Fall 2011

Approximate Entropy Values Demonstrate Impaired Neuromotor Control of Spontaneous Leg Activity in Infants with Myelomeningocele

Beth A. Smith
Oregon Health & Science University

Caroline Teulier
University of Limerick

Jennifer Sansom
University of Michigan - Ann Arbor

Nicholas Stergiou
University of Nebraska at Omaha, nstergiou@unomaha.edu

Beverly D. Ulrich
University of Michigan - Ann Arbor

Approximate Entropy Values Demonstrate Impaired Neuromotor Control of Spontaneous Leg Activity in Infants with Myelomeningocele

ABSTRACT

Purpose: One obstacle to providing early intervention to infants with myelomeningocele (MMC) is the challenge of quantifying impaired neuromotor control of movements early in life. **Methods:** We used the nonlinear analysis tool Approximate Entropy (ApEn) to analyze periodicity and complexity of supine spontaneous lower extremity movements of infants with MMC and typical development (TD) at 1, 3, 6 and 9 months of age. **Results:** Movements of infants with MMC were more regular and repeatable (lower ApEn values) than movements of infants with TD indicating less adaptive and flexible movement patterns. For both groups ApEn values decreased with age, and the movements of infants with MMC were less complex than movements of infants with TD. Further, for infants with MMC, lesion level and age of walking onset correlated negatively with ApEn values. **Conclusions:** Our study begins to demonstrate the feasibility of ApEn to identify impaired neuromotor control in infants with MMC.

INTRODUCTION AND PURPOSE

Myelomeningocele (MMC) is the most common neural tube defect in the United States, affecting 1,500 to 2,000 infants born each year [1]. A primary effect of MMC is impaired sensori-motor function of the lower extremities, negatively influencing the ability to walk. The likelihood that children with MMC will walk ranges from approximately 20% for high lumbar lesions to 80% to 90% for sacral lesions, with a mean onset at 3 years or older [2,3]. Those who do walk tend to expend a high amount of energy on walking, and by late childhood many shift to wheelchairs for community ambulation [2-4].

Although wheelchair use to save energy for other tasks may be the optimal decision at the time, this solution does not represent the optimal outcome overall. Minimizing gait energy costs and maximizing gait function to allow for independent ambulation across the lifespan would be an ideal outcome. Although this ideal outcome is not universally feasible, recent advances in the study of neuroplasticity and neurorehabilitation suggest that better outcomes are possible. Known principles of experience-dependent neuroplasticity include “use it or lose it”, “use it and improve it”, “specificity”, “repetition, intensity, time, salience and age matter” [5]. Based on these principles, we propose that early intervention starting at birth, as opposed to our observations here and previously of physical therapy intervention starting around 3, 6 or even 9 months of age [6], is necessary to promote optimal sensori-motor development of the lower extremities and future walking ability in infants with MMC.

Admittedly, many obstacles exist to providing aggressive early intervention from birth on for infants with MMC. Multiple medical issues may limit the time available for or shift the priority away from therapy interventions concerning long-term goals; parents or caregivers may perceive infants with MMC as fragile; or limited therapist and family resources may make very

early intervention difficult to accomplish. Our focus here is on yet another important obstacle: the challenge of quantifying impaired lower extremity function early in life and relating lower extremity control early in infancy to later functional ambulation outcomes.

The challenge of quantifying impaired lower extremity function early in life and relating it to later functional ambulation outcomes is multi-factorial. Many of the early motor milestones are based on head and upper extremity movements, and infants with MMC generally do not demonstrate difficulty with these types of movements. They do have difficulty with lower extremity movements, which are generally not documented until later in motor milestone progressions on such measures as the Bayley Scales of Infant Development[7] or the Test of Infant Motor Performance[8]. Although therapists can use lesion level and assessment of muscle strength as one component of their clinical decision-making process, these assessments are at the body structure and function level of the World Health Organization International Classification of Functioning, Disability and Health (ICF) model[9] and arguably more removed from the goal of walking than an ICF activity level measure would be. Although many reports show ambulation outcomes are highly related to neurological level, there is still much disparity in outcomes as defined by lesion groups [10,11] or muscle function[12]. Further, manual muscle testing is fairly subjective and unstable in children with MMC under 5 years of age[13] and motor development preceding ambulation varies even among children with MMC who have similar muscle function[14]. There are many factors beyond lesion level that contribute to walking achievement in children with MMC[12]. Our argument here is that an objective activity level assessment will provide more accurate and specific information about impairments and change in infant lower extremity function than current body structure and function level assessments. Although it has been demonstrated at an activity level that infants with MMC spontaneously move their lower

extremities less than infants with typical development (TD) [6,15], less movement quantity alone is not sufficient to justify or guide therapeutic intervention.

In addition to assessing quantity of movements, another possibility is to assess how the movement changes over time. Nonlinear methods of analysis assess qualitative aspects of movement by directly exploring how each point in a movement trajectory influences the next and how movement patterns emerge over time. By showing how the movement trajectory changes across time, nonlinear methods can provide insight into the neuromotor control of the movement. A specific nonlinear tool that can quantify dynamic movement patterns is Approximate Entropy (ApEn). ApEn analyzes the regularity and repeatability of a signal over time. Values at zero signify greatest regularity and absolute rigidity of movement patterns, while values near 2 represent great irregularity and very noisy movement patterns. We define these two ends of the spectrum as movement patterns with low complexity, while mid-range values correspond to movements that are highly complex. Thus, complexity is equated with the most well-controlled and adaptive movement patterns[16,17].

Here we follow the theoretical perspective that health and optimal sensorimotor function is associated with a state of maximum complexity [17-20]. We test the hypothesis that spontaneous lower extremity movements of infants with MMC are less complex and less organized than movements of infants with TD, as indicated by lower ApEn values in infants with MMC. Identifying impaired neuromotor control of lower extremity movements in infants with MMC will provide support for early intervention to promote optimal sensori-motor development of the lower extremities and walking ability. Further, this tool may be used to assess change in underlying control due to development or specific interventions.

METHOD

The infants whose data we present here were participants in two different studies of infant stepping in our laboratory, one longitudinal (Study 1) and one cross-sectional (Study 2). Each study included measurement of treadmill stepping responses as well as separate recording of supine spontaneous leg movements. Although the treadmill stepping protocols were different between the studies, the overall length of testing and the amount of activity the infants performed was similar.

For Study 1, infants with MMC and TD came into the laboratory at 1, 3, 6, 9 and 12 months of age and again at walking onset. We used a 6-camera Vicon Peak Motus real-time system (Vicon Motion Systems, Centennial, CO) to collect reflective marker position data at 60 Hz during treadmill stepping and spontaneous movement testing [6,21]. For Study 2, only infants with MMC participated and were between the ages of 2-5 months or 7-10 months. We used 2 synchronized digital camcorders filming at 60Hz to record reflective marker positions during treadmill stepping and spontaneous movement testing[22]. An additional 12 infants with TD were invited to participate to increase our sample size and match the ages of the infants with MMC in Study 2. We previously published data on the quantity of spontaneous movements for a subset of the infants from Study 1 [6]. Here we have expanded our sample to include additional, older infants, and use a nonlinear analysis of complexity of lower extremity spontaneous movements to look more closely at development of segmental control.

Participants

Overall, we included the data points for 56 infants in our analyses. Infants were 1 month of age (MMC = 5, TD = 9), 3 months of age (MMC = 8, TD = 9), 6 months of age (MMC = 7, TD = 6) or 9 months of age (MMC = 6, TD = 6). The data were a mix of cross-sectional and longitudinal; about half of the infants were tested more than once as they reached the older age

groups. Specifically, two infants with MMC were tested at all 4 time points, 3 were tested 3 times, 3 were tested 2 times and 3 were tested once. Ten infants with TD were tested twice and 10 were tested once. Infants with TD were without known cognitive, sensory or motor impairments. Infants with MMC had lesions (level of repair) at or caudal to L1, and were excluded if they had neuromotor abnormalities other than those associated with MMC (e.g. Arnold Chiari II, hydrocephalus) or if they had a gestational age at birth < 28 weeks. We recruited infants through fliers and MMC clinics in hospitals [redacted]. Approval for the study was granted through the Institutional Review Board at the [redacted] and parents provided written informed consent for their infants to participate in this study. Tables 1 and 2 contain participant characteristics.

Data Collection

For all spontaneous movement testing, we removed clothing and diapers and attached reflective markers (8mm diameter) to the lateral surface of the greater trochanter, ventral surface of the patella and ventral surface of the third metatarsal. We placed infants supine on a towel-covered firm surface. We held their legs extended and parallel for the initial 10 s of each trial, then released their legs for the duration of data collection. A spotter stood near the infants' head and maintained a hand on each shoulder to prevent the infant from rolling or scooting. Infants remained in supine and moved their legs freely. During trials, parents and researchers maintained conversation but did not directly interact with the infant. For Study 1, bilateral lower extremity reflective marker data were collected for 2 2-minute trials and 1 1-minute trial. For Study 2, we collected data from the right leg for 2 minutes and then from the left leg for 2 minutes. Infants were picked up and held by their parent between trials.

For infants with MMC, we recorded aspects of the infant's medical history including lesion

level, surgeries and musculoskeletal conditions. We noted if one leg was more affected than the other. If the legs were equally affected, and for infants with TD, we assigned the right leg as less affected for statistical analysis. For all infants, we took anthropometric measurements including body length, weight, greater trochanter to lateral malleolus length, thigh length, foot length, thigh circumference and leg circumference. We assessed concurrent motor skill development level by administering the motor items from the Bayley Scales of Infant Development II [7]. We recorded the date of administration and whether the infant was able to perform the skill on this day.

Data Analysis

Study 1 data were collected directly in the Vicon Peak Motus software program. Study 2 data were transferred from the digital cameras into the software and synchronized. We then digitized hip, knee and foot markers for each trial. We were able to successfully identify the markers for the first 6147 frames of every trial, corresponding to the first 102.5 seconds of data from each 120-s, 60 Hz recording session. Using the same number of data points for every trial is important for calculating ApEn, so longer trials were shortened to provide a consistent amount of data for every trial. We calculated hip segmental angles as the angle between the thigh segment and the surface on which the infants rested. The angle data were then filtered with a 6 Hz Butterworth filter and exported for further analyses.

Before we could use the nonlinear tool ApEn to assess the complexity of infants' spontaneous movement data we first had to test the hip angle data for a deterministic structure (mathematically defined as non-random). We used Chaos Data Analyzer (CDA) software Professional Version[23] to create randomly shuffled surrogate datasets for all hip angle time series[24,25]. Subsequently, we computed the largest Lyapunov Exponent values for all surrogate and original time series and compared them. Significant differences were found between the

surrogate and original Lyapunov Exponent values, indicating that the original hip angle data were not random, but deterministic.

Next we used MATLab programs to determine the parameters necessary for ApEn calculations (m = 2 and r = 0.2) and then to calculate ApEn. Note that determining parameters m and r involve numerous calculations more detailed than elaborated here. For in-depth description of the process, readers are directed to Stergiou et al., 2004[25]. To calculate quantity of movements, we tested our data to find a threshold for movement identification that was consistent with our observations of spontaneous movements during frame-by-frame video analysis. We wanted to define a threshold that was much more sensitive to small movements than a trained observer could see, while still consistent with observed amounts of movement. We defined a movement as more than 2 degrees of hip flexion or extension in the sagittal plane in 167 ms, and counted the number of times this threshold was exceeded per trial. A lower number for the quantity of movement value indicates fewer and/or shorter movements.

Statistics

We used a 2 (group: MMC or TD) x 2 (leg: more or less affected) x 4 (age: 1, 3, 6 or 9 months) linear mixed model to test for main effects and interactions. Dependent variables were ApEn values in the first test and quantity of movement in the second. Group, leg and age were treated as fixed effects with participant as a repeated measure (by age and leg) with a diagonal structure. To look at relationships between ApEn values, motor development and factors affecting motor development in infants with MMC, we tested for Pearson correlations between ApEn values and lesion level (high = L1, L2, medium = L2/L3, L3, L4, or low = L4/L5, L5, S1), ponderal index and age at which we observed the infant demonstrate selected items of the Bayley scale (as shown in Table 3). We chose five items to represent major milestones across the age

range of our study: sits alone momentarily, sits alone 30 seconds or more, pulls to standing position, walks with minimal help and walks alone, 3 steps or more. We used a two-tailed Pearson correlation to determine if ApEn values were significantly correlated with the selected variables in infants with MMC. For the significantly correlated milestones, we used a one-tailed correlation to follow up and test whether ApEn values at 1, 3, 6 or 9 months of age were significantly correlated with the age at which we observed achievement of the selected milestone. We did not test for correlations in infants with TD because we only had complete Bayley items for 14/30 infants with TD as we did not follow the infants with TD in Study 2 after their 9-month visit to find out when they started walking independently. We used Predictive Analytics Software (SPSS: An IBM Company, Chicago, IL) version 18 for statistical analysis and set our alpha level of significance at 0.05.

RESULTS

ApEn Values

For the ApEn linear mixed model, we obtained a significant group effect ($F[1,80]= 6.40$, $p = 0.01$). There was not a significant leg effect or age effect. There were no significant interactions. As shown in Figure 1, infants with MMC demonstrated lower ApEn values than infants with TD.

Quantity of Movement

For the quantity of movement linear mixed model, we obtained a significant group effect ($F[1,89]= 24.95$, $p < 0.01$) and age effect ($F[3,44]= 5.73$, $p < 0.01$). There was not a significant leg effect or any significant interactions. As demonstrated in Figure 2, the significant group effect was due to infants with MMC producing fewer movements than infants with TD. For the significant age effect, infants produced fewer movements as they got older. Follow-up analysis

revealed that infants produced fewer movements at 6 and 9 months of age as compared to 1 month of age (*p's* < 0.05).

Correlations

For infants with MMC, there was a significant two-tailed negative correlation between ApEn values and the age at which we observed walking alone, 3 steps or more (-0.48, $p = 0.02$). We followed up with one-tailed correlations between the age at which we observed walking alone, 3 steps or more, and ApEn values at 1 month (*NS*), 3 months (-0.82, $p = 0.02$), 6 months (-0.86, $p = 0.01$) and 9 months (-0.79, $p = 0.03$). Lower ApEn values for infants with MMC at 3, 6 and 9 months of age were significantly correlated with later age of walking alone, 3 independent steps. There was also a significant one-tailed negative correlation between ApEn values and lesion level, higher lesion levels were correlated with lower ApEn values (-0.30, $p = 0.02$). Correlations between ApEn values and other motor milestones or ponderal index were not significant.

DISCUSSION

The infants with MMC in our study demonstrated lower overall ApEn values than infants with TD from primarily cross-sectional measurements at 1, 3, 6 and 9 months of age. Lower ApEn values for infants with MMC represent less complex and thus less organized lower extremity movements as compared to their peers with TD. Less organized movements have also been observed in the spontaneous upper extremity movements of infants with brain injury [26] and postural control in infants born preterm [27]. Less organized movements reflect impaired neuromotor control of movement and ApEn values are a sensitive tool for therapists and researchers to use to quantify neuromotor control of movement and show improvement as a result of intervention.

Although the patterns of results for quantity of movement and ApEn values show similar trajectories, ApEn measures aspects of movement beyond mere quantity. This is demonstrated in the 3-month data points, where the group difference in ApEn values (Figure 1) is smaller than the group difference in quantity of movement (Figure 2). If ApEn values were purely reflective of quantity of movement, we would expect to see identical trajectories for ApEn and quantity of movement. Future studies are necessary to see if ApEn measures are more sensitive than current measures to changes in neuromotor control of spontaneous lower extremity movements with intervention, however previous research suggests it might be [27,28].

Beyond quantity of movement, ApEn values reflect the regularity and repeatability of the movement patterns exploring how similar different time points are during the movement, providing a measure of overall complexity. ApEn values exist on a continuum of 0 to 2. An ApEn value of 0 represents complete regularity of a pattern and is a low complexity state. An ApEn value of 2 represents complete irregularity of a pattern and is also a low complexity state. A high complexity state is somewhere in the middle of the range. Our results showed ApEn mean values for all infants ranging from approximately 0.13 to 0.25, indicating that spontaneous leg movements were closer to the regular pattern end of the continuum compared to other types of movement, which makes sense based on the inherent oscillatory nature of leg movements. Studies of supine and sitting postural control in infants found ApEn values of around 1 and 0.23-0.63, respectively, more in the middle of the continuum[27,28]. Additionally, infants with MMC in our study produced leg movements with lower ApEn values than their peers with TD, indicating more regularity and less complexity across their kicking movements, consistent with impaired neuromotor control.

An important point to consider is that both groups have higher ApEn values at one month than at nine months. In general ApEn values are decreasing with age, indicating more regularity and less complexity in kicking movements across time. One could take the values out of context and interpret that MMC one-month ApEn values being approximately equal to TD nine-month values means infants with MMC are "better" than infants with TD and reach the goal of lower ApEn values faster. This interpretation would not be correct, however, as it overlooks the fact that kicking movements change across time, infants at one month of age do not move their legs like infants at nine months of age. As control develops, infants with TD are able to hold their upper leg stable and move only their lower leg [29]. It follows that by moving only one segment, instead of two, movements would become more regular and less complex, leading to lower ApEn values. Additionally, thinking of the emergence through time of more alternating kicks and eventual walking, it also fits that spontaneous leg movements would become more regular and less complex as infants strengthen their patterns of alternating leg movements. Lower ApEn values within age groups for infants with MMC at 3, 6 and 9 months of age, however, were significantly correlated with later age of walking alone, 3 independent steps. This indicates a likely interaction with lesion level, as lower ApEn values were correlated with higher lesion levels. These results imply that neuromotor control of leg movements in infants with MMC is fundamentally different than in infants with TD; we need to design further studies to specifically investigate and understand the factors affecting developmental trajectories in infants with MMC.

ApEn values must always be interpreted in context; for spontaneous leg movements infants with TD show a pattern of decreasing values across time as neuromotor control develops and movement patterns change. Although lower ApEn values appear ideal for infants with TD, this does not appear to be the case for infants with MMC. Infants with MMC start off with lower

ApEn values as compared to their peers with TD and decrease further over time, and those with the lowest values achieve independent walking later. ApEn values for infants with MMC are following the same trajectory as infants with TD, however they have consistently lower ApEn values than their peers with TD at comparable ages. This difference is important as it reflects a unique characteristic of dynamic control between groups in neuromotor control and/or movement patterns of spontaneous leg movements at comparable age and experience levels.

Currently, although they may be evaluated before discharge from the hospital following birth, physical therapy intervention to address impaired neuromotor control for infants with MMC is typically initiated around 3, 6 or even 9 months of age [6] (see Table 2). This is in contrast to adults with spinal cord injury, for whom therapists, researchers and third-party payers recognize the importance of aggressive early intervention to promote positive neural plasticity changes and recovery of function. Adults with spinal cord injury start physical therapy as soon as possible, with aggressive therapy initiated when they are medically stable, within days or weeks of their injury. Infants with MMC, however, are approximately 11-17 months post lesion when therapy is initiated. This approach accepts a loss of plasticity and does not promote the development of optimal neuromotor control.

What happens across the first months of life, before therapy is typically initiated, is of crucial importance to the development of optimal neuromotor control. Although infants with MMC demonstrate the same quantity of spontaneous kicking movements before and at birth, they demonstrate less movement from one month of age on as compared to infants with TD [6,15,30-32]. Lower quantity of movement relates to less organized movement through less repetitions of the perception-action cycle. A lower number of movements provide diminished opportunities to develop coordinated movements and neural networks that support stable leg movement

patterns [33]. Infants with MMC do respond adaptively to external constraints by increasing or decreasing quantity of kicking [15], demonstrating that their lower quantity of movements is amenable to intervention. We propose that increasing the quantity of lower extremity movements and cycles of perception-action from birth on should lead to optimal neuromotor control of the legs, and that this will be reflected in higher ApEn values in infants with MMC indicating more organized movements and better clinical outcomes.

It could be argued that lesser movement quantity alone is a sufficient, easier to obtain measure of neuromotor delay in infants with MMC. Barriers to using movement quantity as a clinical assessment, however, include standardizing the definition of a movement, introducing observer-related variability and addressing the natural variability in infant performance. For these reasons, it would be very difficult for an observer to use a stopwatch and get reliable measurements of quantity of spontaneous leg movements. One could use cameras and software analysis, as we do in the laboratory. While this increases the reliability of the assessment it makes it much less "clinic friendly". ApEn, alternatively, can measure the regularity and complexity of movement patterns as long as some minimal amount of leg movement is recorded. Repeated measurements could theoretically be used to assess changes in the regularity and complexity of spontaneous kicking patterns across time, independent of the fact that an infant kicked more or less at a given session. We did not, however, test the inherent variability of repeated measurements in this study.

In summary, we have shown here that ApEn reflects impaired neuromotor control and less organized, less complex movements of the lower extremities of infants with MMC as compared to infants with TD starting at one month of age. Our study begins to demonstrate the feasibility of ApEn as a valuable tool for identifying and quantifying impaired neuromotor

control in infants with MMC. ApEn assessment adds unique information to current clinical assessments and supports the need for therapeutic intervention early in life.

STUDY LIMITATIONS

The major limitation of our study is that it is not a longitudinal design. Additionally, we report only lesion level of surgical repair, which is not as meaningful for behavior as a functional neurological level. We only tested infants once at each time point, and infant behavior is inherently variable. It would be ideal to test infants twice at each age and follow them from birth through independent walking, and we plan to pursue such a study. Such a design would allow us to test the inherent variability of ApEn measurements as well as rigorously test the relationship between ApEn, factors affecting motor development and outcomes in infants with MMC. This study, however, provides necessary background information on the feasibility and usefulness of ApEn as an outcome measure before recruiting infants and their families for a study design that would be much more demanding of their time. We also appreciate the need for software development to allow clinicians to collect and analyze data without using research laboratory resources.

ACKNOWLEDGEMENTS

We would like to thank the participants and their families for taking part in our studies and the [redacted] for their help with recruiting.

REFERENCES

1. National Institute of Neurological Disorders and Stroke BM. Spina bifida fact sheet. *NIH Publication No 07–309.* 2007.
2. Williams EN, Broughton NS, Menelaus MB. Age-related walking in children with spina bifida. *Dev Med Child Neur.* 1999;41:446-9.
3. Iborra J, Pages E, Cuxart A. Neurological abnormalities, major orthopaedic deformities and ambulation analysis in a myelomeningocele population in Catalonia (Spain). *Spinal Cord.* 1999;37:351-7.
4. van den Berg-Emons HJ, Bussmann JB, Brobbel AS, Roebroeck ME, van Meeteren J, Stam HJ. Everyday physical activity in adolescents and young adults with meningomyelocele as measured with a novel activity monitor. *Pediatrics.* 2001;139:880-6.
5. Kleim JA, Jones TA. Principles of experience-dependent neural plasticity: Implications for rehabilitation after brain damage. *J Speech Lang Hear Res.* 2008;51:S225-39.
6. Rademacher N, Black DP, Ulrich BD. Early spontaneous leg movements in infants born with and without myelomeningocele. *Pediatr Phys Ther.* 2008;20:137.
7. Bayley N. *Bayley scales of infant development: Second edition*. San Antonio, TX: Psychological Corporation; 1993.
8. Campbell S. *The test of infant motor performance*. http://thetimp.com/. Infant Motor Performance Scales, LLC, Chicago, IL.
9. World Health Organization. *International classification of functioning, disability and health.* http://www3.who.int/icf/icftemplate.cfm?myurl=homepage.html&mytitle=Home%20Page. 2007.

10. McDonald CM, Jaffe KM, Mosca VS, Shurtleff DB. Ambulatory outcome of children with myelomeningocele: Effect of lower-extremity muscle strength. *Dev Med Child Neurol.* 1991;33:482-90.
11. Findley TW, Agre JC, Habeck RV, Schmalz R, Birkebak RR, McNally MC. Ambulation in the adolescent with myelomeningocele. I: Early childhood predictors. *Arch Phys Med Rehabil.* 1987;68:518-22.
12. Bartonek A, Saraste H. Factors influencing ambulation in myelomeningocele: A cross-sectional study. *Dev Med Child Neurol.* 2001;43:253-60.
13. McDonald CM, Jaffe KM, Shurtleff DB. Assessment of muscle strength in children with meningomyelocele: Accuracy and stability of measurements over time. *Arch Phys Med Rehabil.* 1986;67:855-61.
14. Bartonek A. Motor development toward ambulation in preschool children with myelomeningocele-a prospective study. *Pediatr Phys Ther.* 2010;22:52-60.
15. Chapman D. Context effects on the spontaneous leg movements of infants with spina bifida. *Pediatr Phys Ther.* 2002;14:62-73.
16. Harbourne RT, Stergiou N. Movement variability and the use of nonlinear tools: Principles to guide physical therapist practice. *Phys Ther.* 2009;89:267-82.
17. Stergiou N, Harbourne R, Cavanaugh J. Optimal movement variability: A new theoretical perspective for neurologic physical therapy. *J Neurol Phys Ther.* 2006;30:120-9.
18. Goldberger AL, Amaral LA, Hausdorff JM, Ivanov PC, Peng CK, Stanley HE. Fractal dynamics in physiology: Alterations with disease and aging. *Proc Natl Acad Sci U S A.* 2002;99(Suppl 1):2466-2472.

19. Peng CK, Havlin S, Stanley HE, Goldberger AL. Quantification of scaling exponents and crossover phenomena in nonstationary heartbeat time series. *Chaos.* 1995;5:82-7.
20. Seely AJ, Macklem PT. Complex systems and the technology of variability analysis [review]. *Crit Care.* 2004;8:R367-84.
21. Teulier C, Smith BA, Kubo M, et al. Stepping responses of infants with myelomeningocele when supported on a motorized treadmill. *Phys Ther.* 2009;89:60-72.
22. Pantall A, Teulier C, Smith BA, Moerchen V, Ulrich BD. Optimization of the treadmill context to elicit stepping in infants born with myelomeningocele. *Ped Phys Ther*. 2011;23(1):42-52.
23. Sprott JC, Rowlands G. *Chaos data analyzer*. New York: American Institute of Physics; 1992.
24. Smith BA, Stergiou N, Ulrich BD. Lyapunov exponent and surrogation analysis of patterns of variability: Profiles in new walkers with and without Down syndrome. *Motor control.* 2010;14:16.
25. Stergiou N. *Innovative analyses of human movement*. Champaign, IL: Human Kinetics; 2004.
26. Ohgi S, Morita S, Loo KK, Mizuike C. Time series analysis of spontaneous upper-extremity movements of premature infants with brain injuries. *Phys Ther.* 2008;88:1022-33.
27. Dusing SC, Kyvelidou A, Mercer VS, Stergiou N. Infants born preterm exhibit different patterns of center-of-pressure movement than infants born at full term. *Phys Ther.* 2009;89:1354-62.
28. Harbourne RT, Stergiou N. Nonlinear analysis of the development of sitting postural control. *Dev Psychobiol.* 2003;42:368-77.

29. Jensen JL, Thelen E, Ulrich BD, Schneider K, Zernicke RF. Adaptive dynamics of the leg movement patterns of human infants: III. Age-related differences in limb control. *J Mot Behav.* 1995;27:366-74.

30. Hobbins JC, Grannum PA, Berkowitz RL, Silverman R, Mahoney MJ. Ultrasound in the diagnosis of congenital anomalies. *Am J Obstet Gynecol.* 1979;134:331-45.

31. Korenromp MJ, van Gool JD, Bruinese HW, Kriek R. Early fetal leg movements in myelomeningocele. *Lancet.* 1986;1:917-8.

32. Warsof SL, Abramowicz JS, Sayegh SK, Levy DL. Lower limb movements and urologic function in fetuses with neural tube and other central nervous system defects. *Fetal Ther.* 1988;3:129-34.

33. Thelen E. *A dynamic systems approach to the development of cognition and action.* Cambridge, MA.: The MIT Press; 1994.

FIGURE LEGENDS

Figure 1. Mean Approximate Entropy values for each group by age. Error bars represent standard error of the mean. The overall group main effect is significant. TD = typical development, MMC = myelomeningocele.

Figure 2. Mean quantity of movement (defined as greater than 2 degrees of hip flexion or extension in 167 ms) per 6147 frames per trial for each group by age. A lower value indicates fewer and/or shorter movements. Error bars are the standard error of the mean. The overall group and age main effects are significant. TD = typical development, MMC = myelomeningocele.