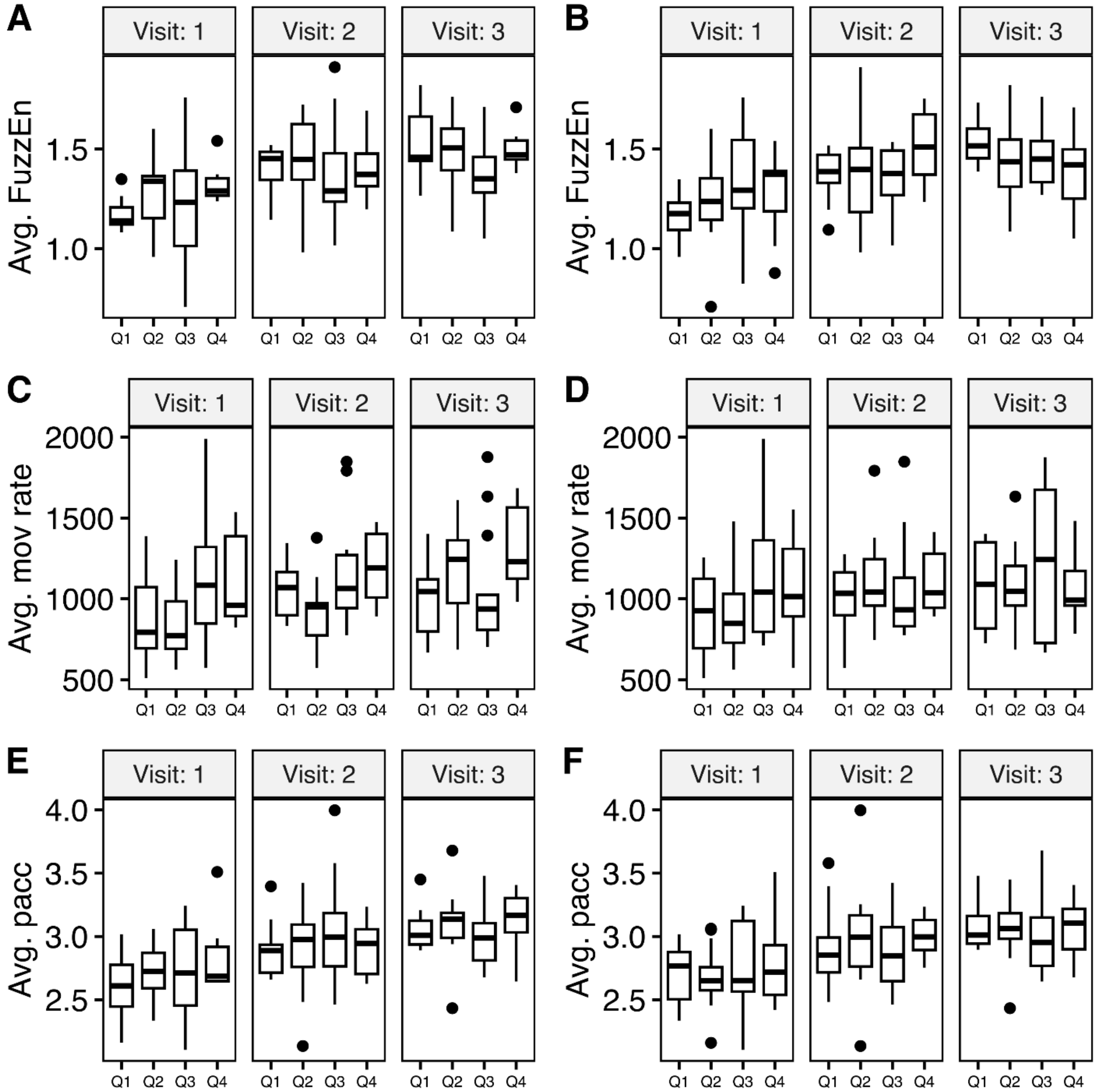
Note. Quartile medians (IQRs in parentheses) are reported; Q: score quartiles for motor, language or cognitive composite scores of infants

Appendix C

Associations between sensor variables and quartiles based on different BSID-III composite scores

Figure C1

Boxplots of infants' sensor measures and their language / cognitive composite score quartiles across the three visits.



Note. Quartiles are estimated based on infants' language (A, C, E) or cognitive (B, D, F) composite scores; black points are outliers. Avg. FuzzEn: limb averaged fuzzy entropy; Avg. mov rate: limb averaged leg movement rate; Avg. pacc: limb averaged peak acceleration per leg movement

Appendix D

Median regression results

Table D1

Summary of the median regression model investigating the association between fuzzy entropy and the language composite score at 12 months.

Predictors	*Coefficient*	*95% C.I.*	*P*
Limb-averaged fuzzy entropy	1.31	-15.55 – 18.18	0.88
Study Visit			
Visit 1	--	--	--
Visit 2	-5.86	-39.51 – 27.80	0.73
Visit 3	10.94	-32.37 – 54.24	0.62
Visit:Entropy interaction term			
Visit 1	--	--	--
Visit 2	-3.24	-27.74 – 21.27	0.79
Visit 3	-21.20	-51.95 – 9.56	0.18
Age (days)	0.28	0.11 – 0.45	0.001
Observations	118		

Note. Standard errors of the coefficients are adjusted for 40 clusters of infants.

Table D2

Summary of the median regression model investigating the association between fuzzy entropy and the cognitive composite score at 12 months.

Predictors	*Coefficient*	*95% C.I.*	*P*
Limb-averaged fuzzy entropy	7.99	-12.50 – 28.49	0.77
Study Visit			
Visit 1	--	--	--
Visit 2	-0.44	-29.41 – 28.53	0.98
Visit 3	19.14	-37.09 – 75.37	0.50
Visit:Entropy interaction term			
Visit 1	--	--	--
Visit 2	-2.10	-23.91 – 19.70	0.85
Visit 3	-18.20	-54.12 – 17.72	0.32
Age (days)	0.05	-0.15 – 0.26	0.61
Observations	118		

Note. Standard errors of the coefficients are adjusted for 40 clusters of infants.

Table D3

Summary of the median regression model investigating the association between averaged leg movement rate and the motor composite score at 12 months.

Predictors	*Coefficient*	*95% C.I.*	*P*
Limb-averaged movement rate	1.66e-16	-0.01 – 0.01	1.00
Study Visit			
Visit 1	--	--	--
Visit 2	-8.62	-25.63 – 8.40	0.32
Visit 3	2.95e-13	-11.38 – 11.38	1.00
Visit:movement rate interaction term			
Visit 1	--	--	--
Visit 2	0.01	-0.01 – 0.03	0.27
Visit 3	-1.91e-16	-0.01 – 0.01	1.00
Age (days)	-9.60e-16	-0.10 – 0.10	1.00
Observations	118		

Note. Standard errors of the coefficients are adjusted for 40 clusters of infants.

Table D4

Summary of the median regression model investigating the association between average leg movement rate and the language composite score at 12 months.

Predictors	*Coefficient*	*95% C.I.*	*P*
Limb-averaged movement rate	1.20e-3	-0.01 – 0.02	0.87
Study Visit			
Visit 1	--	--	--
Visit 2	-11.96	-35.80 – 11.87	0.32
Visit 3	-17.06	-48.80 – 14.67	0.29
Visit:movement rate interaction term			
Visit 1	--	--	--
Visit 2	2.29e-3	-0.02 – 0.03	0.85
Visit 3	-1.32e-3	-0.03 – 0.02	0.92
Age (days)	0.28	0.07 – 0.50	0.01
Observations	118		

Note. Standard errors of the coefficients are adjusted for 40 clusters of infants.

Table D5

Summary of the median regression model investigating the association between average leg movement rate and the cognitive composite score at 12 months.

Predictors	*Coefficient*	*95% C.I.*	*P*
Limb-averaged movement rate	0.00	-0.01 – 0.02	0.41
Study Visit			
Visit 1	--	--	--
Visit 2	9.12	-16.33 – 34.57	0.48
Visit 3	-3.40	-27.76 – 19.97	0.77

Visit:movement rate interaction term			
Visit 1	--	--	--
Visit 2	-0.01	-0.04 – 0.02	0.51
Visit 3	-1.08e-3	-0.02 – 0.02	0.90
Age (days)	0.04	-0.19 – 0.27	0.74
Observations	118		

Note. Standard errors of the coefficients are adjusted for 40 clusters of infants.

Table D6

Summary of the median regression model investigating the association between peak acceleration per leg movement and the motor composite score at 12 months.

Predictors	*Coefficient*	*95% C.I.*	*P*
Limb-averaged peak acceleration	-1.02e-12	-8.92 – 8.92	1.00
Study Visit			
Visit 1	--	--	--
Visit 2	-19.33	-49.06 – 10.41	0.20
Visit 3	-4.74e-12	-28.76 – 28.76	1.00
Visit:peak acceleration interaction term			
Visit 1	--	--	--
Visit 2	7.08	-3.54 – 17.70	0.19
Visit 3	1.60e-12	-9.63 – 9.63	1.00
Age (days)	2.04e-15	-0.11 – 0.11	1.00
Observations	118		

Note. Standard errors of the coefficients are adjusted for 40 clusters of infants.

Table D7

Summary of the median regression model investigating the association between peak acceleration per leg movement and the language composite score at 12 months.

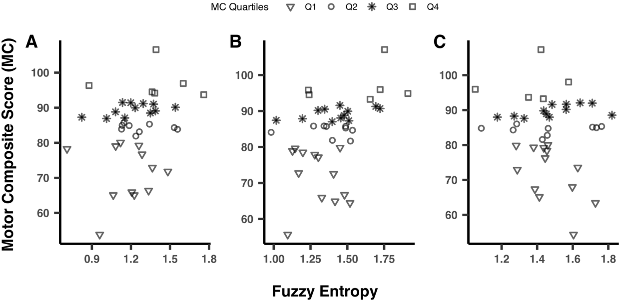
Predictors	*Coefficient*	*95% C.I.*	*P*
Limb-averaged peak acceleration	0.24	-13.82 – 14.30	0.97
Study Visit			
Visit 1	--	--	--
Visit 2	-0.82	-45.92 – 44.28	0.97
Visit 3	-13.01	-93.13 – 67.11	0.75
Visit:peak acceleration interaction term			
Visit 1	--	--	--
Visit 2	-3.34	-19.71 – 13.04	0.69
Visit 3	-2.43	-28.36 – 23.49	0.85
Age (days)	0.30	0.12 – 0.49	0.002
Observations	118		

Table D8

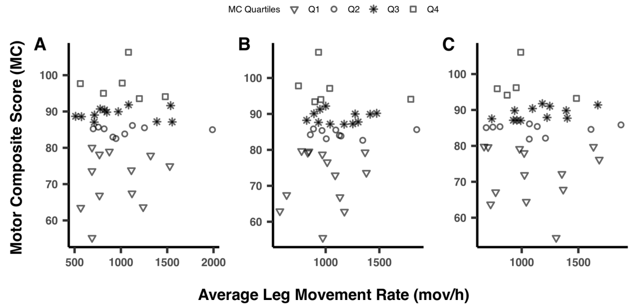
Summary of the median regression model investigating the association between peak acceleration per leg movement and the cognitive composite score at 12 months.

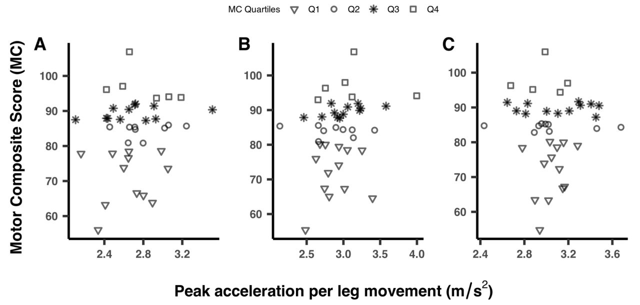
Predictors	*Coefficient*	*95% C.I.*	*P*
Limb-averaged peak acceleration	-3.79	-22.12 – 14.54	0.68
Study Visit			
Visit 1	--	--	--
Visit 2	-1.97	-57.58 – 53.65	0.94
Visit 3	-23.06	-76.66 – 30.54	0.40
Visit:peak acceleration interaction term			
Visit 1	--	--	--
Visit 2	-0.47	-19.86 – 20.81	0.96
Visit 3	6.91	-10.86 – 24.69	0.44
Age (days)	0.07	-0.16 – 0.29	0.58
Observations	118		

PM
1:35
2023-10-18
OPAL



MC Quartiles
Q1
Q2
Q3
Q4
A
B
C
Motor Composite Score (MC)
100
90
80
70
60
0.9
1.2
1.5
1.8
1.00
1.25
1.50
1.75
Fuzzy Entropy


MC Quartiles
Q1
Q2
Q3
Q4
A
B
C
Motor Composite Score (MC)
Average Leg Movement Rate (mov/h)
100
90
80
70
60
500
1000
1500
2000



MC Quartiles
Q1
Q2
Q3
Q4
A
B
C
Motor Composite Score (MC)
100
90
80
70
60
2.4
2.8
3.2
2.5
3.0
3.5
4.0
3.6
Peak acceleration per leg movement (m/s^2)