Automated movement detection reveals features of maturation in preterm infants

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***Abstract*— Nearly 10% of all births in the United States are preterm. Preterm birth is a major risk for developmental neuromotor disorders. Early characterization of a future developmental outcome is necessary to design early interventions. However, such evaluations are currently subjective and typically happen only several months after birth. The aim of this study was to quantify movement bouts after birth and to determine if features of maturation might be characterized. Four preterm infants were continuously monitored for several months, from a few days after birth until discharge, in the Neonatal Intensive Care Unit. Movement was quantified from the photoplethysmogram using a wavelet-based algorithm. In all 4 infants, maturation was associated with a decrease ($p < 0.001$) in the occurrence of movement bouts ≤ 30s and an increase ($p < 0.001$) in longer movement bouts (> 30s). The distribution of movement durations followed a power law function with its exponent defining the characteristic of the distribution. The exponent significantly increased with post-menstrual age. Future research will test whether these maturational changes can predict developmental outcomes.**

***Clinical Relevance*— Early identification of changes in features of preterm infant movement may be useful in predicting neuromotor development and potential disorders.**

I. Introduction

The human nervous system spontaneously generates a wide range of movement patterns starting as early as 8 weeks of gestational age (GA) [1]. These movements are an expression of spontaneous neural activity, continuing after birth. Infants that are born very preterm (GA <28 week) are at an increased risk for adverse neurodevelopmental disorders including motor impairments, intellectual disabilities, hearing loss, and visual impairments. The prevalence of motor disorders, cerebral palsy being the most common, is 15% in preterm infants born between 24 and 27 weeks of gestation [2]. A potential early marker of motor dysfunction might assist in designing early therapeutic interventions to treat these disorders. For example, early intervention has been shown to improve motor outcomes in infancy, with longer-term benefits in childhood and in adolescence [3].

Current methods to diagnose motor disorders involve assessing infant movement at several months of post-natal age and correlating them with outcomes at a later age. However, such assessments typically involve subjective tests administered by trained clinicians. More automated and objective measurements of spontaneous preterm movement while in the Neonatal Intensive Care Unit (NICU) could provide a better understanding of how features of movement change with development. Further, continuous assessment of motor function over longer periods may reveal important pathologies earlier and more accurately than single or sporadically repeated assessments.

The current study aimed to quantify features of movements in preterm infants over a period of months during their stay in the NICU, using an algorithm [4] that detected movement from the photoplethysmograph (PPG) signal; PPG is routinely used for oximetry in preterm infants. Maturational changes in movement patterns were quantified as a function of post-menstrual age (PMA). Additionally, the distribution of movement durations across time was examined using power law regression. A significant correlation was observed in the exponent of the power law with the post-menstrual age of the infant. This information might be clinically important for assessing long-term neurodevelopmental outcomes of preterm infants and as a tool to implement early interventions.

II. Methods

A. Subjects and data acquisition

The study protocol was approved by the Institutional Review Board at The University of Texas at Austin. Four preterm infants were studied in the Level 3 NICU at Seton Medical Center in Austin, Texas, with PMA as early as 24 4/7 weeks until discharge (mean duration: 13 1/7 weeks) (Table 1). All vital signals were continuously recorded with their native sampling rates via an RS232 connection and laptop from their bedside monitor (IntelliVue MX450, Philips) using a data acquisition system (TrendFace, ixellence GmbH, Wildau, Germany or MediCollector BEDSIDE, MediCollector LLC, Boston, MA, USA). This study analyzed only the PPG signal (sampled at 125 Hz). During their stay, infants transitioned from ventilation to spontaneous room air breathing, with feeding scheduled every 3 hours. In two subjects, there was an interruption in streaming of data due to failure of the data acquisition (Table 1).

B. Measurement of movement

The PPG signal was used to estimate movement using a wavelet-based algorithm developed and validated previously

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[4]. Briefly, the PPG signal is naturally disrupted by movement, producing non-stationary fluctuations of frequency that are lower than that of a typical PPG signal. This low-frequency artifact was analyzed using a wavelet-based algorithm to obtain an estimate of movement. The algorithm computed duration of movement bursts by identifying its onsets and offsets. Fig. 1 shows an example of a one-hour-long PPG time series (Fig. 1A) with the estimated movement waveform (Fig. 1B). Additionally, the figure shows the binary markers of movement onset and offset (Fig. 1C). In an initial analysis we divided movement durations for each day into only two categories: ≤ 30s and > 30s. To test the relation between PMA and movement in each category, a linear mixed-model regression was used with PMA as fixed effects. Subjects were entered as random effects to account for repeated observations of a single infant. The null hypothesis - no change in movement with age - was evaluated at the 0.05 significance level.

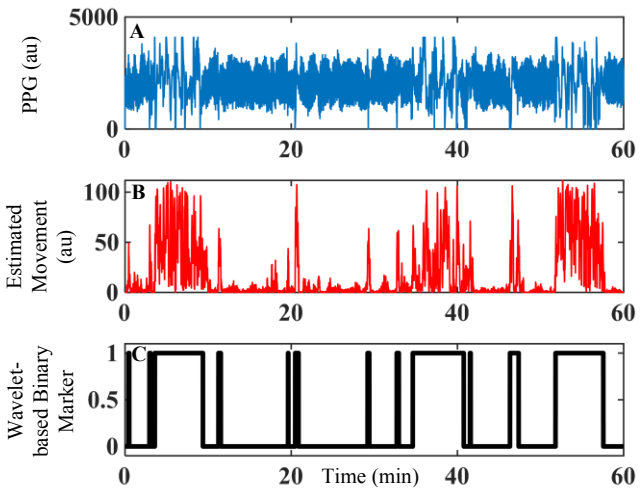

Figure 1. Detection of movement: A. PPG signal. B. Estimated movement from the wavelet-based algorithm. C. Binary markers of the onset and offset of movements determined by the wavelet algorithm.

TABLE I. SUBJECT CHARACTERISTICS

Sub #	GA (week)	PMA on day 1 of recording (week)	Birth Weight (g)	Weight on day 1 of recording (g)	Total recording time (week)	Missing data (week)
1	26 4/7	26 5/7	990	735	10 5/7	0
2	24 4/7	26 1/7	785	675	16 5/7	1 5/7
3	26 2/7	26 5/7	1065	975	10 4/7	0
4	24 4/7	25 1/7	495	520	14 6/7	1/7

GA: Gestational age; PMA: Post menstrual age

C. Distribution of movement durations

To further analyze how movement bouts changed across days, movement durations were separated into time bins with durations incremented by 5s (e.g. 10s, 15s, etc). The histograms of these movement durations, plotted for each 24-hour day, exhibited a long tail, suggesting a power law distribution. To compare distributions across days, histograms were normalized as each day had a different recording time; the area under the curve was set to 1. The power law function is defined as:

$$P(m) \sim m^{\alpha}$$

where, m is the bin number; P(m) is the normalized count of movement incidences in bin m; and α is the exponent in the power law. This exponent could be obtained by non-linear regression, which involves fitting the data to a power law function in the linear domain. Another way to compute the exponent is through linear regression of the log-log transformation of the distribution. As noted in previous studies [5, 6], the distribution of the residuals from each regression type can be used to identify the better method. Non-linear regression in the linear domain is better when the residuals are normally distributed in the linear domain, whereas linear regression in the log-log domain is better when the residuals are normally distributed on the logarithmic scale. Hence, both methods were performed and their residuals were obtained using the MATLAB function *chi2gof*. The distribution of residuals obtained by fits in the log-log scale proved to be better as will be detailed in the results (see Section IIIB).

An estimate of the exponent obtained from the fit was computed for each day of the study to assess the change in the distribution with development. A linear mixed-model regression tested the relation between PMA and the exponent, with PMA as fixed effects and subjects as random effects. Statistical analyses were performed using RStudio version 1.2.5019. The mixed models were implemented with the *lmer* function from the *lme4* package [7]. R^2-values were estimated with the *r.squaredGLMM* function from the *MuMIn* package [8].

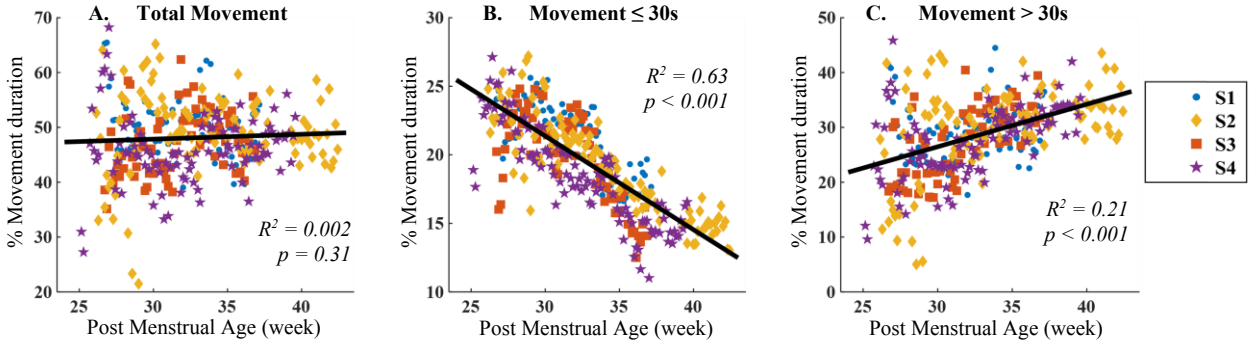

Figure 2. Movement duration as percentage of total study time by post menstrual age. A. Total movement duration. B. Movement duration ≤ 30 s. C. Movement duration > 30 s. The four colors of the symbols represent the individual subjects. The regression lines were obtained using mixed-model regression p-values indicate significance of slope of the grouped data.

III. Results

A. Change in movement duration with maturation

The percentage of total movement duration as a function of PMA is shown in Fig. 2A. While there was no change in the total time of movement with age, movements with a duration ≤ 30s gradually decreased with PMA in each of the 4 infants (Fig. 2B). The mixed-model regression rendered $R^2 = 0.63$ and $p < 0.001$. We also observed an increase in the percentage of movement duration in the > 30s category with age with $R^2 = 0.21$, and $p < 0.001$ from the mixed model analysis (Fig. 2C).

B. Power law relation

The change in movement duration with age was further characterized by the distribution of different movement durations parsed into bins of 5s increment. Given the visible long tails, the distributions were fit with a power law (Fig. 3A, B). To determine whether linear or non-linear fitting was better, the distribution of the residuals was examined. This analysis was conducted separately for each day for all subjects. Figs. 3A and 3B show the distributions of movement in one day in the linear and the log-log transformed domain, along with their best fit. The residuals from the respective fits are plotted in Figs. 3C and 3D. The log-transformed linear regressions resulted in fits with residuals that were close to a normal distribution in 310 out of 357 days of recording. The non-linear regression yielded residuals that were normally distributed in only 30 of the 357 days. Therefore, all further analyses were performed on the log-log transformed data.

Fig. 4A shows the change in the movement distributions of one infant across its PMA (subject 3). The plots reveal an increase in the incidences of more prolonged movement with increasing days of study. For better visualization, the same data is plotted in Fig. 4B after applying the logarithmic transformation of the density. Using a linear regression in the log-log domain, the exponent of the power law distribution was estimated as the slope of the linear fit for each day. Fig. 4C shows that the single day exponent during an earlier age (PMA = 30 week) was -2.19 and that for a later day of study it was -1.82 (PMA = 37 week).

Fig.5 shows the changes in the exponent across age for each of the four subjects. The colored shaded areas represent the confidence intervals in the estimation of the exponent for each day. The value of the exponent α shows a significant increase with PMA in each of the 4 infants (mixed-model analysis: $R^2 = 0.55$, $p < 0.001$). Gaps in the plot indicate missing data. The shaded gray boxes masks data before PMA of week 30. These data show more variability due to frequent procedures including artificial ventilation during this period. If these data are excluded from the analysis, the R^2 value increases to 0.7 ($p < 0.001$).

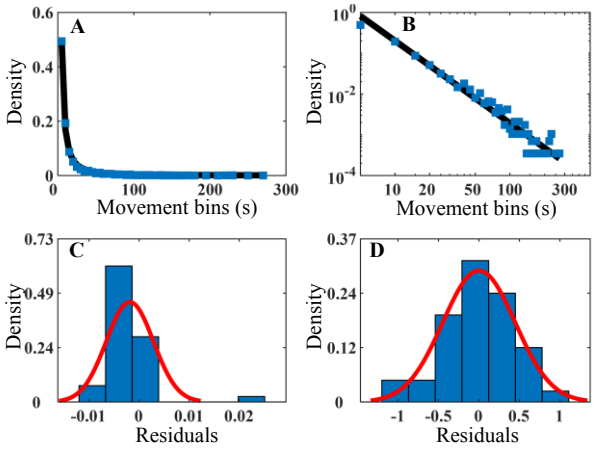

Figure 3. Fitting a power law function to movement duration in the linear domain (A) vs log-log transformed domain (B). C and D. Histogram of residuals obtained from each of the fits. Normal density functions (red) are superimposed on the histograms. Goodness-of-fit: Distribution of residuals are closer to normal in the log-log transformed domain.

IV. Discussion

This study examined two different indices that can be used to characterize the change in relative movement duration with development in preterm infants. Given the need for early identification of potential neurodevelopmental disorders, these markers could help design and implement better and earlier intervention methods.

A. Change in percentage of movement duration

In this longitudinal study we first measured duration of movement each day. Although there was no change in the total duration of movement as a percentage of recording time, there was a decrease in shorter movements ≤ 30s and an increase in longer movements > 30s. These findings are consistent with other studies on preterm infants [9, 10]. Short movements (≤30s) may correspond to twitches, sighs, startles and jitters which have shown to decrease with maturity over the preterm period. An increase in the incidences of longer movements could indicate maturation of the central nervous system where simpler and shorter movements progress into complex and more prolonged movements involving the entire body.

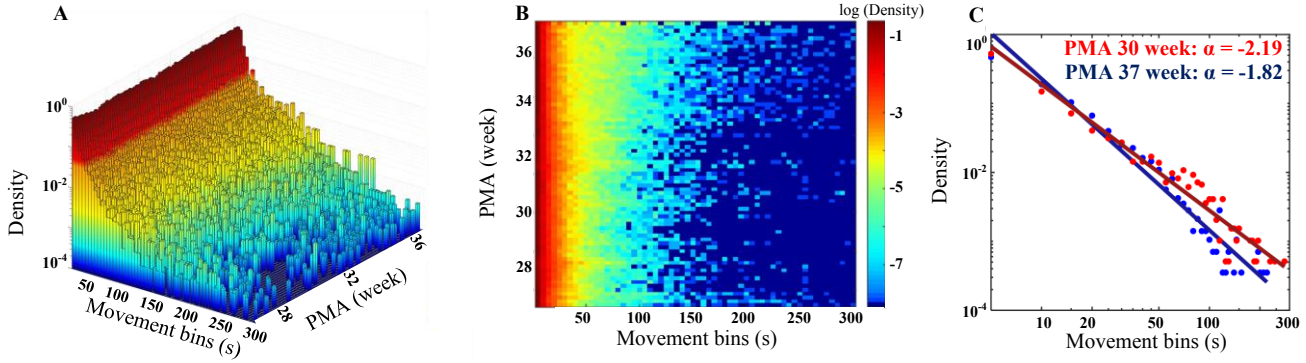

Figure 4. Power law distributions of movement duration. A. Each day of recording in a single infant (subject 3). B. Log transformation of density. C. Slope of the regression-line in the log-log domain for an earlier and later age.

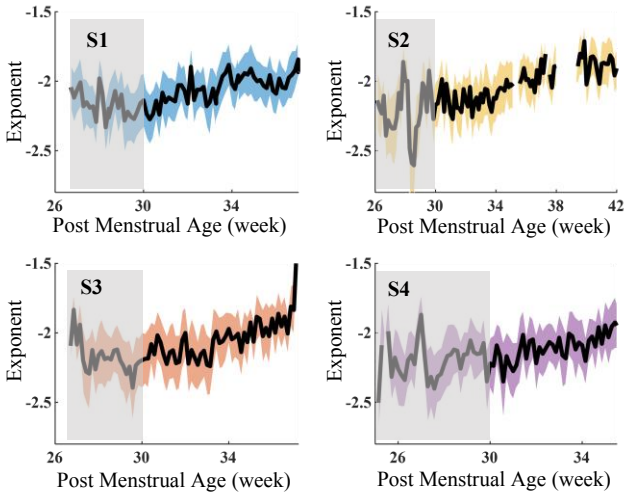

Figure 5. Change of the exponent of the power law distribution with post menstrual age. PMA < 30week are indicated by shaded grey bands. Colored shaded areas indicate the confidence interval of the estimate of the exponent.

B. Power law and physiological interpretations

When movement duration was analyzed in 5s bins, a power law distribution emerged that could be characterized by a single number, the exponent α of the power law, which is the slope of the long-tail distribution in the log-log domain. As the infants matured, the slope of the power law distribution became less steep. This is more evident beyond the PMA of 30 weeks. The variability below 30 weeks could arise from procedures during early care of the infant. Physiologically, the change in exponent could indicate several mechanisms. A first mechanism is synaptic pruning, a process during early brain development, where the brain starts out with a relatively high density of synapses [11]. As the infant matures, synapses are pruned, i.e., the number of synapses diminish. One may speculate that the high-density neural network in the brain has preferential generation of movements of shorter durations, thus generating the power law distribution [12]. As the incidences of longer movement start to increase, the exponent of the power law distribution also shifts. A second possible mechanism explaining this observation could be the increase in myelination during development. The extent of myelination has been linked to psychomotor development [13, 14]. Myelination increases the conduction speed of the nerve impulses, thus allowing for higher incidences of longer movement duration. Lastly, the maturation of neurotransmitter and neuromodulator systems such as serotonin and dopamine may be another mechanism causing the change in movement distribution [15].

C. Caveats

This study examined the change in the characteristics of movement with age. While this algorithm reliably recorded generalized movement using a routine sensor in the NICU, the algorithm was unable to capture qualitative features of movement such as intensity or limb-specificity of these movements. More features of the movements can be obtained by attaching additional sensors (accelerometers, IMUs, etc.) on the infants. However, this is not only difficult in clinical settings, but also impractical for data collection over months. Due to similar practical reasons, our data contained some confounds, such as passively generated movement on these infants from handling by nursing staff, and other procedures. Nevertheless, even without removing these events from the analyses, a visible trend in the movement characteristics was evident. This is important as for any clinical applicability, it is necessary to use data that do not require selected removal of data or other extended post-processing.

V. Conclusion

The features derived from preterm infants at such an early age might be useful when compared with outcomes at a later age, thus enabling identification of infants at risk for neurodevelopmental delays and disorders.

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