2009

Nonlinear Dynamics of Infant Sitting Postural Control

Joan E. Deffeyes
University of Nebraska at Lincoln, joan_deffeyes@yahoo.com

NONLINEAR DYNAMICS OF INFANT SITTING POSTURAL CONTROL

by

Joan E. Deffeyes

A DISSERTATION

Presented to the Faculty of

The Graduate College at the University of Nebraska

In Partial Fulfillment of Requirements

For the Degree of Doctor of Philosophy

Major: Psychology

Under the Supervision of Professor Nicholas Stergiou

Lincoln, Nebraska

December, 2009

NONLINEAR DYNAMICS OF INFANT SITTING POSTURAL CONTROL

Joan Elizabeth Deffeyes, Ph.D.

University of Nebraska, 2009

Advisor: Nicholas Stergiou

Sitting is one of the first developmental milestones that an infant achieves. Thus measurements of sitting posture present an opportunity to assess sensorimotor development at a young age, in order to identify infants who might benefit from therapeutic intervention, and to monitor the efficacy of the intervention. Sitting postural sway data was collected using a force plate from infants with typical development, and from infants with delayed development, where the delay in development was due to cerebral palsy in most of the infants in the study. The center of pressure time series from the infant sitting was subjected to a number of different analyses, both traditional linear analyses, and a number of nonlinear analyses based on information theory, nonlinear dynamics, and artificial intelligence. The traditional linear measures of postural sway did not detect a difference between the two groups, but several of the nonlinear measures did detect differences. Postural sway of infants with delayed development was found to have more repeated patterns in their postural sway, and to control posture on a slower time scale than infants with typical development. Additionally, spectral analysis was performed, and high frequency (20 -30 Hz) features were observed in the postural sway of infants with typical development that were not apparent in the postural sway of infants with delayed development, and these high frequency features were particularly prominent in the posterior sway in the anterior-posterior axis in early sitting. The origins of the features are not certain, but the fastest control is from stretch reflexes, and stretch reflexes

may be contributing to the postural sway control in infant sitting. Dynamic systems theory, as applied in developmental psychology, suggests that infants need to explore a wide range of postural sway control muscle synergies, in order that the upright sitting behavior emerge. Infants with cerebral palsy often have muscle spasticity associated with altered stretch reflexes, and this may limit the exploration of a wide a range of postural control strategies, as compared to infants with typical development.

Acknowledgments

First I would like to thank all of the babies and their families who took the time from their busy lives to paricipate in this study. I would like to thank my committee for comments and suggestions on this work, including Professors Nicholas Stergiou (committee chairman and research advisor), Wayne Stuberg, Dora Matache, and Jeff French. A number of professors at University of Nebraska contributed greatly to my education with the excellent classes they taught, including Professors John Konvalina (Mathematics), Jim Rogers (Mathematics), Dora Matache (Mathematics), Joe Brown (Psychology), Roni Reiter-Palmon (Psychology), and Qiuming Zhu (Computer Science). I would also like to thank Natasha Kyvelidou who helped with the data collection for these studies, Sara Meyers, Jessie Husinga, Tim Judkins, David Miller, and all my other friends from the Biomechanics Lab. I would especially like to thank Kim Ryland and Naomi Kochi with whom I had many long discussions on such topics as the interpretation of Lyapunov exponents, the importance of nonstationarity in time series data, and the meaning of life.

During the course of my studies here in Nebraska, I was privileged to work with several members of the University of Nebraska Medical Center Munroe-Meyer Institute Physical Therapy department, including Reggie Harbourne, Stacey DeJong, Max Kurz, Brad Corr, and Wayne Stuberg. The things that these people do to help kids is amazing, and if there is any glimmer of hope that this dissertation research will ever help anyone with cerebral palsy, it will be through the work that these good people do. In particular, I would like to thank my dissertation buddy, Reggie Harbourne, whose devotion to making

the world a better place for kids with cerebral palsy has driven this project, and whose expertise in infant development has provided guidance for this project from its inception.

Prior to coming to Nebraska, a number of people helped me to define the path that I am on, including Professor Guy Genin (Washington University in Saint Louis) who taught me to appreciate mathematics, dynamics, and Godzilla; and Professor Ross Sanders (University of Edinburgh) and Roozbeh Naemi (University of Edinburgh), with whom I share a lifelong devotion to swimming and a love of the smell of chlorine in the morning.

Stanford University is a magical place, with a beautiful campus, but most importantly, amazing people, and the time I spent there had a profound influence on my work. I could not hope to name all of the professors and fellow students who contributed to my education and development during my time at Stanford, and without whom I would not have been prepared to do the work in this dissertation. Certainly among those are Professors Juan Santiago, John Eaton, Mark Denny, Scott Delp, Dennis Carter, Chris Jacobs, and Tom Andriacchi, and fellow students Karl Stahl and Chris Dyrby. Stanford's swim coach Skip Kenney may never have taken a class in nonlinear dynamics, but he understands better than anyone I have ever met how to manipulate the control parameters that allow excellent motor skills to emerge in a human being, and I probably learned as much from him as from anyone.

Finally, I would like to thank Michelle, Stephanie, and Allison Goodman for helping to keep me young at heart, Ray Goodman for his enduring love and support (not to mention the occasional sushi dinner!), and my parents for being so supportive of my quest to find beauty and truth in this world.

Grant information: This work was supported by NIDRR (H133G040118) and the University of Nebraska Presidential Graduate Fellowship.

TABLE OF CONTENTS

LIST OF MULTIMEDIA OBJECTS

CHAPTER1

INTRODUCTION TO THE DISSERTATION

The control of movement in humans is a complicated process as multiple sensory signals must be integrated, and appropriate responses determined and executed. Even for an apparently simple task such as upright sitting information from millions of sensory cells, including retinal cells, vestibular cells, cutaneous sensory cells, sensory cells in muscle spindles and Golgi tendon organs, and joint proprioceptive cells. Information must be extracted from all of the various sensory input, and control decisions made and implemented for hundreds of muscles. As complicated as control of sitting posture is, infants with typical development still are able to acquire upright sitting skill early in life, at about age 6 to 8 months, while infants with certain motor pathologies, such as cerebral palsy, take longer to acquire the skill. Stable sitting allows the infant to reach for objects in his environment, and allows visual inspection of the environment. Additionally, sitting is a major developmental milestone. Infants who don't learn to sit by age 2 years, typically never learn to walk (Fedrizzi, et al., 2000). Thus sitting is not only important in itself, but can serve as a window into the sensorimotor system of the developing infant, and provide insight into deficits in motor control in infants with developmental delay.

Human development can be viewed as an emergent process (Smith & Thelen, 2003), where behaviors such as sitting emerge as the organism matures in a manner that depends on the interaction of genetic and environmental influences. The old debate of nature versus nurture is seen to be nonsensical, just as asking whether 5 times 3 is 15 because of the 5 or is it because of the 3? The answer is 15 because of the interaction between the 3 and the 5, just as in the human emergent behaviors are a result of the

nature-nurture interaction. In African societies where early sitting is encouraged by parents' manipulating of infants' posture, the infants develop sitting at an earlier age and spend more time in an unsupported sitting posture than American infants (Bril & Sabatier, 1986). Thus the development of postural control is not entirely a matter of maturation of biological control systems, but also is influenced by the environment in which the infant develops. However, there is no culture in which infants develop independent sitting skills at age 1 month, as the neuromuscular system apparently cannot control sitting at that age regardless of environmental influences. The development of postural control is not entirely a matter of the environment in which the infant develops, but also depends on the maturation of the biological control systems. It is the interaction of the biological system and the environment in which it develops that determines the outcome of the infant's motor development, not simply biology or environment acting alone. In a complex system, the property of emergence is a result of many interactions among many individual agents. The patterns formed by a flock of birds or a school of fish, for example, emerge due to relatively simple rules being executed by each individual as they respond to each other and to the environment (Grimm, et al. 2005). Similarly, a multi-cellular human being, along with their behaviors including upright sitting, emerge based on the interactions. Each neuron may be executing a relatively simple integrate-and-fire logic, but the complex behavior patterns that emerge as a result of the interactions of over 10,000,000,000 of them are not easily predicted just from a knowledge of the integrate-and-fire logic that each is implementing.

The question arises then, if we want to characterize the emergence of sitting behavior in infants, and if we want to quantify differences between infants with typical

development and infants with developmental delay, as occurs in cerebral palsy, what are the appropriate measures to use? In this dissertation, postural sway data from sitting infants was characterized using a number of measures from nonlinear dynamics, with the hope that features of system complexity that are overlooked by more conventional, linear measures would be apparent using the nonlinear measures. These measures are described in detail in the relevant chapters, but include measures from information theory, chaos theory, and fractal measures. What these measures have in common is sensitivity to the system dynamic that linear measures of variability are lacking. However, the application of these nonlinear measures is not straight forward, as compared to the linear measures. For example, calculation of the standard deviation is straight forward with a single formula. However, each of the nonlinear analyses measures requires the use of several parameters that must be decided on in order to perform the analysis. The parameters that have been developed for use in heart rate analysis in cardiology, for example, may not be appropriate for use in postural sway analysis, and vise-versa. This much of the work performed for this dissertation is simply trying to understand how these parameters affect the analysis, and what values of the parameters are best for distinguishing differences between sitting postural sway of infants with typical development from infants with delayed development.

The dissertation is divided into five chapters, each of which is a separate paper in itself, three of which are already in print (Deffeyes, Harbourne, DeJong, Kyvelidou, Stuberg, & Stergiou, 2009; Deffeyes, Harbourne, Kyvelidou, Stuberg, & Stergiou, 2009; Deffeyes, Kochi, Harbourne, Kyvelidou, Stuberg, & Stergiou, 2009). In short, the five chapters are:

1. Analysis of infant sitting postural sway, comparing a variety of linear and nonlinear measures.

2. Analysis of late infant sitting postural sway using entropy measures.

3. Analysis of early infant sitting postural sway using approximate entropy.

4. Analysis of fractal properties of infant sitting postural sway using detrended fluctuation analysis.

5. Analysis of infant sitting postural sway using an artificial neural network model.

References

Bril, B. & Sabatier, C. (1986). The cultural context of motor development: postural manipulations in the daily life of Bambara babies (Mali). International Journal of Behavioral Development, 9, 439-453.

Deffeyes, J.E., Harbourne, R.T., DeJong, S.L., Kyvelidou, A., Stuberg, W.A., & Stergiou N. (2009). Use of information entropy measures of sitting postural sway to quantify developmental delay in infants. Journal of Neuroengineering Rehabilitation, 6, 34.

Deffeyes, J.E., Harbourne, R.T., Kyvelidou, A., Stuberg, W.A., & Stergiou, N. (2009). Nonlinear analysis of sitting postural sway indicates developmental delay in infants. Clinical Biomechanics 24(7), 564-570.

Deffeyes, J.E., Kochi, N., Harbourne, R.T., Kyvelidou, A., Stuberg, W.A., & Stergiou N. (2009). Nonlinear Detrended Fluctuation Analysis of Sitting Center-of-Pressure

Data as an Early Measure of Motor Development Pathology in Infants.vNonlinear Dynamics in Psychology and the Life Sciences, 13(4), 351-368.

Fedrizzi, E., Facchin, P., Marzaroli, M., Pagliano, E., Botteon, G., Percivalle, L., & Fazzi, E. (2000). Predictors of independent walking in children with spastic diplegia. *Journal of Child Neurology*, *15*, 228-234.

Grimm, V., Revilla, E., Berger, U., Jeltsch, F., Mooij, W.M., Railsback, S.F., Thulke, H.H., Weiner, J., Wiegand, T., DeAngelis, D.L. (2005). Pattern-oriented modeling of agent-based complex systems: lessons from ecology. Science, 310(5750), 987-91.

Smith L.B. & Thelen E. (2003). Development as a dynamic system. Trends in Cognitive Science, 7(8), 343-348.

CHAPTER 2

NONLINEAR ANALYSIS OF SITTING POSTURAL SWAY INDICATES DEVELOPMENTAL DELAY IN INFANTS

Abstract

Background: Upright sitting is one of the first developmental motor milestones achieved by infants, and sitting postural sway provides a window into the developing motor control system. A variety of posture sway measures can be used, but the optimal measures for infant development have not been identified.

Methods: We have collected sitting postural sway data from two groups of infants, one with typical development (n=33), and one with delayed development and either diagnosed with or at risk for cerebral palsy (n=26), when the infants had developed to the point where they could just maintain sitting for about ten seconds. Postural sway data was collected while infants were sitting on a force platform, and the center of pressure was analyzed using both linear and nonlinear measures.

Findings: Our results showed that a nonlinear measure, the largest Lyapunov exponent, was the only parameter of postural sway that revealed significant differences between infants with typical versus delayed development. The largest Lyapunov exponent was found to be higher for typically developing infants, indicating less repeated patterning in their movement coordination.

Interpretations: A nonlinear measure such as largest Lyapunov exponent may be useful as an identifier of pathology, and thus is a potential candidate for measuring the success of therapeutic interventions.

1. Introduction

Cerebral palsy is a result of damage that occurs to the brain early in development, typically before, during or shortly after birth. While cerebral palsy is non-progressive in that there is no further expansion of the lesion with age, the result of the early damage influences the rest of the infant's life in many ways, both medical and social. Motor control abnormalities due to the initial neurological insult give rise to atypical movement patterns, which in turn give rise to atypical development (Bleck, 1990). Motor development in infants with cerebral palsy is delayed, meaning that developmental milestones such as sitting, standing, or walking may occur later than in infants with typical development, and in severe cases these milestones may never be met (Wu, et al., 2004; Fedrizzi, et al., 2000).

There is both strong theoretical support for the idea that early intervention may result in more desirable outcome (Landsman, 2006), as well as evidence-based support (Blauw-Hospers, et al., 2007; Blauw-Hospers & Hadders-Algra, 2005). Certainly intervention early in development is seen as being beneficial among clinical practitioners (Gardner, 2005). Early intervention requires early identification of infants who would benefit from the intervention, however current methods for early identification of cerebral palsy are inadequate (Donohue & Graham, 2007). Not only are many infants with cerebral palsy difficult to identify early, but false positives can occur (Nelson & Ellenberg, 1982). Early and accurate identification of infants with cerebral palsy allows appropriate allocation of resources to help those who would benefit, avoid use of resources on those who would not, and avoids the unnecessary anxiety for parents that an incorrect identification brings. Unfortunately, early identification is difficult; however, a

lack of complexity and low variation of movement is thought to be an indication that physical therapy intervention would be indicated (Hadders-Algra, 2001).

Learning how to maintain upright sitting posture is an important motor developmental milestone. Upright sitting allows visual exploration of the environment and serves as a stable platform for reaching nearby objects. If sitting posture is not developed by age 2 years, there is a significant chance that walking will never be achieved (Wu, et al., 2004; Fedrizzi, et al., 2000). Additionally, because sitting is one of the first motor developmental milestones an infant achieves in life, detecting abnormalities in infants' sitting posture control provides an opportunity to identify infants with motor control pathologies much earlier in life than, for example, waiting until the walking or talking milestones have been missed. Thus characterizing sitting posture differences in infants with cerebral palsy and infants with typical development has the potential to allow early and objective identification of infants who would benefit from intervention (de Graaf-Peters, et al., 2007).

Linear techniques such as path length or range of movement can be used to describe how much the center of pressure moves around (quantity of movement), but these techniques don't give any information about how well controlled the movement is (quality of movement) (Stergiou, et al., 2006). For example, one infant may have a large amount of postural sway due to poor control of movement, whereas another infant may have a large amount of postural sway due to exploration of the environment after good posture control skills have been learned. Thus measures of the quantity of movement do not necessarily indicate the progress that an infant has made in control of movement. What are needed are measures of the quality of the center of pressure (COP) movement

in order to develop a more complete understanding of the development of postural control. Measures from nonlinear dynamics, such as the largest Lyapunov exponent (LyE), approximate entropy (ApEn), and correlation dimension (CorrDim) are promising new additions to the analytical tools used for physiologic time series analysis (Stergiou, et al., 2004). Because these nonlinear analysis techniques are sensitive to patterns in the data, rather than the overall magnitude of the fluctuations, they could be ideal tools for quantifying the quality of postural sway, thus making them potentially clinically useful for studying both the typical and pathological development of motor control in infants. ApEn is a measure of system complexity made by counting how often patterns of different lengths repeat in the time series (Pincus, 1991). The LyE is a measure of how rapidly trajectories diverge in phase space, and the CorrDim estimates the dimensionality of the system (Sprott & Rowlands, 1998). See Stergiou, et al., (2004) for a more complete discussion of these nonlinear measures.

These three nonlinear measures are derived from chaos theory and from information theory, and have higher values for a random signal and lower values for a periodic signal. A random signal has no patterns in it, and a periodic signal, such as a sine function has a simple pattern that repeats over and over again. While the analysis of the ideal signals can often be interpreted in terms of randomness or complexity, the interpretation of physiologic signals is considerably more difficult. Part of the difficulty lies in the fact that precise definitions of basic terminology are still evolving. For example, whether a high value for approximate entropy should be interpreted as higher complexity of the system (Vaillancourt & Newell, 2002a; Vaillancourt & Newell, 2002b) or merely as more random (Goldberger, et al., 2002) has not been resolved. A clear

definition of “complexity” is lacking. In comparing the results from different studies, one must be careful with the language used, as “complexity” defined by one author may differ from “complexity” defined by a different author.

In this paper we will speak of “optimal movement variability” as being indicative of the middle ground between random and periodic (Stergiou, et al., 2006). A random response to a stimulus would be maladaptive, just as an overly rigid pattern of response would be maladaptive. In fact, the mid-ground between these extremes is likely the best control region for maintaining appropriate responses. The mathematical theory of chaos, a branch of dynamical systems theory, suggests that the middle-ground, the region of optimal movement variability, may be chaotic. The nonlinear measures that we have selected to use, ApEn, LyE, and CorrDim, all have high values for random signal (no structure), low values for a periodic sine function (overly rigid structure), and intermediate values for chaotic region where optimal movement variability is found.

The actual assessment of chaos in experimental data is somewhat controversial due to limitations of the experimental data (Rapp, 1994), but despite the mathematical controversy, these algorithms have been successfully applied to many different biological and physiological systems, including postural sway data. In standing posture, nonlinear techniques have been used successfully to give insight into posture control. Nonlinear measures have been shown to be able to discriminate between pathologic and non-pathologic populations using standing COP data, and thus someday may be clinically useful measures. Patients with stroke (Roerdink, et al., 2006), traumatic brain injury (Cavanaugh, et al., 2006), and Parkinson’s disease (Vaillancourt & Newell, 2000; Schmit, et al., 2006) have all been shown to differ from non-pathologic controls using

nonlinear measures applied to standing COP data. Most encouraging for the present study is that COP data from standing posture in children with cerebral palsy has been found to differ from typically developing children, using both linear and nonlinear measures (Rose, et al., 2002; Donker, et al., 2008). Nonlinear measures of posture sway tend to decrease with pathology, when significant changes are observed. This might be interpreted as being more periodic, less complex, or less random.

The purpose of this paper was to investigate the use of sitting postural sway as a measure of health of the motor control system in infants. To accomplish this, we have used several linear and nonlinear time series analysis techniques to determine how sitting postural sway in typically developing infants differs from developmentally delayed infants. We hypothesized that the infants with developmental delay will have more periodic postural sway than typically developing infants. Additionally, to further explore the relationships between these various measures of postural sway, Pearson product-moment correlation coefficients were calculated, since highly correlated measures may be providing redundant information.

2. Methods

2.1. Participants

Twenty six infants with developmental delay and thirty three typically developing infants participated in the study. Recruitment was done through newsletters, flyers, and pediatric physical therapists employed at the University. Infants in the developmentally delayed group were diagnosed with cerebral palsy, or else were developmentally delayed and at risk for cerebral palsy (Table 2.1). At risk infants met one or more of the following

conditions: premature delivery, brain abnormality based on ultrasound or MRI, or significantly delayed gross motor development as measured on standardized testing with no current diagnosis. Because a definitive diagnosis of cerebral palsy had not been made, we refer to these infants as developmentally delayed, because all scored below 1.5 standard deviations below the mean for their corrected age on the Peabody Gross Motor Scale (Folio & Fewell, 2000). However, the development is likely not just delayed, but also atypical (Chen & Wollacott, 2007).

This study was part of a longitudinal study in which the infants with developmental delay received one of two different interventions. This analysis was of the data from the first month only, before any interventions had started, so all infants with developmentally delay were analyzed as a single group. A consent form was signed by a parent or guardian of all infant participants, and all procedures were approved by the University of Nebraska Medical Center Institutional Review Board.

2.2. Inclusion and exclusion criteria

Inclusion criteria for entry into the study for the typically developing infants were: a score on the Gross Motor Quotient of the Peabody Developmental Motor Scale-2 of greater than 0.5 SD below the mean, age of five months at the time of initial data collection, and sitting skills as described below in beginning sitting. Exclusion criteria for the sample of infants who are typically developing were: a score on the Gross Motor Quotient of the Peabody Developmental Motor Scale-2 of greater than 0.5 SD below the mean, diagnosed visual deficits, or diagnosed musculoskeletal problems. If a typically developing infant was found to be less than 0.5 SD below the mean, and did not qualify

for the study, the parents were informed of the score, the possibility of error in the measurement, and advised to have the infant re-evaluated within the next 3 months. Operational definitions of beginning sitting were used to determine the child's readiness for entry into the study. Beginning sitting was defined as (a) head control such that when trunk is supported at the mid-trunk, head is maintained for over one minute without bobbing; (b) infant can track an object across midline without losing head control; (c) infant may prop hands on floor or legs to lean on arms, but should not be able to reach and maintain balance in the prop sit position; (d) when supported in sitting can reach for toy; (e) can prop on elbows in the prone position for at least 30 seconds.

For the infants with developmental delay the inclusion and exclusion criteria were as follows. Inclusion criteria were: age from five months to two years, score less than 1.5 SD below the mean for their corrected age on the Peabody Gross Motor Scales, and sitting skills as described above for beginning sitting. Exclusion criteria were: age over two years, a score greater than 1.5 SD below the mean for their corrected age on the Peabody Gross Motor Scale, a diagnosed visual impairment, or a diagnosed hip dislocation or subluxation greater than 50%.

2.3. Data Collection

For data acquisition (Figure 2.1), infants sat on an AMTI force plate (Watertown, MA), interfaced to a computer system running Vicon data acquisition software (Lake Forest, CA). Markers can be seen on the infant in Figure 2.1, and kinematic data was also collected, but is not discussed in this paper. COP data were acquired through the Vicon software at 240 Hz. A frequency analysis of both the medial-lateral and anterior-posterior

components of all the COP time series from our preliminary data indicated that the range of signal frequencies that contain 99.99% of the overall signal power is between 1 and 29 Hz. Therefore, the sampling frequency was set at 240 Hz in order to be above a factor of ten higher than the highest frequency that might contain relevant signal.

For all data collection sessions, the infants were allowed time to get used to the laboratory setting, and were at their parent's side or on their lap for preparation and data collection. Infants were provided with a standard set of infant toys for distraction and comfort. All attempts were made to maintain a calm, alert state by allowing the infant to eat if hungry, be held by a parent for comforting, or adapting the temperature of the room to the infant's comfort level. Testing was only proceeded when the infant was in a calm and relaxed state, not crying or otherwise making extended vocalization. A blanket was placed over the plate for warmth and was securely adhered with double sided tape on the ground. The investigator and the parent remained at one side and in front of the infant respectively during all data collection, to assure the infant did not fall or became insecure. The child was held at the trunk for support, and gradually the infant was guided into a prop sitting position while being distracted by toys presented by the parent. Once the examiner could completely let go of the infant, data were collected for 10 seconds while the child attempted to maintain sitting postural control. Trials were performed until we had collected three trials that are acceptable for our criteria, or until the infant was indicating that they were done. At any time the child became irritated; the session was halted for comforting by the parent or a chance for feeding, and then resumed only when the child was again in a calm state. In some cases, if the infant was crying for a long period of time, then data was not collected at that session. Infants came to the lab twice

within a single week, and we attempted to get three trials in each of the two sessions.

Segments of usable (described below) data were analyzed using custom MatLab software (MathWorks, Nantick, MA). No filtering was performed on the data in order to not alter the nonlinear results (Rapp, et al., 1993). Trials were recorded including force plate data and video data from the back and side views. Afterwards segments were selected by viewing the corresponding video. Segments of data with 2000 time steps (8.3 seconds at 240 Hz) were selected from these trials by examination of the video. Acceptable segments were required to have no crying or long vocalization, no extraneous items (e.g. toys) on the force platform, neither the assistant nor the mother were touching the infant, the infant was not engaged in rhythmic behavior (e.g. flapping arms), and the infant had to be sitting and could not be in the process of falling.

2.4. Data analysis

Linear measures of the variability present in postural sway were calculated using customized MatLab software from the COP time series, using the methodology of Prieto, et al., (1996), and included root-mean-square (RMS), maximum minus minimum (range), length of the path traced by the COP (sway path), the area of a circle (circle area) that contains 95% of the COP data points, and the area of an ellipse (ellipse area) that contains 95% of the COP data points. These parameters were selected according to Chiari, et al., (2002), as being relatively independent of biomechanical factors (e.g. height and weight), which might be expected to change with development. These linear measures characterize the quantity or amount of movement variability present in the data (Stergiou, et al., 2006).

Three nonlinear measures of variability were used, approximate entropy, largest

Lyapunov exponent, and correlation dimension. Nonlinear measures of the variability present in postural sway were calculated from the COP time series as described by Harbourne and Stergiou (2003) and Stergiou, et al., (2004). Specifically, the nonlinear measures of largest Lyapunov Exponent (LyE) and the Correlation Dimension (CorDim) were calculated using the Chaos Data Analyzer software (professional version, Physics Academic Software; Sprott & Rowlands, 1998) using an embedding dimension of 6 for all files, which had been determined as one higher than the highest value for a representative sample of data segments using the Tools for Dynamics software (Applied Nonlinear Sciences, LLC and Randle, Inc, Del Mar, CA). Using too low of an embedding dimension results in points being next to each other in the phase space that do not belong next to each other (i.e. too many false nearest neighbors); using too high of an embedding dimension can lead to too few nearby trajectories to do the analysis. For consistency in the analysis, the same embedding dimension was used for all files, even if they had a dimension lower than 6. The Approximate Entropy (ApEn) was calculated using MatLab code developed by Kaplan and Staffin (1996), implementing the methodology of Pincus (1991), using a lag value of 4, an r value of 0.2 times the standard deviation of the data file, and a vector length m of 2. These r and m values are typically used in the calculation of ApEn for physiologic time series (Pincus & Goldberger, 1994), and the lag 4 values was used due to slight contamination of the 240 Hz signal with a 60 Hz sinusoidal line noise. This noise was due to the electric power distribution in North America being at 60 Hz, which can result in contamination at this frequency, and at harmonics of this frequency. All the above mentioned nonlinear measures characterize the “quality” of movement variability present in the data by examining the patterns and the order that

exist in the COP time series by evaluating point-by-point the entire data set (Stergiou, et al., 2006).

Infants came to the lab twice within a single week, and we attempted to get three trials in each of the two sessions. Sometimes the infant would cry, or not stay seated on the force plate, and data could not be collected for these sessions. Thus the analysis results for six trials in most cases, or fewer if we could not collect all six trials, were averaged, and statistical analysis performed on the average. The infants in the developmental delay group were somewhat less willing to sit for multiple trials, compared to infants in the typical development group. Infants with developmental delay on average had 5.15 trials per infant; where as infants with typical development had 5.55 trials per infant.

2.5. Statistical Analysis

Independent t-tests were used to compare the measures of postural sway from the infants with typically development and the infants with delayed development. There were thirteen different measures of postural sway that were compared, so significance was set at $p < .004$, based on a Bonferroni correction for multiple comparisons (.05/13). Additionally, Pearson product-moment correlation coefficients were calculated between the different measures of postural sway for the infants with typical development, and again for the infants with delayed development. For the correlation analyses, there were 156 total correlations calculated, so the significance level was set at $p < .000321$, based on the Bonferroni correction (.05/156). For independent t-tests and correlation analysis (described in detail below), all the data available was used.

3. Results

The age of the infants with typical development was 5.0 months (std 0.6 months). The age of the infants with delayed development was 13.3 months (std 3.4) months. Thus the infants with delayed development were older than those with typical development, as would be expected since all the infants entered the study when they were at a similar level of motor skill development (able to sit for about ten seconds).

Results of independent t-tests showed significant differences between the typically developing and delayed developing infants only for the Lyapunov exponent (Table 2.2), both in the anterior-posterior direction and in the medial-lateral direction.

The correlation analysis showed that the linear measures of postural sway were often strongly positively correlated with each other, except for sway path, for both infants with typical development (Table 2.3) and infants with developmental delay (Table 2.4). The nonlinear measures tended to not be strongly correlated with each other, except for the approximate entropy in the anterior-posterior direction and the approximate entropy in the medial-lateral direction were positively correlated.

Approximate entropy and correlation dimension were strongly negatively correlated with many of the linear measures, but never with sway path. The Lyapunov exponent was not significantly correlated with any of the linear or other nonlinear measures. These trends were seen in postural sway from both infants with typical development and infants with delayed development. There were more significant correlations of the postural sway measures for infants with typical development, which may be due to a somewhat larger sample size (n=33 for typical development group versus n=26 for delayed development group, over 25% more in the group with typical

development).

4. Discussion

We hypothesized that the infants with developmental delay likely due to cerebral palsy will have more periodic postural sway than typically developing infants, and our data supported this hypothesis. In fact, the Lyapunov exponent was found to be significantly higher for sitting postural sway of typically developing infants than for delayed infants. Optimal variability theory (Stergiou, et al., 2006) does not require that the LyE be less for the pathologic condition. Instead, it suggests that there is an optimal value, and the pathology exists if the LyE is either too high or too low. However, for posture data, with a fixed point intrinsic dynamic, the tendency is for more regular postural sway to be associated with pathology (Vaillancourt & Newell, 2002a). The ApEn and the CorrDim were not sensitive to differences between the two groups in the present study, while the LyE was found to be more sensitive to the differences in postural sway dynamics between these two populations than ApEn or CorrDim.

We included a variety of different linear and nonlinear analytical techniques for analysis of postural sway data from sitting infants. The linear measures used in this study include range, root-mean-square, length of the sway path, and area covered by the sway path. These linear techniques were chosen from those considered by Chiari, et al., (2002) for postural sway data as being relatively insensitive to body mass parameters, an important consideration for a methodology to be applied to developing infants whose mass is changing rapidly with growth. The other class of postural sway measures that we included was nonlinear analysis techniques, which were taken from nonlinear dynamics

(chaos theory) and information theory. The nonlinear analysis techniques included ApEn, LyE and CorrDim.

From all these measures, the LyE measure of postural sway was the only one of these measures that was significantly different between infants with typical versus delayed development. The infants with delayed development were found to have postural sway with a lower LyE than infants with typical development. The Lyapunov exponent is derived from chaos theory, and is a measure of how rapidly trajectories diverge in phase space (Alligood, et al., 1996). The LyE is a classic test of whether a system is chaotic or not, with a positive LyE being consistent with the system being chaotic. We would like to understand the nature of the difference in the LyE between these groups.

As mentioned in the introduction, there are a wide variety of differences to be expected between infants with cerebral palsy and infants with typical development. Dynamic systems theory has been used to describe infant sitting (Thelen & Spencer, 1998), and we expect the postural control system dynamics to be altered in infants with developmental delay or cerebral palsy, as compared to infants with typical development. A limitation of this study is that because we enrolled infants just as they were able to sit upright, the developmentally delayed infants were older than the infants with typical development. Thus it is possible that age is a contributing factor to the observed differences. However, we find that none of the linear measures showed a significant difference between the postural sway of infants with delayed versus typical development. Instead, the difference between the two groups was seen in the LyE, a measure that is sensitive to patterns in the movement.

Mathematically, the LyE indicates exponential divergence of trajectories in phase

space. Embedding the postural sway data in a phase space means that, for example in a two dimensional phase space, velocity would be plotted versus position. Imagine that at some point in time, the postural COP data has a certain velocity and position. Then the infant sways around, but at a later time the infant has the same velocity and position as the previous time. These two points would be close to each other in the phase space plot. Does the infant's sway the second time follow a similar trajectory as the first time, or does it diverge from the first trajectory, and if so how much? The LyE quantifies this divergence. For our analysis, the data was embedded in a six dimensional phase space, using position plus 5 derivatives. A higher LyE indicates more divergence of the trajectories.

Our interpretation of the LyE relevant to clinical considerations, which is somewhat speculative, is that the COP from an infant with more diversity in motor control strategies will follow different trajectories, whereas the COP from an infant with limited diversity in motor control strategies will tend to follow a similar trajectory each time, with the result being less divergence in the trajectories, and a correspondingly lower LyE. Thus the infants with delayed development appear to have less diversity in their motor control strategies than infants with typical development, based on the lower LyE values seen in the COP from sitting postural sway. Our assumption is that the infants with typical development have better motor control, and thus we speculate that the diversity in motor control strategies has a benefit, perhaps that the infants with typical development are exploring a wider variety of solutions to postural control, and/or that infants with delayed development are freezing degrees of freedom in order to have fewer control parameters to have to manipulate as they maintain upright posture. This

interpretation supports the notion that the therapist should select activities that allow and encourage the infant to explore different strategies in motor control, rather than identical repetition of a single task.

In order to gain additional insight into the relationships between these various measures of postural sway, we looked at the correlations between the variables. If two variables are highly correlated, measuring one does not provide new ability to discriminate between two populations that the other has not already provided. Variables with low correlations to other variables are of interest because they potentially measure different aspects of the system. For example, the Lyapunov exponent and COP root-mean-square were two such variables with low correlation in this study. Of these, it was the Lyapunov exponent that was sensitive to whatever aspect of movement that was different about the sitting postural sway of infants with developmental delay and infants with typical development, where as root-mean-square was not. In fact, the LyE was not highly correlated with any of the other variables, consistent with it being a uniquely useful measure. A more in-depth analysis of the relationships between these variables using principle component analysis is published elsewhere (Harbourne, Deffeyes, Kyvelidou, & Stergiou, 2009).

5. Conclusion

The ability to discriminate between the typical and delayed development groups using nonlinear analysis of postural sway has the potential to add to the specificity of diagnosis in the early months of life, when most standardized tests of infant development have little predictive value. In addition, information from postural measures may aid the therapist in decision-making for therapeutic intervention and goal setting. Furthermore, it

is desirable to be able to objectively quantify progress being made by intervention in the developmentally delayed population, assuming that the therapeutic intervention moves the quality of their movement patterns towards that of the typically developing population. Sensitive objective measures that can quantify changes in motor control of specific tasks would be useful in assessment of various interventions designed to assist developmentally delayed infants to achieve more typical movement patterns. An approach that includes nonlinear measures of postural sway, optimized for infant sitting posture data, may contribute to these goals in the future. More work is needed to determine if these potential benefits of nonlinear analysis can be realized in clinical work.

References

Alligood, K.T., Sauer, T.D., Yorke, J.A., 1996. Chaos: An Introduction to Dynamical Systems. Springer-Verlag, New York.

Blauw-Hospers, C.H., de Graaf-Peters, V.B., Dirks, T., Bos, A.F., Hadders-Algra, M., 2007. Does early intervention in infants at high risk for a developmental motor disorder improve motor and cognitive development? Neurosci. Biobehav. Rev. In press.

Blauw-Hospers, C.H., Hadders-Algra, M., 2005. A systematic review of the effects of early intervention on motor development. Dev. Med. Child Neurol. 47(6), 421-32.

Bleck, E.E., 1990. Management of the lower extremities in children who have cerebral palsy. J. Bone Joint Surg. 72-A(1), 140-144.

Cavanaugh, J.T., Guskiewicz, K.M., Giuliani, C., Marshall S., Mercer V.S., Stergiou, N., 2006. Recovery of postural control after cerebral concussion: new insights using approximate entropy. J. Athl. Train. 41(3), 305-313.

Chen, J., Wollacott, M.H., 2007. Lower extremity kinetics for balance control in children with cerebral palsy. J. Mot. Behav. 39(4), 306-316.

Chiari L, Rocchi L, Cappello A., 2002. Stabilometric parameters are affected by anthropometry and foot placement. Clin. Biomech. 17(9-10), 666-677.

de Graaf-Peters, V.B., Blauw-Hospers, C.H., Dirks, T., Bakker, H., Bos, A.F., Hadders-Algra, M., 2007. Development of postural control in typically developing children and children with cerebral palsy: Possibilities for intervention? Neurosci. Biobehav. Rev. In press.

Donker, S.F., Ledebt, A., Roerdink, M., Savelsbergh, G.J., Beek, P.J., 2008. Children

with cerebral palsy exhibit greater and more regular postural sway than typically developing children. Exp. Brain. Res. 184(3), 363-370.

Donohue, P.K. Graham, E.M., 2007. Earlier markers for cerebral palsy and clinical research in premature infants. J. Perinatol. 27, 259–261.

Fedrizzi, E., Facchin, P., Marzaroli, M., Pagliano, E., Botteon, G., Percivalle, L., Fazzi, E., 2000. Predictors of independent walking in children with spastic diplegia. J. Child Neurol. 15(4), 228-234.

Folio, M.R., Fewell, R.R., 2000. Peabody Developmental Motor Scales (2nd ed.). Austin, TX : Pro-ed, Inc.

Gardner, M.R., 2005. Outcomes in children experiencing neurologic insults as preterm neonates. Pediatr. Nurs. 31(6), 448, 451-6

Goldberger, A.L., Peng, C.K., Lipsitz, L.A., 2002. What is physiologic complexity and how does it change with aging and disease? Neurobiol. Aging 23(1), 23-26.

Hadders-Algra, M., 2001. Evaluation of Motor Function in young infants by means of the assessment of general movements: a review. Pediatr. Phys. Ther. 13(1), 27-36.

Harbourne, R.T., Deffeyes, J.E., Kyvelidou, A., Stergiou, N., 2009. Complexity of Postural Control in Infants: Linear and Nonlinear Features Revealed by Principal Component Analysis. Nonlinear Dynamics Psychol Life Sci. 13(1), 123-144.

Harbourne, R.T., Stergiou, N., 2003. Nonlinear analysis of the development of sitting postural control. Dev. Psychobiol. 42, 368-77.

Kaplan, D., Staffin, P., 1996. Software for heart rate variability. [Computer software]. Retrieved from: http://www.macalester.edu/~kaplan/hrv/doc/

Landsman, G.H., 2006. What evidence, whose evidence?: Physical therapy in New York

State's clinical practice guideline and in the lives of mothers of disabled children. Soc. Sci. Med. 62(11), 2670-2680.

Nelson, K.B., Ellenberg, J.H., 1982. Children who “outgrew” cerebral palsy. Pediatrics 69(5), 529-536.

Palisano, R., Rosenbaum, P., Walter, S., Russel, D., Wood, E., Galuppi, B., 1997. Development and reliability of a system to classify gross motor function in children with cerebral palsy. Dev Med Child Neurol. 39, 214–23.

Pincus, S.M. Goldberger, A.L., 1994. Physiological time-series analysis: what does regularity quantify? Am. J. Physiol. Heart Circ. Physiol. 266(4), H1643-H1656.

Pincus, S.M., 1991. Approximate entropy as a measure of system complexity. Proc. Natl. Acad. Sci. U.S.A. 88, 2297-2301.

Rapp, P.E., 1994. A guide to dynamical analysis. Integr. Psychol. Behav. Sci. 29(3),311-327.

Rapp, P.E., Albano, A.M., Schmah, T.I., Farwell, L.A., 1993. Filtered noise can mimic low-dimensional chaotic attractors. Phys. Rev. E, 47(4), 2289-2297.

Roerdink, M., De Haart, M., Daffertshofer, A., Donker, S.F., Geurts, A.C., Beek, P.J., 2006. Dynamical structure of center-of-pressure trajectories in patients recovering from stroke. Exp. Brain Res. 174(2), 256-269.

Rose, J., Wolff, D.R., Jones, V.K., Bloch, D.A., Oehlert, J.W., Gamble, J.G., 2002. Postural balance in children with cerebral palsy. Dev. Med. Child Neurol. 44(1), 58-63.

Schmit, J.M., Riley, M.A., Dalvi, A., Sahay, A., Shear, P.K., Shockley, K.D., Pun, R.Y., 2006. Deterministic center of pressure patterns characterize postural instability in

Parkinson's disease. Exp. Brain Res. 168(3), 357-67.

Sprott, J.C., Rowlands, G., 1998. Chaos data analyzer: the professional version. Raleigh, NC: Physics Academic Software.

Stergiou, N., Buzzi, U.H., Kurz, M.J., Heidel, J., 2004. Nonlinear tools in human movement. In Stergiou (Ed.), Innovative Analysis of Human Movement: Analytical Tools for Human Movement Research (pp. 63-90). Human Kinetics, Champaign, IL.

Stergiou, N., Harbourne, R.T., Cavanaugh, J.T., 2006. Optimal movement variability: a new theoretical perspective for neurologic physical therapy. J. Neurol. Phys. Ther. 30(3), 120-129.

Thelen, E., Spencer, J.P., 1998. Posture control during reaching in young infants: A dynamic systems approach. Neurosci. Biobehav. Rev. (224), 507-514.

Vaillancourt, D.E., Newell, K.M. , 2002b. Changing complexity in human behavior and physiology through aging and disease. Neurobiol. Aging 23, 27-29.

Vaillancourt, D.E., Newell, K.M., 2000. The dynamics of resting and postural tremor in Parkinson's disease. Clin. Neurophysiol. 111(11), 2046-2056.

Vaillancourt, D.E., Newell, K.M., 2002a. Changing complexity in human behavior and physiology through aging and disease. Neurobiol. Aging 23, 1–11.

Wu, Y.W., Day, S.M., Strauss, D.J., Shavelle, R.M., 2004. Prognosis for ambulation in cerebral palsy: A population based study. Pediatrics 114(5), 1264-1271.

Table 2.1

Subject information for infants included in the developmentally delayed group

Subject	Diagnosis at 2 years old	Severity	GMFCS
1. C01	Spastic Quadriplegic CP	Severe	4
2. C02	Right Hemiplegic CP	Mild	1
3. C03	Right Hemiplegic CP	Mild	1
4. C04	Hypotonic, overall delays	Moderate	3
5. C05	Hypotonic, overall delays	Mild*	n/a
6. C06	Premature (28 weeks), BPD	Mild*	n/a
7. C07	Premature (28 weeks), BPD	Mild*	n/a
8. C08	Spastic lower extremities	Moderate	1
9. C09	Hypotonic, overall delays	Severe	3
10. C10	Athetoid CP	Moderate	2
11. C12	Mixed Quadriplegic CP	Moderate	3
12. C13	Spastic Quadriplegic CP	Severe	4
13. C14	Spastic Quadriplegic CP	Severe	4
14. C15	Right Hemiplegic CP	Mild	1
15. C17	Noonan's Syndrome	Mild*	n/a
16. C18	Athetoid CP	Moderate	3
17. C19	Spastic Quad CP & MD	Moderate	3
18. C20	Spastic Quadriplegic CP	Severe	4
19. C21	Undiagnosed; motor delay	Moderate	2

20. C23	Spastic Quadriplegic CP	Severe	4
21. C24	Mental Retardation	Mild*	n/a
22. C25	Spastic Diplegia	Moderate	2
23. C26	Premature, hearing impaired	Mild*	n/a
24. C27	Premature	Mild*	n/a
25. C29	Premature, left side weakness	Mild	1
26. C30	Premature	Mild*	n/a

Note. *Diagnosis of CP excluded, BPD=Brochial Pulmonary Dysplasia, MD=Muscular Dystrophy (Duchenne's), GMFCS=Gross Motor Function Classification Scale, n/a indicates GMFCS is not applicable unless infant is diagnosed with cerebral palsy (Palisano, et al., 1997)

Table 2.2

Independent t-tests comparing postural sway measures of infants with typical development with infants who have delayed development

	DD [a]		TD[b]		p
	mean	std	mean	std	
Linear					
RMS AP	6.61	3.22	6.88	2.67	0.729
RMS ML	6.31	2.90	7.30	2.24	0.143
Range AP	32.63	12.96	37.86	11.70	0.110
Range ML	29.92	12.11	36.46	10.23	0.028
Sway Path	1024.26	222.31	1110.80	221.84	0.143
Circle	1037.32	834.03	1139.52	678.28	0.606
Ellipse	823.07	649.81	1017.00	661.95	0.265
Nonlinear					
ApEn AP	0.613	0.245	0.695	0.213	0.171
ApEn ML	0.528	0.187	0.533	0.196	0.923
LyE AP	0.092	0.016	0.108	0.011	0.000
LyE ML	0.077	0.012	0.087	0.008	0.000
CorDim AP	4.262	0.306	4.357	0.261	0.204
CorDim ML	4.268	0.328	4.274	0.231	0.934

* Note. Significant at $p < .004$
a. n=26
b. n=33

Table 2.3

Correlations between different measures of postural sway for infants with typical development

	Linear						Nonlinear					
		Range					ApEn		LyE		CorDim	
Linear	RMS ML	AP	ML	SwayPath	Circle	Ellipse	AP	ML	AP	ML	AP	ML
RMS AP	0.63*	0.94*	0.65*	0.10	0.93*	0.91*	-0.63*	-0.40	-0.04	0.10	-0.83*	-0.27
RMS ML		0.58	0.96*	-0.04	0.82*	0.80*	-0.67*	-0.79*	0.15	-0.23	-0.59	-0.62*
Range AP			0.63*	0.26	0.86*	0.86*	-0.55	-0.37	0.02	0.20	-0.72*	-0.24
Range ML				0.00	0.81*	0.78*	-0.64*	-0.74*	0.18	-0.13	-0.63*	-0.54
SwayPath					0.01	0.04	0.14	0.10	0.29	0.33	0.12	0.04
Circle						0.99*	-0.66*	-0.56	0.05	-0.03	-0.79*	-0.36
Ellipse							-0.65*	-0.54	0.04	-0.06	-0.76*	-0.31
Nonlinear												
ApEn AP								0.82*	0.19	0.16	0.54	0.42
ApEn ML									-0.10	0.23	0.36	0.52
LyE AP										0.45	0.15	-0.07
LyE ML											0.07	0.21
CorDim AP												0.42

* Note. Significant at p< .000321; n=33

Table 2.4

Correlations between different measures of postural sway for infants with delayed development

	Linear						Nonlinear					
		Range					ApEn		LyE		CorDim	
Linear	RMS ML	AP	ML	SwayPath	Circle	Ellipse	AP	ML	AP	ML	AP	ML
RMS AP	0.49	0.94*	0.52	0.23	0.85*	0.85*	-0.56	-0.44	-0.23	0.11	-0.81*	-0.30
RMS ML		0.50	0.97*	-0.20	0.80*	0.82*	-0.22	-0.73*	0.18	-0.14	-0.31	-0.44
Range AP			0.57	0.30	0.80*	0.81*	-0.50	-0.36	-0.17	0.24	-0.71*	-0.26
Range ML				-0.10	0.81*	0.84*	-0.16	-0.63	0.24	-0.01	-0.31	-0.44
SwayPath					0.08	0.03	0.05	0.44	-0.16	0.19	0.02	0.27
Circle						0.98*	-0.41	-0.58	-0.07	-0.08	-0.66*	-0.37
Ellipse							-0.44	-0.65	-0.02	0.00	-0.66*	-0.40
Nonlinear												
ApEn AP								0.63	0.53	0.21	0.63	0.19
ApEn ML									0.14	0.34	0.42	0.39
LyE AP										0.55	0.37	0.14
LyE ML											0.01	0.08
CorDim AP												0.40

* Note. Significant at p< .000321; n=26

Figure 2.1. Infant sits on force plate for data collection, with researcher, parent and sibling nearby.

CHAPTER 3

USE OF INFORMATION ENTROPY MEASURES OF SITTING POSTURAL SWAY TO QUANTIFY DEVELOPMENTAL DELAY IN INFANTS

Abstract

Background

By quantifying the information entropy of postural sway data, the complexity of the postural movement of different populations can be assessed, giving insight into pathologic motor control functioning.

Methods

In this study, developmental delay of motor control function in infants was assessed by analysis of sitting postural sway data acquired from force plate center of pressure measurements. Two types of entropy measures were used: symbolic entropy, including a new asymmetric symbolic entropy measure, and approximate entropy, a more widely used entropy measure. For each method of analysis, parameters were adjusted to optimize the separation of the results from the infants with delayed development from infants with typical development.

Results

The method that gave the widest separation between the populations was the asymmetric symbolic entropy method, which we developed by modification of the symbolic entropy algorithm. The approximate entropy algorithm also performed well, using parameters optimized for the infant sitting data. The infants with delayed

development were found to have less complex patterns of postural sway in the medial-lateral direction, and were found to have different left-right symmetry in their postural sway, as compared to typically developing infants.

Conclusions

The results of this study indicate that optimization of the entropy algorithm for infant sitting postural sway data can greatly improve the ability to separate the infants with developmental delay from typically developing infants.

Background

Cerebral palsy, and other motor pathologies, give rise to altered patterns of movement. In order to quantify altered movement patterns in infants, postural sway during infant sitting can be analyzed for patterns using measures derived from information theory, such as approximate entropy and symbolic entropy. Measures such as these quantify patterns in time series data, making them potentially well suited for assessment of altered patterns of movement in a variety of movement pathologies, and may also provide insight into the nature of movement variability in human motor control pathologies [1, 2, 3, 4].

Variability in control of human movement has historically been thought of in terms of error in a control system [5]. For example, if one is tossing darts, sometimes one might toss a bull's eye (meaning the dart goes in the very center of the circular pattern of the target), but the dart doesn't always go in the bull's eye because of variability in the motor control system. This leads some to the conclusion that a motor program was not executed correctly when the dart fails to go in the bull's eye, and from this perspective, variability is always an error in the motor control system. A more recent theory of motor control, based on dynamic systems theory, views the

variability in motor control as part of the natural dynamics of the system [6]. Dynamic systems theory represents behaviors as being local minima on a potential surface, with the system proceeding towards a potential well like a marble rolling towards the bottom of a dish. Motor learning involves deepening the system's potential well associated with the behavior, and thus reducing variability. From this perspective, the potential well can never be infinitely deep, so there will always be some variability in the behavior. While a person tossing darts may wish for zero variability in their tosses, current theories on variability find that there are benefits to having some variability in movement. The theory of optimal movement variability focuses on the benefits of having a balance between rigid control and randomness in movement; i.e. complexity [7]. Having complexity in movement allows for exploration of new solutions to motor control in order to find optimal solutions. As stated by Hadders-Algra and colleagues, "Complexity points to the spatial variation of movements. It is brought about by the independent exploration of degrees of freedom in all body joints." [8,9]. Thus entropy, a measure of complexity from information theory, might be expected to differ in postural sway of infants with typical development, as compared to infants with motor development pathologies such as cerebral palsy.

The application of the concept of entropy to information theory has resulted in mathematical algorithms that are useful for describing randomness in experimental data from physiological systems. Information is a concept used in information theory, and is used in the sense that the string "ABABABABAB" has only a small amount of information in it (it is easy to guess what the next letter is – so the next letter adds no new information, hence a low information content) but "ABAABABABB" has more information (you could not determine for sure the next letter), even though both are strings of characters of the same length. Claude Shannon [10, 11], developed the

Shannon Entropy to describe the information content of a signal, with the idea that transmission of the signal for communication purposes needs to preserve the information content. If the goal of one's research is to characterize information in experimental physiologic time series, rather than in communication applications as Shannon did, there are some modifications that can be made to the algorithm. Perhaps the most widely used entropy measurement for experimental data from physiologic systems is the approximate entropy developed by Pincus [12]. The approximate entropy may serve as an indicator for the complexity of the underlying physiologic processes that give rise to the variability in the time series data [12]. In instances where pathology alters the complexity of the physiological process, the entropy value may serve as a means to identify the pathological state. For example, cardiac pathology may be identified by loss of complexity in heart rate data [13], concussions have been shown to cause loss of complexity in standing postural sway data [1], and knee ligament injury alters complexity in gait [14].

Other authors have developed different algorithms to assess entropy in experimental time series data [15, 16, 17], often with the goal of improving some aspect of the analysis. For example, one might desire to find a measure of randomness that does not depend on the length of the time series, i.e. the entropy should remain within a well defined range, regardless of the length of the time series. This would facilitate comparisons with data acquired in different laboratories, for example. Sample entropy has been used for this reason [15]. Both the approximate entropy and the sample entropy look at changes comparing patterns of length L with patterns of length L+1. Alternatively, the scaling of patterns at greatly different lengths, i.e. a pattern repeats but one repeat is longer or shorter than another, has been studied using multiscale entropy [16]. A data vector from time series data is a continuous subset of

the list of numbers that comprise the time series data. Comparison of data vectors at different points along the time series is typically done by comparing the values, with similarity of the vectors being defined as one vector having values within a specified range of those in the comparison vector. However, comparison of the vectors can be performed using fuzzy logic, resulting in the fuzzy entropy [17], where the term "fuzzy" indicates that the similarity between the vectors is not a simple binary "yes" or "no", but rather the degree of similarity is calculated.

Different types of data may be best analyzed using different measures of complexity, and it is not clear a priori which type of analysis will be best for a particular type of data. For infant sitting postural sway data, approximate entropy has been used previously [18], but other methods have not been explored. For this work we have chosen to use the approximate entropy [12], the symbolic entropy [19], and asymmetric symbolic entropy, which is a modification of the symbolic entropy. While in our Methods section we provide more details on the algorithm, in short the symbolic entropy measures how much the infant's postural sway crosses certain locations on the force plate, called "threshold values". Typically only one threshold is used, the mean of the data. We modified the symbolic entropy algorithm to allow multiple threshold values to be used. These thresholds need not be symmetric – i.e. thresholds in one direction could be set differently from thresholds in the opposite direction in order to investigate asymmetry in the data. The use of two thresholds is motivated by the idea that the postural sway needs to be confined within the base of support to avoid a fall. Therefore control of posture near the center of the base of support might not be as critical as control of posture near the boundary. In order to investigate postural control near the boundaries of the base of support, two threshold values were used. Additionally, the use of different thresholds in the left and right

directions allows the investigation of asymmetry of the postural sway, which can not be addressed with other measures of complexity.

Learning how to maintain upright sitting posture is an important motor developmental milestone. Infants use the upright sitting posture as a base from which to explore their immediate environment by reaching for nearby objects and to allow visual inspection of their immediate environment [20, 21]. Additionally, sitting is important because it is one of first developmental milestones an infant achieves, and thus serves as an early indicator of the health of the motor control system [22]. The achievement of the sitting milestone is delayed in some pathologic populations, such as those with cerebral palsy. Identification of infants with delayed motor development at the youngest age possible is of interest because treatment early in life when neural plasticity is greatest may confer greater benefits. Some intervention methods for infants with cerebral palsy may prove better than others [23]. Quantifying the differences between various interventions using sitting postural sway will assist researchers evaluating the various interventions. Specifically, cerebral palsy is a multifaceted pathology, and there is great variability in the pathology among the affected population [24]. Thus what works best for one infant may not be optimal for another infant. Early evaluation of the effectiveness of one intervention may allow early change of treatment, while neural plasticity is still greatest. For example, if an infant is found to not be responding to a particular intervention, an alternative could be implemented as soon as the first intervention can be determined to not be optimal. Thus, use of sitting postural sway as an early window into the developing motor control system could have potential clinical benefits.

While being able to extract information about the infant's motor control capabilities from sitting postural sway data could be beneficial, the best analytical

method to do so has not yet been identified. Linear measures, such as standard deviation or range of sway, may be used to describe how much movement there is in the postural sway. However, the complexity of the movements that an infant makes may be a better predictor of pathology that simply how much movement [9]. The entropy measures discussed above are promising because they have been developed to assess the complexity of a time series, rather than just assessing the amount of movement. We anticipate that the complexity of the postural sway will give insight into the motor control pathology in cerebral palsy, as it has in other motor control studies, including concussion [1], grip force in Parkinson's disease [2], stereotypical rocking in severe retardation [3], and loss of visual/cutaneous feedback [4]. However, the best algorithm to use for infant sitting needs to be determined. The reason for comparing different parameter values is to understand the impact of parameter choice on the outcome of the analysis, as different researchers will use different parameters in their analysis. But more importantly, in order for a measure to be clinically useful, it needs to maximize the ability to classify individuals correctly into one population or the other. The approach used here was to examine t-scores, the statistic used in the independent t-test to compare two populations, with the goal of maximizing the ability of the algorithm to separate the two populations.

Therefore, the goal of this investigation was to determine the utility of several different entropy algorithms in differentiating between sitting posture data of infants who have typical motor skills from sitting posture data of infants who have delayed development of motor skills. We hypothesized that infants with developmental delay will have altered complexity of postural control, because optimal variability theory suggests that pathology can be associated with either higher or lower complexity of movement [7]. Further, we hypothesized that asymmetric measures of postural control

will vary in the infants with developmental delay as compared to typically developing infants in the anterior-posterior direction (forward-backwards direction), since falling forward results in a soft landing on the legs, but falling backwards needs to be more carefully controlled.

Methods

Subjects

Infants were recruited into the study when they were just developing the ability to sit upright, and all infants participated for several months. However, the data used for this analysis is only from the last session for each infant, so it represents the most mature sitting behavior that was collected for each infant. Recruitment was done through newsletters, flyers, and pediatric physical therapists employed at the University. Twenty-two developmentally delayed infants, age 11.97 months to 27.8 months (mean=17.70, std=3.93); and nineteen typically developing infants, age 7.03 to 9.8 months (mean=8.13, std=0.71) participated in the study. Infants in the developmentally delayed group were diagnosed with cerebral palsy, or else were developmentally delayed and at risk for cerebral palsy. At risk infants met one or more of the following conditions: premature delivery, brain bleeding (of any level of severity), diagnosis of periventricular leukomalacia, or significantly delayed gross motor development as measured on standardized testing. Because a definitive diagnosis of cerebral palsy could not been made by our collaborating physicians, we refer to these infants as developmentally delayed, and all scored below 1.5 standard deviations below the mean for their corrected age on the Peabody Gross Motor Scale [25]. Exclusion criteria included having an untreated, diagnosed visual impairment, a diagnosed hip dislocation or subluxation greater than 50%, or an age outside the range

5 months to 24 months at the start of the study, which was 4 months prior to the data collection session used for this analysis. Typically developing infants were screened for normal development by a physical therapist prior to admission into the study, being excluded if they failed to score above 0.5 standard deviations below the mean on the Peabody Gross Motor Scale, had a diagnosed visual impairment, had a diagnosed musculoskeletal problem, or were older than five months at the start of the study. A consent form was signed by a parent of all infant participants, and all procedures were approved by the University of Nebraska Medical Center Institutional Review Board.

Data collection

For data acquisition, infants sat on an AMTI force plate (Watertown, MA), interfaced to a computer system running Vicon data acquisition software (Lake Forest, CA). Center of Pressure (COP) data were acquired through the Vicon software at 240 Hz, in order to be above a factor of ten higher than the highest frequency that contained relevant signal as established via spectral analysis from pilot work. Segments of usable (described below) data were analyzed using custom MatLab software (MathWorks, Nantick, MA). No filtering was performed in order to not alter the entropy results [26]. Trunk and pelvis markers were also placed on the infant, but the marker data was not analyzed for this study. An assistant sat to the left side of the infant during data acquisition, and a parent or relative (typically the mother) sat in front of the infant, for comfort and support, as well as to keep the infant's attention focused on toys held in front of the infant (Figure 3.1).

Trials were recorded including force plate data and video data from the back and side views. Afterwards segments were selected by viewing the corresponding video. Segments of data with 2000 time steps (8.3 seconds at 240 Hz) were selected

from these trials by examination of the video. The COP data allows medial-lateral (side-to-side) and anterior-posterior (front to back) to be analyzed separately. Acceptable segments were required to have no crying or long vocalization, no extraneous items (e.g. toys) on the force platform, neither the assistant nor the mother were touching the infant, the infant was not engaged in rhythmic behavior (e.g. flapping arms), and the infant had to be sitting and could not be in the process of falling.

Data analysis

Symbolic entropy. Calculation of symbolic entropy was performed on postural sway data in both the medial-lateral movement, and in the anterior-posterior movement, using the methodology presented by Aziz and Arif [19]. It is a four step process:

1. Convert the time series into a binary symbol series based on a threshold value. Time series data points below the threshold are replaced by 0, those above the threshold value are replaced by 1.

Example time series:

{ 0.6073 0.8768 0.7129 0.4104 0.3791 0.1073 0.4267 0.6073 0.8768 0.7129 }

With a threshold of 0.5718 (mean of the data) is converted to the following symbol series:

Symbol series: {1 1 1 0 0 0 0 1 1 1}

2. Words are formed from the symbols, each with a word length L. For our example, using a word length of three:

{1 1 1 0 0 0 0 1 1 1}

etc…

that is then represented as a word series (Figure 3.2c):

{ (111) (110) (100) (000) (000) (001) (011) (111)}

3. The word series can be transformed by conversion of the binary into decimal: (000=0, 001=1, 010=2, 011=3, 100=4, 101=5, 110=6, 111=7) into a word symbol series:

{7 6 4 0 0 1 3 7 }

4. Shannon's entropy can be calculated from this word symbol series, and then corrected and normalized as described by Aziz and Arif [19]. However, it is this process of conversion to a symbolic time series that is critical in finding relevant patterns in the time series.

The threshold value is a key aspect of the process, as points in the time series are either above or below the threshold value. Selection of too low of a threshold produces more ones than zeros, with a correspondingly high number of words with mostly ones. Conversely selecting too high of a threshold value results in more zeros in the symbol series, with a correspondingly high number of words with mostly zeros. If the symbol series is mostly ones (or mostly zeros) then the corresponding entropy will be low, and the complexity of the time series will not be appropriately captured in the result. Thus selection of a threshold value must be done carefully. One method is to select the mean value for the time series, thereby ensuring that half of the symbols will be zeros and half will be ones, as was done by Aziz and Arif [19]. As an example, consider the analysis with a word length of three. The words that are encoded with this approach will have a value 0 (000) if the infant stays on the low side of the mean for the time interval that corresponds to that word; or a value of 7

(111) if the infant stays on the high side of the mean for the time interval that corresponds to that word. The only way the word will have a value of other than 0 or 7 will be if the infant moves past the average value during the time interval that corresponds to that particular word. The entropy value calculated with this approach will then be a reflection of the movement back and forth past this mean value. The important question is whether this reflects a clinically meaningful measure or not.

Control of the system near the average value may not be the most sensitive measure of physiologic function of the postural control system. It may be that control towards the extreme values of postural sway, where there is a greater likelihood of falling over, would be more diagnostic of pathology in neuromuscular control. With just a single threshold value in the symbolic entropy, this can not really be explored fully. Thus a second method of calculating the symbolic entropy was devised with two threshold values. Choosing values of 0.3 and 0.8 for the threshold values, the time series

{ 0.6073 0.8768 0.7129 0.4104 0.3791 0.1073 0.4267 0.6073 0.8768 0.7129 }

is converted to the symbol series (Figure 3.2d):

{1 2 1 1 1 0 1 1 2 1}

where 0 indicates a data point below the lower threshold, 2 indicates a data point above the upper threshold, and 1 indicates a data point in between the thresholds. Again, using a word length of three for this example, the following words are obtained:

{(121), (211), (111), (110), (101), (011), (112), (121)}

with a word length of three and three symbols possible, there are 3^3= 27 possible

words, coded from 0 to 26 as follows:

000 = 0 100 = 9 200 = 18

001 = 1 101 = 10 201 = 19

002 = 2 102 = 11 202 = 20

010 = 3 110 = 12 210 = 21

011 = 4 111 = 13 211 = 22

012 = 5 112 = 14 212 = 23

020 = 6 120 = 15 220 = 24

021 = 7 121 = 16 221 = 25

022 = 8 122 = 17 222 = 26

So that the word series formed is:

{16, 22, 13, 12, 10, 4, 14, 16}

As with the single threshold symbolic entropy, Shannon's entropy is calculated from the word series, and then the normalized corrected Shannon's entropy is calculated.

The thresholds in all cases were based on the mean value of each time series, and new threshold values were calculated for each time series. In some cases of multiple thresholds, the thresholds were determined from the standard deviation of the time series. The strategy in these calculations is to examine a movement at each time step as it relates to the overall movement in that time series. In other cases, the thresholds were set as a certain number of millimeters above or below the mean. The strategy in these calculations is to examine at the actual distance moved in millimeters at each time step. In most cases the thresholds were set symmetrically, with the same distance above and below the mean being used. However, a few non-symmetric thresholds were also investigated. For example, 0 might be assigned to data points below minus three standard deviations, 1 assigned to data points between minus three

standard deviations and plus one standard deviations, and 2 assigned to all data points above one standard deviation. In this example, excursions have to be three standard deviations away from the mean in the left direction, but only one standard deviation in right direction, to trigger the assignment of a different symbol. Once the symbols have been assigned, the Shannon entropy is calculated, and then normalized, as was done for the symbolic entropy, using the method of Aziz and Arif [19]. The entire procedure is performed twice, once for data from the anterior-posterior direction, and once for the data from the medial-lateral direction.

Approximate entropy The approximate entropy (ApEn) was calculated using MatLab code developed by Kaplan and Staffin [27], implementing the methodology of Pincus [12]. Approximate entropy is a measure of how disorderly a time series is [12] and can be used to assess disorderliness in movement when applied to COP time series data. The general strategy in the calculation of approximate entropy is to examine all the points in the data set for short pattern repeats (Figure 3.2a). The length of the repeat pattern is defined by a parameter m. This is done by using a vector of length m starting at point p_i, and then counting how many other vectors at other points p_j ($j \neq i$) in the time series have a similar pattern, repeating the procedure for all vectors of length m in the time series, and summing the logarithm of the results. The r parameter defines how similar a second vector has to be in order to be counted. Another parameter, lag, indicates how many time steps there are between points in one of the length m vectors. For example, if lag=1, then adjacent points are used. To calculate approximate entropy, the log of this similarity count is normalized by the number of points in the time series. Thus three parameters are used in this algorithm, m, r, and lag. Typical values for biomechanics data analysis are lag = 1, r = 0.2 to 0.25 times the standard deviation of the time series, and m = 2 [2, 28, 29].

Statistical analysis

One goal of the statistical analysis was to find the best entropy measure to separate the two populations, since the entropy measure identified in this manner would presumably have the best chance of having clinically useful sensitivity to changes in postural control with physical therapy interventions, a long range goal of this research. In order to assess the effectiveness in separating the two populations (delayed versus typical development), we used the t-score, which is a measure of the separation between the two populations relative to the variances of the populations. The t-scores, also called t-statistics or t-values that are commonly used in independent t-tests [30], were calculated by dividing the difference in means between the two populations (mean of delayed development minus mean of typically developing) by the root mean square of the standard deviations, for each set of parameters used for each type of entropy, for COP data from both anterior-posterior and medial-lateral directions. A negative sign on the t-score indicates that the mean of the data from the typically developing is larger than the mean of the data from delayed development. The t-score indicates how much the two populations overlap for the given measure, with larger magnitude indicating less overlap.

The analysis includes multiple comparisons, but they are not all independent. In other words, the entropy calculated with one set of parameters is correlated with the entropy calculated with a slightly different set of parameters, and values of t scores in the tables 1-4 are similar to values nearby. We have 2 types of entropy (approximate entropy and symbolic entropy) and 3 parameters for each (approximate entropy has m, r, and lag; symbolic entropy has number of threshold values, position of threshold, and symmetry of thresholds). Thus, there are 2 times 3 equal with 6 parameters that we have adjusted independently. This number times 2 (for postural

sway in the two directions: the anterior-posterior and medial-lateral) gives a total of 12. The Bonferroni correction requires the p-value to be adjusted for the number of independent comparisons. Thus, we set the p_{crit} =.05/12 = .00417, corresponding to a t-score of magnitude 3.04 for a t-tailed test with 39 degrees of freedom (dof = n_1 + n_2 – 2; where n_1 and n_2 are the number of subjects sampled from the two populations).

Results

The t-score results (Table 3.1) indicated that the symbolic entropy does find significant differences between the medial-lateral postural sway of typically developing infants compared to infants with delayed development. The t-score results in the anterior-posterior direction were less able to detect separation between the two populations (Table 3.2). The largest t-scores are for two threshold analysis with non-symmetric thresholds, as presented in last row of two-threshold analyses in Table 3.1. The larger magnitude t-scores (Table 3.1) are connected with two threshold values being assigned relatively far away from the mean, with the thresholds assigned on the order of three standard deviations above and below the mean value of the COP. This is consistent with the notion that control near the extreme positions (i.e. far to the right or far to the left) is important, since poor control near the extreme values of the COP may result in a fall. The best threshold of those tested was the mean-3 std, mean+1 std. This means that excursions farther away from the mean to the left side (mean -3 std) and excursions not as far away to the right side (mean + 1 std) were the important differences between the populations. A word length of about 4 to 7 was found to be the most successful. The largest magnitude t-score of -3.48 corresponds to p-value equal with 0.00125 for a two-tailed test and for degrees of freedom equal with 39. While the separation found between the two populations by this measure of entropy is considered statistically significant, the clinical significance of the measure

identified here would have to be determined with additional experimentation.

The approximate entropy algorithm was also capable of detecting separation between the infants with typical development and the infants with delayed development. As with the symbolic entropy, the largest separations were seen between typical development and delayed development in the medial-lateral direction. Also, as with symbolic entropy, the larger t-scores for approximate entropy were negative, indicating that entropy calculated from postural sway data of infants with typical development is higher that entropy calculated from postural sway data of infants with delayed development. Overall, the best approximate entropy result (t-score=-3.48) was with lag = 4, m =2, and r= 3*std. However several other combinations presented also larger values than the critical t value of 3.04, indicating significant differences between the two populations.

In order to visually examine the effect of these parameters on the distribution of the entropy values, plots of the entropy values for the medial-lateral postural sway were calculated with two different methods (Figure 3.3). The top plot in Figure 3.3 shows the approximate entropy values that were obtained using the following parameters: m = 2, r = 0.2 std, and lag = 4. The bottom plot shows asymmetric symbolic entropy values that were obtained using two thresholds, mean – 3 std and mean + 1 std, and a word length of seven. This plot visually illustrates the benefit of using a method with a larger magnitude t-score for analysis of sitting postural sway in the medial-lateral direction to compare these two populations, as the populations can be seen to overlap quite a bit with the standard approximate entropy analysis (top) where as the separation is better in the asymmetric symbolic entropy analysis (bottom).

Discussion

One aspect of this work was the exploration of the effects of various parameters in the entropy algorithms. While selection of the parameters used in the calculation of entropy was found to affect the results, the parameter values that give rise to statistically significant comparisons show consistent trends, with the typically developing infants having higher entropy values in sitting postural sway, and sway in the medial-lateral having the bigger differences between the populations.

Furthermore, two hypotheses were proposed in the introduction. One was that the complexity of postural sway of infants with delayed development would be altered as compared to that for infants with typical development. Importantly, a finding of this study was that the medial-lateral postural sway in sitting is a useful type of data to compare infants with delayed development with those who are typically developing, and that infants with typical development are seen to have more information entropy in their movement in this dimension than infants with delayed development, as measured by approximate entropy and symbolic entropy. This is consistent with the notion that development of a postural control strategy involves an exploration of the many possible solutions to Bernstein's degrees of freedom problem in order to arrive at a control strategy with optimal variability [7]. In this study we found that infants with typical development appear to be exploring more varied motor strategies, giving rise to a higher level of complexity in their postural sway. Therefore, healthy postural control is seen to be more complex as predicted by the optimal movement variability [7].

The second hypothesis, that lack of symmetry in anterior-posterior posterior control would be different between infants with delayed development and those with typical development, was not supported. A surprising result of this study was that the asymmetric symbolic entropy in the medial-lateral direction (left-right movement)

found larger separation between postural sway in infants with developmental delay and those with typical development. We had expected this result in the anterior-posterior axis, since the result of a large excursion in the posterior direction is falling over, whereas a large excursion in the anterior direction merely results in the infant resting the torso on top of the legs. In fact, this was the motivation for trying the non-symmetric thresholds. However, the impact of the non-symmetric threshold was actually seen in the medial-lateral direction. As described in the experimental section, a researcher is always positioned to the left of the infant. Perhaps having a large object in the visual field unilaterally alters the infants' postural sway, as vision has been shown to impact standing postural sway in infants, although the effect was only seen in infants after walking skills had been acquired [31]. If integration of visual information is different in the two populations of infants, differences in postural sway could result. Alternatively, the non-symmetric postural sway may be due to some type of psychological response that the infants have to the presence of the adult on the left side, and this response is different in the two populations of infants. Infants develop a protective extension reaction [32], which is a reaction of the arms to falling from a seated position. The protective extension reaction develops first in the anterior direction, typically at around 6 months. Then it develops sideways, typically at around eight months. Finally, from about the tenth month, they are able to use their arms to prevent backwards falls. An infant who has developed this reaction for sideways falling may well respond differently to the presence of a researcher on one side than an infant who has not yet developed this reaction. Based on this typical development schedule of the protective extension reaction [32], we would expect that the typically developing infants would have developed this response, where as the infants with delayed development may not. However we did not test the infants for the protective

extension response, so this is a speculative explanation. An alternative explanation which should be considered is that there may be some unconscious bias in how the researcher sitting next to the infants responds to near falls in the two populations, perhaps being more protective of falling movement away from themselves in infants that they perceive as having less control. The reason for the success of non-symmetric thresholding in the medial-lateral axis is not clear and warrants further investigation.

The results of this study indicate that optimization of the entropy algorithm for infant sitting postural sway data can greatly improve the ability to separate the infants with developmental delay from typically developing infants. However, there is still significant overlap of even the best entropy measures, which could result in false positives or false negatives if used in a clinical setting. Further improvements may be possible, such as optimization of the number of thresholds used in the calculation of symbolic entropy, optimization of the actual threshold values, and further exploration of non-symmetric thresholds. Additionally, there are other entropy algorithms that have not yet been applied to infant sitting postural sway data, which may offer an improvement. Multiscale entropy analysis [16] has been used on gait data [33] and on heart rate data [34]. Von Newman entropy, originally derived for quantum mechanics applications, has been applied to EEG data [35]. Kolmogorov entropy has been used on EEG data for epileptic seizure prediction [36] and on cell patch-clamp recordings [37]. Success in finding an algorithm that can objectively quantify pathologic motor patterns will help to identify infants who would benefit from therapeutic intervention, as well as provide an important research tool for assessment of various interventions for developmentally delayed infants.

Based on our exploration of different parameter combinations, we can make

the following suggestions to researchers interested in using entropy measures in their work. Asymmetry can be an interesting aspect of postural sway data and of other time series data. However, asymmetry is not often probed, or if it is, then two separate force plates are required [38]. Use of the asymmetric symbolic entropy provides a means to investigate asymmetry on postural sway with data from a single force plate. Approximate entropy is a useful choice for an entropy measure, but the values for the parameters of m, lag, and r need to be optimized for the data set under investigation, rather than accepting standard values for these parameters.

Conclusions

Information entropy measures can be used to characterize randomness in time series data. We have used approximate entropy and symbolic entropy in infant sitting postural sway for infants with typical development, and infants with delayed development, where the developmental delay was likely due to cerebral palsy. While selection of the parameters used in the calculation of entropy was found to affect the results, differences between the two populations found were to be consistent for statistically significant results. The significant results were that infants with typical development were found to have less repetition of fixed patterns in the medial-lateral direction of postural sway than infants with developmental delay. This result is consistent with the notion that infants with typical development are exploring a wider range of movement patterns as they learn to control upright sitting posture. This result also suggests that therapeutic interventions that encourage the exploration of varied movement patterns would be beneficial.

References

1. Cavanaugh JT, Guskiewicz KM, Giuliani C, Marshall S, Mercer VS, Stergiou N: **Recovery of Postural Control after Cerebral Concussion: New Insights Using Approximate Entropy**. J Athl Train 2006, **41(3)**:305-313
2. Vaillancourt DE, Slifkin AB, Newell KM: **Regularity of Force Tremor in Parkinson's Disease**. Clin Neurophysiol 2001, **112(9)**:1594-603
3. Hong SL, Bodfish JW, Newell KM: **Power-Law Scaling for Macroscopic Entropy and Microscopic Complexity: Evidence from Human Movement and Posture**. Chaos 2006, **16(1)**:013135
4. Hong SL, Manor B, Li, L: **Stance and Sensory Feedback Influence on Postural Dynamics**. Neurosci Lett 2007, **423(2)**:104-8
5. Schmidt RA: **A Schema Theory of Discrete Motor Skill Learning**. Psychol Rev 1975, **82**:225-260
6. Kelso JAS: Dynamic Patterns: The Self Organization of Brain and Behavior. Cambridge, MIT Press 1995
7. Stergiou N, Harbourne RT, Cavanaugh JT: **Optimal Movement Variability: A New Theoretical Perspective for Neurologic Physical Therapy**. J Neurol Phys Ther 2006, **30(3)**:120-129
8. Hadders-Algra M: Putative neural substrate of normal and abnormal general movements. Neurosci Biobehav Rev 2007, 31(8):1181-90
9. Hadders-Algra M: **General Movements: A Window for Early Identification of Children at High Risk for Developmental Disorders**. J Pediatr 2004, **145(2 Suppl)**:S12-S18
10. Shannon CE: **A Mathematical Theory of Communication**. Bell System Technical Journal 1948, **27:**379-423

11. Shannon CE: **A Mathematical Theory of Communication**. Bell System Technical Journal 1948, **27**:623-656

12. Pincus SM: **Approximate Entropy as a Measure of System Complexity**. Proc Natl Acad Sci USA 1991, **88**:2297-2301

13. Pincus SM, Goldberger AL: **Physiological Time-Series Analysis: What Does Regularity Quantify?** Am J Physiol Heart Circ Physiol 1994, **266(4)**:H1643-H1656

14. Georgoulis AD, Moraiti C, Ristanis S, Stergiou N: **A Novel Approach to Measure Variability in the Anterior Cruciate Ligament Deficient Knee During Walking: The Use of the Approximate Entropy in Orthopaedics.** J Clin Monit Comput 2006, **20(1)**:11-18

15. Richman JS, Moorman JR: **Physiological Time-Series Analysis using Approximate Entropy and Sample Entropy**. Am J Physiol Heart Circ Physiol 2000, **278(6)**:H2039-H2049

16. Costa M, Goldberger AL, Peng C-K: **Multiscale Entropy Analysis of Complex Physiologic Time Series**. Phys Rev Lett 2002, **89(6)**:068102-1-4

17. Chen W, Wang Z, Xie H, Yu, W: **Characterization of Surface EMG Signal Based on Fuzzy Entropy**. IEEE Trans Neural Syst Rehabil Eng 2007, **15(2)**:266-72

18. Harbourne RT, Stergiou N: **Nonlinear Analysis of the Development of Sitting Postural Control**. Dev Psychobiol 2003, **42**:368-77

19. Aziz W and Arif M: **Complexity Analysis of Stride Interval Time Series by Threshold Dependent Symbolic Entropy**. Eur J Appl Physiol 2006, **98**:30-40

20. Harbourne RT, Giuliani C, Neela JM: **A Kinematic and Electromyographic**

Analysis of the Development of Sitting Posture in Infants. Dev Psychobiol 1993, **26(1)**:51-64

21. de Graaf-Peters VB, Bakker H, van Eykern LA, Otten B, Hadders-Algra M: **Postural Adjustments and Reaching in 4- and 6-Month-Old Infants: An EMG and Kinematical Study**. Exp Brain Res 2007, **181(4)**:647-56
22. Carlberg EB Hadders-Algra M: **Postural Dysfunction in Children with Cerebral Palsy: Some Implications for Therapeutic Guidance**. Neural Plast 2005, **12(2-3)**:221-228
23. Blauw-Hospers CH, de Graaf-Peters VB, Dirks T, Bos AF, Hadders-Algra M: **Does Early Intervention in Infants at High Risk for a Developmental Motor Disorder Improve Motor and Cognitive Development?** Neurosci Biobehav Rev 2007, **31(8):**1201-1212
24. Shapiro BK: **Cerebral Palsy: A Reconceptualization of the Spectrum**. J Pediatr 2004, **145(2 Suppl)**:S3-7
25. Folio MR, Fewell RR: Peabody Developmental Motor Scales (2nd ed.). Austin TX, Pro-ed Inc 2000
26. Rapp PE, Albano AM, Schmah TI, Farwell LA: **Filtered Noise Can Mimic Low-Dimensional Chaotic Attractors**. Phys Rev E 1993, **47(4)**:2289-2297
27. Kaplan D, Staffin P: **Software for Heart Rate Variability** 1996. Retrieved from: http://www.macalester.edu/~kaplan/hrv/doc/
28. Stergiou N, Buzzi UH, Kurz MJ, & Heidel J: **Nonlinear Tools in Human Movement.** In: Innovative Analysis of Human Movement: Analytical Tools for Human Movement Research. Edited by Stergiou N. Champaign IL, Human Kinetics 2004, 63-90
29. Vaillancourt DE Newell KM: **The Dynamics of Resting and Postural**

Tremor in Parkinson's Disease. Clin Neurophysiol 2000, **111(11)**:2046-2056

30. Zar JH: Biostatistical Analysis, 4th Ed. Upper Saddle River, NJ: Prentice-Hall; 1999.
31. Sundermier L, Woollacott MH: The influence of vision on the automatic postural muscle responses of newly standing and newly walking infants. Exp Brain Res 1998, 120(4):537-540
32. Pearson PH, Williams CE: Physical Therapy Services in the Developmental Disabilities. Springfield IL, Thomas Books 1972
33. Costa M, Peng C-K, Goldberger AL, and Hausdorff JM: **Multiscale Entropy Analysis of Human Gait Dynamics**. Physica A 2003, **330**:53-60
34. Costa M, Cygankiewicz I, Zareba W, Bayes de Luna A, Goldberger AL, Lobodzinski S: **Multiscale Complexity Analysis of Heart Rate Dynamics in Heart Failure: Preliminary Findings from the MUSIC Study**. Comput Cardiol 2006, **33**:101-103
35. Kamousi B, Amini A N, and He, B: **Classification of Motor Imagery by Means of Cortical Current Density Estimation and Von Neuman Entropy**. J Neural Eng 2007, **4**:7-25
36. van Drongelen W, Nayak S, Frim DM, Kohrman MH, Towle VL, Lee HC, McGee AB, Chico MS, Hecox KE: **Seizure Anticipation in Pediatric Epilepsy: Use of Kolmogorov Entropy**. Pediatr Neurol 2003, **29(3)**:207-213
37. Kleppe IC, Robinson HPC: **Correlation Entropy of Synaptic Input-Output Dynamics.** Physical Review E 2006, Statistical, Nonlinear, and Soft Matter Physics, **74(4 pt 1)**:041909
38. Myklebust JB, Lovett EG, Myklebust BM, Reynolds N, Milkowski L, Prieto TE: Two-dimensional coherence for measurement of asymmetry in postural

steadiness. Gait Posture 2009, 29(1):1-5

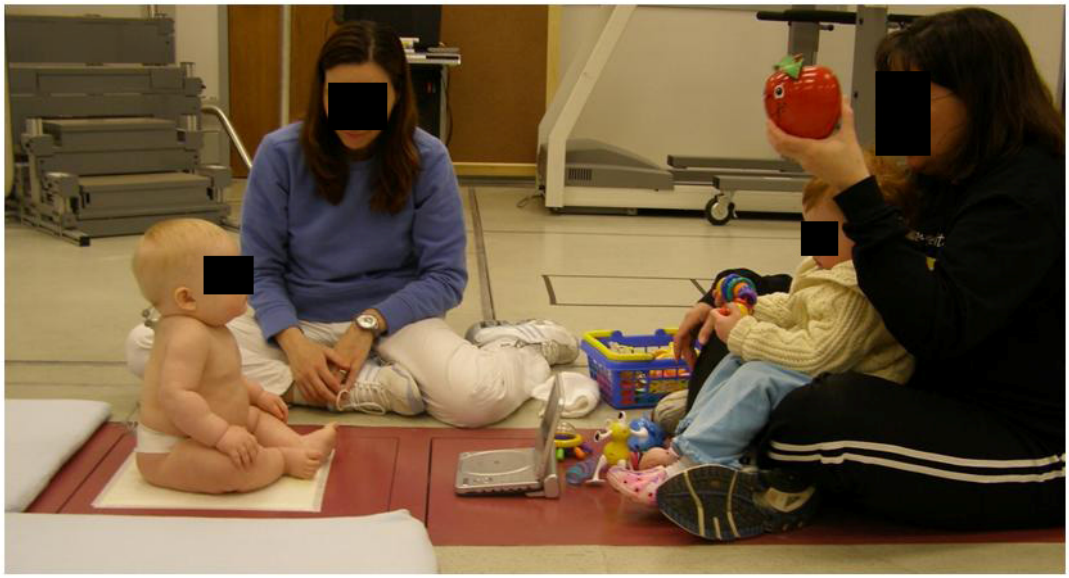

Figure 3.1. Infant sits on force platform for data collection, with researcher and parent near by.

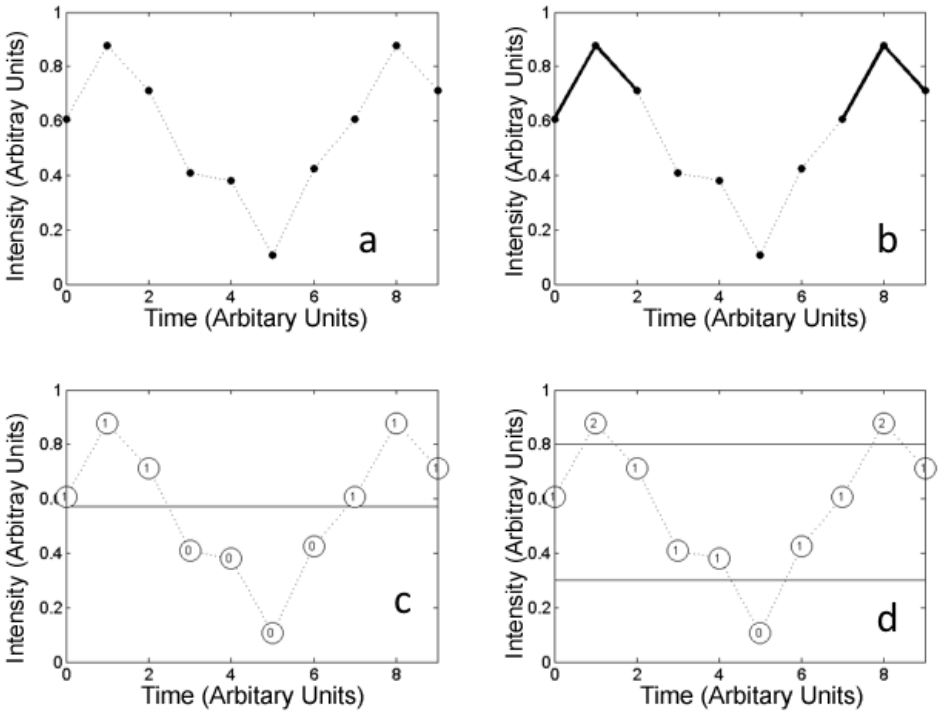

Figure 3.2. Entropy calculations

Entropy calculations: A. time series data. B. Approximate entropy counts similar vectors; here two similar vectors are shown in bold. C. Symbolic entropy with one threshold creates a time series based on whether a point is above or below the mean. Note that the value changes as the time series crosses the threshold. D. Two thresholds allow sensitivity to movement that is not close to the center, and thus closer to the presumed edge of the base of support.

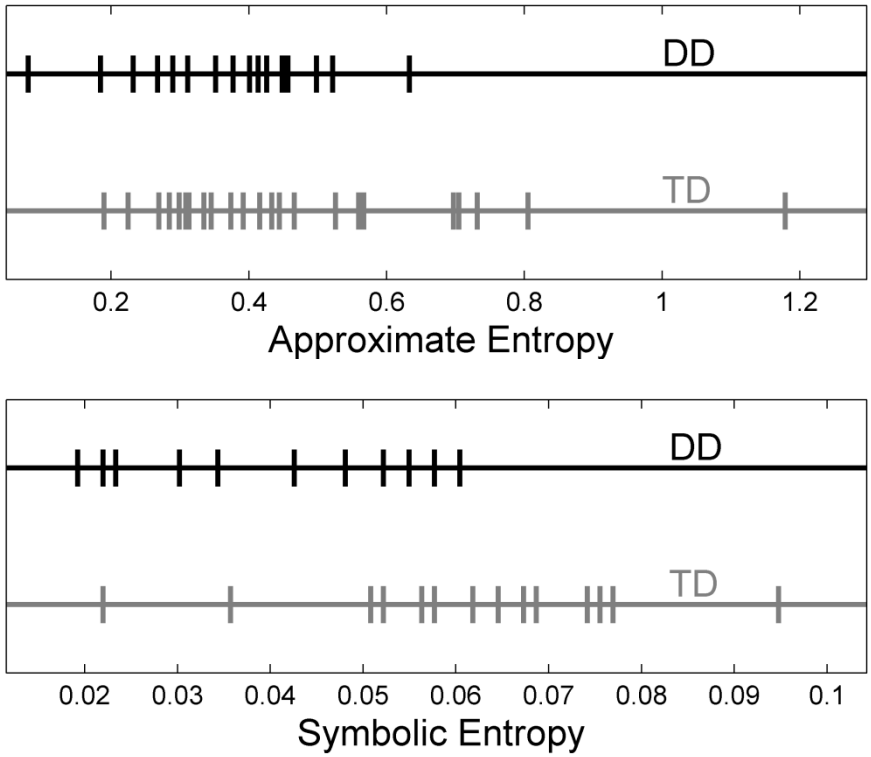

Figure 3.3. Distribution of entropy values

Distribution of entropy values for medial-lateral postural sway for infants who are typically developing versus those who have delayed development. Top plot (t-score = -1.94) is approximate entropy with r = 0.2 std, lag = 4, m = 2. Bottom plot (t-score = -3.48) is symbolic entropy with word length=6, thresholds of -3 std and +1 std. Several of the subjects have the same symbolic entropy values as other subjects; the same number time series were analyzed for both top and bottom plots. The populations (DD and TD) are much better separated by use of symbolic entropy than approximate entropy.

Table 3.1. Symbolic entropy t-scores for comparison of medial-lateral postural sway

t-scores for comparison of medial-lateral postural sway of infants with typical development and with delayed development, based on symbolic entropy calculated with various thresholds and word lengths, -3.48 is the largest magnitude t-score.

	Word length used in symbolic entropy calculation									
One threshold	1	2	3	4	5	6	7	8	9	10
M	-0.93	-0.68	0.77	-1.85	-1.44	-1.40	-1.13	-1.05	-1.12	-1.18
Two thresholds										
m - .01 std, m + .01 std	-1.20	-1.61	-1.62	-1.47	-1.39	-1.25	-1.24	-1.22	-1.31	-1.33
m - .1 std, m + .1 std	-1.26	-0.32	-0.41	-0.71	-0.72	-0.88	-1.07	-1.23	-1.30	-1.31
m - .2std, m + .2std	-0.48	-0.86	-0.67	-1.19	-1.35	-1.53	-1.46	-1.42	-1.32	-1.21
m - .5 std, m + .5 std	0.37	-1.23	-1.15	-0.51	-0.61	-0.77	-0.84	-1.03	-1.13	-1.21
m - 1 std, m + 1 std	0.44	0.29	-0.53	-1.70	-1.98	-2.10	-1.86	-1.64	-1.38	-1.22
m - 2 std, m + 2 std	-0.61	-1.07	-1.15	-0.71	-0.49	-0.43	-0.39	-0.36	-0.33	-0.31
m - 2.5 std, m + 2.5 std	-1.13	-1.04	-1.20	-1.13	-0.93	-0.82	-0.77	-0.76	-0.75	-0.77
m - 2.8 std, m + 2.8 std	-0.98	-1.30	-1.52	-1.70	-1.95	-1.99	-2.01	-2.02	-2.00	-1.97
m - 2.9 std, m + 2.9 std	-0.97	-1.38	-1.66	-1.74	-1.81	-1.82	-1.84	-1.92	-2.00	-2.05
m - 3 std, m + 3 std	-2.68	-2.76	-2.57	-2.36	-2.52	-2.59	-2.64	-2.68	-2.71	-2.79
m - 3.1 std, m + 3.1 std	-2.31	-2.67	-2.85	-2.85	-2.73	-2.62	-2.55	-2.56	-2.59	-2.62
m - 3.2 std, m + 3.2 std	-1.56	-1.92	-2.16	-2.24	-2.30	-2.32	-2.31	-2.31	-2.34	-2.35
m - 3.5 std, m + 3.5 std	-2.10	-2.24	-2.25	-2.24	-2.25	-2.25	-2.25	-2.26	-2.27	-2.29
m - 1 mm, m + 1 mm	-0.34	-1.79	-1.85	-1.69	-1.11	-1.08	-1.18	-1.34	-1.41	-1.45
m - 10 mm, m + 10 mm	-0.30	-0.49	-0.25	-0.17	-0.30	-0.46	-0.57	-0.64	-0.67	-0.67

m - 15 mm, m + 15 mm	0.61	0.59	0.42	0.19	0.06	-0.05	-0.04	-0.03	0.00	0.04
m - 20 mm, m + 20 mm	0.64	0.65	0.58	0.59	0.60	0.57	0.54	0.54	0.55	0.55
m - 25 mm, m + 25 mm	-0.39	-0.53	-0.39	-0.38	-0.30	-0.26	-0.27	-0.28	-0.29	-0.32
m - 22 mm, m+ 22 mm	-0.40	-0.53	-0.52	-0.54	-0.51	-0.45	-0.47	-0.47	-0.47	-0.50
m - 30 mm, m + 30 mm	-0.07	-0.14	0.14	0.43	0.48	0.50	0.51	0.50	0.48	0.46
m - 35 mm, m + 35 mm	0.30	0.46	0.65	0.77	0.82	0.84	0.85	0.85	0.84	0.83
m - 40 mm, m + 40 mm	0.22	0.45	0.65	0.77	0.82	0.82	0.82	0.81	0.80	0.79
m - 2 std, m + 3 std (A)	-1.30	-1.40	-1.20	-0.86	-0.73	-0.63	-0.60	-0.62	-0.65	-0.68
m - 1std, m + 3 std (A)	-1.39	-1.54	-1.45	-1.04	-1.07	-1.06	-0.95	-0.81	-0.67	-0.63
m - 3 std, m + 2 std (A)	-1.86	-2.19	-2.28	-1.85	-1.57	-1.46	-1.34	-1.22	-1.13	-1.08
m - 3 std, m + 1 std (A)	-2.52	-2.64	-2.61	**-3.33***	**-3.42***	**-3.48***	**-3.05***	-2.68	-2.28	-1.99
<u>Three thresholds</u>										
m - .01 std, m, m + .01 std	-1.16	-1.77	-2.23	-2.76	-2.25	-1.20	-0.72	-1.05	-1.14	-1.85
m - .1 std, m, m + .1 std	-1.49	0.91	-1.11	-1.16	-2.50	-2.15	-1.47	-2.08	-2.77	-1.60
m - .2std, m, m + .2std	-2.67	-1.38	-1.43	-0.54	0.57	0.64	-0.58	-0.58	-0.19	0.43
m - .5 std, m, m + .5 std	-0.27	0.19	0.15	-1.13	-1.33	-1.51	-1.91	-2.51	-1.69	-0.70
m - 1 std, m, m + 1 std	-0.18	-0.31	-0.60	-1.30	-0.68	-0.93	-0.63	-1.11	-2.70	-2.17
m - 2 std, m, m + 2 std	-2.89	-2.58	-2.35	-2.66	**-3.07**	-2.29	-1.57	-0.61	-0.37	0.10
m - 2.5 std, m, m + 2.5 std	-2.24	-1.45	-0.95	-1.41	-1.24	-1.40	-0.99	-1.33	-2.59	-2.21
m - 2.8 std, m, m + 2.8 std	-1.32	-1.05	-0.92	-1.16	-1.71	-1.46	-1.64	-1.57	-1.71	-1.53
m - 2.9 std, m, m + 2.9 std	-1.62	-1.44	-1.54	-1.54	-1.62	-1.51	-1.53	-2.37	-1.37	-1.04
m - 3 std, m, m + 3 std	-1.25	-0.96	-1.04	-1.50	-1.16	-1.67	-2.09	**-3.06**	-1.90	-1.42
m - 3.1 std, m, m + 3.1 std	-1.32	-0.94	-1.21	-1.24	-1.09	-1.01	-1.04	-1.15	-1.08	-1.22
m - 3.2 std, m, m + 3.2 std	-1.02	-1.26	-1.55	-2.10	-1.52	-1.46	-1.07	-1.46	-1.41	-1.12
m - 3.5 std, m, m + 3.5 std	-2.04	-1.74	-1.68	-1.63	-1.15	-0.69	-1.28	-1.34	-1.05	-0.89

m - 1 mm, m, m + 1 mm	0.80	0.88	1.68	1.73	1.15	0.67	0.96	0.37	0.24	-0.13
m - 10 mm, m, m + 10 mm	-1.24	-2.08	-2.20	-1.86	0.91	-0.22	0.24	0.92	1.43	1.48
m - 15 mm, m, m + 15 mm	0.41	0.57	1.52	-0.09	-0.21	-1.07	-0.55	-0.54	-0.92	-2.06
m - 20 mm, m, m + 20 mm	0.49	1.46	1.76	1.45	1.28	0.41	1.21	0.90	0.95	0.96
m - 25 mm, m, m + 25 mm	1.80	0.55	1.04	1.76	0.70	0.80	0.85	1.24	0.55	0.82
m - 22 mm, m, m+ 22 mm	-0.03	-1.25	-0.57	-0.45	-0.76	-1.78	-1.50	-1.21	1.63	0.61
m - 30 mm, m, m + 30 mm	1.26	0.59	1.09	0.97	1.00	1.11	0.83	-0.41	-0.27	-1.44
m - 35 mm, m, m + 35 mm	0.06	0.48	1.04	1.73	1.04	0.52	0.62	1.14	1.02	0.55
m - 40 mm, m, m + 40 mm	-0.23	-0.20	-0.21	-0.12	0.81	0.17	0.75	0.68	0.14	0.64
m - 2 std, m, m + 3 std (A)	1.26	0.80	0.62	1.15	1.04	0.79	1.00	0.92	0.90	1.01
m - 1std, m, m + 3 std (A)	0.85	0.37	0.75	0.61	0.26	0.84	1.30	1.84	1.33	0.91
m - 3 std, m, m + 2 std (A)	-0.37	-0.12	0.65	0.65	0.61	0.64	0.64	0.66	0.92	0.42
m - 3 std, m, m + 1 std (A)	1.08	0.94	1.09	1.02	0.99	1.06	1.45	0.02	-0.25	0.13

Note: t-scores with magnitude equal or larger than 3.04 are indicated with * and are in bold. The “m” indicates mean value for the time series, “std” indicates the standard deviation for the time series, and “mm” indicates millimetres of movement in the COP. (A) indicates asymmetric thresholds were used

Table 3.2. Symbolic entropy t-scores for comparison of anterior-posterior postural sway

t-scores for comparison of anterior-posterior postural sway of infants with typical development and with delayed development, based on symbolic entropy calculated with various thresholds and word lengths, -3.29 is the largest magnitude t-score.

	Word length used in symbolic entropy calculation									
One threshold	1	2	3	4	5	6	7	8	9	10
M	0.67	1.63	1.48	0.83	0.68	0.52	0.69	0.80	0.91	0.95
Two thresholds										
m - 1 std, m + 1 std	0.34	1.01	1.27	0.86	0.25	-0.13	-0.20	-0.25	-0.25	-0.23
m - .5 std, m + .5 std	-0.25	1.17	0.51	0.11	-0.21	-0.42	-0.13	0.15	0.31	0.40
m - .2std, m + .2std	1.53	1.24	1.12	1.01	1.20	1.14	1.04	0.98	0.97	1.02
m - .1 std, m + .1 std	1.67	0.52	0.80	0.86	1.08	1.31	1.62	1.79	1.87	1.92
m - .01 std, m + .01 std	1.32	0.41	0.75	0.53	0.72	0.85	0.96	1.12	1.25	1.32
m - 2 std, m + 2 std	0.94	1.24	1.54	1.36	0.99	0.47	0.27	0.17	0.11	0.07
m - 2.5 std, m + 2.5 std	0.38	0.80	1.17	1.51	1.52	1.39	1.35	1.32	1.37	1.43
m - 3 std, m + 3 std	0.21	0.54	0.93	1.16	1.16	1.13	1.09	1.07	1.05	1.01
m - 3.5 std, m + 3.5 std	-0.16	-0.07	0.01	0.12	0.20	0.26	0.31	0.29	0.29	0.30
m - 2.8 std, m + 2.8 std	0.98	0.89	0.90	0.94	1.04	1.08	1.08	1.09	1.11	1.16
m - 3.2 std, m + 3.2 std	0.25	0.36	0.55	0.69	0.77	0.76	0.77	0.78	0.78	0.77
m - 3.1 std, m + 3.1 std	0.02	0.21	0.60	0.84	0.81	0.78	0.76	0.70	0.69	0.67
m - 2.9 std, m + 2.9 std	0.22	0.38	0.65	0.86	1.01	1.03	1.03	1.01	0.98	0.97

m - 1 mm, m + 1 mm	1.63	1.29	1.15	1.40	1.32	1.21	1.06	0.98	1.01	1.09
m - 10 mm, m + 10 mm	-0.60	-0.28	-0.47	-0.56	-0.58	-0.67	-0.70	-0.73	-0.73	-0.74
m - 15 mm, m + 15 mm	-0.74	-0.36	-0.19	-0.20	-0.45	-0.74	-0.87	-0.97	-1.08	-1.18
m - 20 mm, m + 20 mm	-1.33	-1.19	-1.27	-1.39	-1.48	-1.57	-1.66	-1.69	-1.66	-1.66
m - 25 mm, m + 25 mm	-0.94	-0.74	-0.89	-0.89	-0.94	-0.99	-1.02	-1.01	-1.03	-1.03
m - 22 mm, m+ 22 mm	-0.81	-0.69	-0.68	-0.69	-0.77	-0.80	-0.85	-0.91	-0.95	-0.98
m - 30 mm, m + 30 mm	-1.40	-1.12	-1.14	-1.20	-1.22	-1.25	-1.27	-1.30	-1.30	-1.31
m - 35 mm, m + 35 mm	-2.03	-2.08	-2.11	-2.13	-2.13	-2.13	-2.12	-2.12	-2.12	-2.12
m - 40 mm, m + 40 mm	-2.13	-2.15	-2.13	-2.11	-2.09	-2.07	-2.07	-2.06	-2.06	-2.05
m - 2 std, m + 3 std	0.93	1.29	1.58	1.53	1.16	0.79	0.65	0.62	0.61	0.58
m - 1std, m + 3 std	-0.02	-0.07	0.25	0.51	0.31	-0.06	-0.11	-0.18	-0.26	-0.37
m - 3 std, m + 2 std	0.16	0.40	0.73	0.80	0.82	0.56	0.36	0.20	0.05	-0.02
m - 3 std, m + 1 std	0.54	1.08	1.50	1.53	1.04	0.66	0.42	0.29	0.27	0.34
Three thresholds										
m - 1 std, m, m + 1 std	-0.95	-1.58	-2.34	-0.94	-0.59	-0.50	0.51	0.60	-0.59	-0.60
m - .5 std, m, m + .5 std	-0.53	-0.98	-1.46	-0.68	-1.09	-1.04	-2.76	-2.25	-1.29	-1.93
m - .2std, m, m + .2std	0.43	-1.09	-1.40	-1.70	-2.21	-2.88	-1.63	-0.99	-0.37	-0.96
m - .1 std, m, m + .1 std	-1.18	-0.23	0.45	0.61	-0.33	-0.45	0.22	0.74	0.74	-0.65
m - .01 std, m, m + .01 std	-1.01	-1.40	-2.76	-2.81	-2.02	-2.73	**-3.27***	-2.12	-1.38	-0.36
m - 2 std, m, m + 2 std	-1.61	-1.67	-0.78	-0.40	-0.40	-1.65	-1.12	-1.83	-2.06	**-3.29***
m - 2.5 std, m, m + 2.5 std	-2.28	-2.37	-2.66	-2.15	-1.70	-1.13	-0.90	-0.43	-1.64	-1.70
m - 3 std, m, m + 3 std	-0.99	-1.49	-1.31	-1.13	-0.94	-1.22	-2.02	-1.68	-1.89	-1.82
m - 3.5 std, m, m + 3.5 std	-0.95	-1.18	-1.05	-1.41	-1.78	-2.46	-1.68	-1.47	-1.02	-1.50
m - 2.8 std, m, m + 2.8 std	-1.69	-2.01	-1.22	-0.79	-1.16	-1.20	-1.01	-0.89	-0.93	-1.09
m - 3.2 std, m, m + 3.2 std	-0.97	-1.17	-1.64	-1.43	-1.57	-1.54	-1.65	-1.51	-1.61	-2.30

m - 3.1 std, m, m + 3.1 std	-1.49	-1.89	-1.44	-1.45	-1.11	-1.42	-1.43	-1.18	-1.03	-1.20
m - 2.9 std, m, m + 2.9 std	-1.26	-1.29	-1.16	-1.10	-1.12	-1.21	-1.15	-1.23	-1.47	-1.76
m - 1 mm, m, m + 1 mm	1.03	0.30	0.06	0.24	1.73	-0.38	-0.53	-1.19	-0.75	-0.61
m - 10 mm, m, m + 10 mm	1.20	0.98	0.30	1.56	1.39	0.98	0.74	0.15	1.08	0.57
m - 15 mm, m, m + 15 mm	-2.07	-1.73	1.43	0.14	0.59	1.34	1.21	1.20	1.02	0.92
m - 20 mm, m, m + 20 mm	0.87	-0.23	0.01	-1.07	-0.58	-0.42	-0.75	-2.00	-1.75	-1.61
m - 25 mm, m, m + 25 mm	1.49	1.60	1.41	0.49	1.15	0.97	1.11	1.10	0.88	-0.38
m - 22 mm, m, m+ 22 mm	1.06	1.53	0.30	0.58	0.89	1.51	0.88	0.67	1.09	1.44
m - 30 mm, m, m + 30 mm	-0.45	-0.46	-0.50	-0.66	-0.62	-0.40	1.19	0.40	1.04	1.03
m - 35 mm, m, m + 35 mm	0.93	0.79	0.82	0.95	1.05	-0.52	-0.62	-1.55	-0.29	-0.33
m - 40 mm, m, m + 40 mm	1.18	1.80	1.14	0.69	0.59	1.14	1.03	0.70	0.97	0.86
m - 2 std, m, m + 3 std (A)	1.30	-0.31	-0.52	-0.59	0.43	0.42	0.41	0.45	0.45	0.47
m - 1std, m, m + 3 std (A)	0.69	1.22	1.08	0.90	1.07	1.00	0.98	1.06	1.39	-0.12
m - 3 std, m, m + 2 std (A)	0.79	0.70	0.32	0.86	1.37	1.82	1.37	0.95	0.71	1.24
m - 3 std, m, m + 1 std (A)	0.74	0.74	0.69	0.72	0.72	0.73	0.93	0.43	0.81	0.77

Note: t-scores with magnitude equal or larger than 3.04 are indicated with * and are in bold. The “m” indicates mean value for the time series, “std” indicates the standard deviation for the time series, and “mm” indicates millimetres of movement in the COP. **(A) indicates asymmetric thresholds were used**

Table 3.3. Approximate entropy t-scores for comparison of medial-lateral postural sway

t-scores for comparison of medial-lateral postural sway of infants with typical development and with delayed development, based on approximate entropy calculated with various lag and r values, -3.32 is the largest magnitude t-score.

		r value used in ApEn calculation										
m	lag	0.05*std	0.1*std	0.2*std	0.4*std	0.8*std	1.5*std	2.5*std	3*std	3.5*std	4*std	5*std
2	1	-0.94	-0.55	-0.46	-0.47	-0.56	-0.67	-0.20	-0.26	-1.14	-2.12	-0.76
4	1	0.58	-1.08	-1.22	-1.20	-1.37	-1.67	-1.62	-1.40	-2.26	**-3.17***	-2.04
8	1	1.05	-0.14	-0.63	-1.69	-1.92	-2.40	-2.52	-2.54	-2.88	**-3.27***	-2.69
2	4	-1.26	-1.41	-1.94	-2.46	-2.72	-2.68	**-3.09**	**-3.32***	**-3.27***	**-3.17***	-2.04
4	4	1.23	-0.17	-1.55	-2.41	-2.84	-2.81	**-3.07**	**-3.24***	**-3.20***	**-3.10***	-1.67
8	4	1.34	0.33	0.16	-2.39	-2.64	-2.64	-2.49	-2.93	**-3.16***	**-3.13***	-1.32
2	8	-1.32	-1.50	-2.18	-2.72	-2.82	-2.71	-3.02	**-3.16***	**-3.08**	-2.90	-1.54
4	8	1.64	0.46	-1.51	-2.68	-2.60	-2.47	-2.45	-2.86	-3.03	-2.91	-1.15
8	8	1.35	0.50	1.29	-1.96	-2.91	-2.06	-1.96	-2.20	-2.49	-2.83	-1.73

Note: t-scores with magnitude equal or larger than 3.04 are indicated with * and are in bold.

Table 3.4. Approximate entropy t- scores for comparison of anterior-posterior postural sway

t- scores for comparison of anterior-posterior postural sway of infants with typical development and with delayed development, based on approximate entropy calculated with various m, lag and r values, are all lower than 3.04.

		r value used in ApEn calculation										
m	lag	0.05*std	0.1*std	0.2*std	0.4*std	0.8*std	1.5*std	2.5*std	3*std	3.5*std	4*std	5*std
2	1	0.83	0.82	0.84	0.99	0.99	1.03	0.92	1.46	1.14	0.54	0.69
4	1	0.50	0.17	0.25	0.60	0.61	0.73	0.36	0.87	0.59	0.28	0.12
8	1	-1.04	0.68	0.41	0.28	0.24	0.40	-0.19	0.53	0.30	0.22	0.17
2	4	0.61	0.60	0.46	0.16	0.02	0.40	-0.30	0.41	0.23	0.24	0.04
4	4	1.15	1.05	0.84	0.48	0.17	0.17	-0.38	0.39	0.24	0.31	0.20
8	4	-0.80	0.55	1.03	1.01	0.39	0.49	-0.48	0.44	0.12	0.36	0.46
2	8	1.27	1.01	0.90	0.36	0.10	0.21	-0.33	0.39	0.25	0.35	0.17
4	8	0.15	1.26	1.09	0.90	0.36	0.54	-0.42	0.32	0.18	0.42	0.39
8	8	-1.04	-0.49	0.90	1.47	0.85	0.34	-0.05	0.21	0.20	0.34	0.43

Note: No t-scores with magnitude equal or larger than 3.04 are in this table.

CHAPTER 4

DEVELOPMENTAL DELAY AND TYPICAL DEVELOPMENT INVESTIGATED USING APPROXIMATE ENTROPY AND SPECTRAL ANALYSIS OF INFANT SITTING POSTURAL SWAY

Abstract: We have applied approximate entropy to infant sitting postural sway center of pressure (COP) data, with the goal of distinguishing between the postural sway dynamics of infants with typical development, and infants with delayed motor development, where the delayed development is due to cerebral palsy for many of our subjects. By trying to find approximate entropy parameters that are effective in separating these populations, we hope to find a measure that will be able to quantify improvements that occur in motor control due to physical therapy. In order to assess the impact that experimental noise has on the analysis, we included a periodic single pendulum and a chaotic double pendulum in the analysis, however comparison of the single and double pendulum COP data was not very sensitive to the parameters used in the approximate entropy analysis, due to the very different dynamics of the periodic single pendulum and chaotic double pendulum. We find that best approximate entropy parameters for the infant sitting data set are ApEn(m=1, r=1*std(Data), t=8.33sec@240Hz, lag=8), and a significant difference is seen in the anterior-posterior axis, but not in the medial-lateral axis with these parameters. The analysis is not very sensitive to the m value selected, but is sensitive to the values of r and lag. Use of the full time series, 8.33 sec at 240 Hz, was the best value of N we obtained for the data, but we cannot rule out that longer time series could have improved the analysis. The choice of lag value of 8 to 12 in the

approximate entropy analysis corresponded to a time lag of 33 to 50 msec, or a frequency of 20 to 30 Hz. Spectral analysis confirmed features in the postural sway of early sitting of infants with typical development in this frequency range. The high frequency of these features suggests a stretch reflex or tissue vibration may be active, perhaps activated by a near-fall. Voluntary movements, medium and long latency reflexes are not as fast. Suggestions for implementation of the approximate entropy algorithm to experimental data are discussed.

Introduction

Cerebral palsy occurs because of brain injury sustained very early in life, either before, during, or shortly after birth, and is characterized by motor dysfunction. Identifying affected infants when they are very young allows for physical therapy to be started early when brain plasticity is maximal, with the goal of improving the long-term outcome for these infants (Blauw-Hospers, Hadders-Algra, 2005; Blauw-Hospers, de Graaf-Peters, Dirks, Bos, Hadders-Algra, 2007; de Graaf-Peters, Blauw-Hospers, Dirks, Bakker, Bos, & Hadders-Algra, 2007). Sitting is a motor skill acquired early in life, typically at about age 4-9 months, and thus can serve as a window into the development of motor skills in very young infants (Harbourne & Stergiou, 2003). Studying sitting dynamics affords the possibility of objectively quantifying motor coordination in order to identify infants who might benefit from physical therapy, and to assess improvements as therapy progresses, even in infants who cannot yet stand. Lack of general movement complexity in young infants may be a useful indicator of cerebral palsy and that therapeutic intervention is appropriate (Hadders-Algra, 2004), but it is not yet clear how

best to objectively quantify movement complexity. To explore the dynamics of sitting postural sway in infant sitting, a measure of time series dynamics is needed that is sensitive to differences between affected and unaffected infants, and which is robust to experimental noise, and also robust to shorter time series segments since many infants can not sit for extended periods of time. The long term goal of this work is to develop a measure that can assess developmental delay early in life, is sensitive enough that it can be used to monitor the effectiveness of a course of therapy, and is robust enough to real-world data limitations such as noise and limited time for analysis, that it could someday be applied in a clinical setting.

Approximate entropy was developed by Pincus (1991) as a measure of "complexity" for time series data, where "complexity" is defined as being low for time series with a repetitive pattern such as a sine function, high for a random variable, and intermediate for systems with chaotic dynamics. Alternatively, it can be described as a measure of "regularity" where time series data with repeated patterns has low approximate entropy and high regularity (Pincus & Goldberger, 1994), i.e. approximate entropy is a measure of lack of regularity. Because approximate entropy is sensitive to the system dynamics, it is a potentially useful measure for a wide range of medical conditions that alter physiological or motor control dynamics. There are a number of medical fields where the use of approximate entropy has been investigated, including cardiology (Pincus & Goldberger, 1994; Kaplan, Furman, Pincus, Ryan, Lipsitz & Goldberger, 1991), endocrinology (Liu, Iranmanesh, Keenan, Pincus, and Veldhuis, 2007; Veldhuis, Keenan, & Pincus, 2008), anesthesiology (Kumar, Anand, Chari, Yaddanapudi, & Srivastava, 2007), traumatic brain injury (Cavanaugh, Guskiewicz,

Giuliani, Marshall, Mercer, & Stergiou, 2005, Cavanaugh, Guskiewicz, Giuliani, Marshall, Mercer, & Stergiou, 2006), Parkinson's disease (Morrison, Kerr, Newell, & Silburn, 2008), and orthopedics (Georgoulis, Moraiti, Ristanis, Stergiou, 2006). Both the loss of complexity hypothesis (Goldberger, Peng, & Lipsitz, 2002) and the optimal movement variability hypothesis (Stergiou, Harbourne, & Cavanaugh, 2006) suggest that approximate entropy of time series data from physiological systems may be clinically useful, as pathology can shift the regularity of system dynamics away from the optimal values. A measure like approximate entropy, with the ability to quantify regularity of system dynamics, may someday be used clinically to discriminate typically developing children from those with pathology, help assess severity of pathology, and assess efficacy of treatment.

Despite the wide range of research applications of approximate entropy, the methodology of application of the approximate entropy algorithm to experimental data has yet to be fully optimized for widespread clinical implementation. Experimentally measured time series data is necessarily of limited length, and often, if not always, corrupted by experimental noise of unknown dynamics. Experimental noise is often assumed to be white noise, or independent and identically distributed error, allowing for statistical treatment based on these assumptions. The reality is that the measurement noise is generated by physical processes that have certain dynamics associated with them, which may lead to noise dynamics being something other than the statistical ideal of white noise. For example, time series data acquired at high enough frequency will often have a 60 Hz noise component due to electrical power distribution using 60 Hz frequency (or 50 Hz in Europe). The 60 Hz noise is certainly not well represented as white noise.

The dynamics of the noise may not be important if the measure used on the time series data is range or standard deviation, but in using measures of the dynamics of the time series, including approximate entropy, the dynamics of the noise may interfere with the measurement of the dynamics of the system under study. One way the impact of noise can be studied is to add in computer generated white noise to time series data, and investigate the impact that the added white noise has on the approximate entropy analysis. However, this method leaves open the possibility that real experimental noise, which is not pure white noise, may have a different effect on the analysis.

Another approach to understanding the impact of experimental noise on measures of system dynamics is to use a model system that has known dynamics, and see if the dynamical analysis gives a result in reasonable agreement with the known dynamics. For example, a mechanical single pendulum has limit cycle dynamics, and thus would be expected to have a low value for the approximate entropy. Higher values of approximate entropy from experimental measurements of the dynamics of a single pendulum are likely a result of contamination of the measured signal with experimental noise with more complex dynamics. Data acquired from the single pendulum with the same experimental equipment as the infant sitting data would be contaminated with noise having the same dynamics as noise contaminating the infant sitting data. Thus it is possible to select analysis parameters for the approximate entropy analysis using pendulum data that minimize the impact of experimental noise on the analysis. A double pendulum is a pendulum with two linked segments that are each free to rotate, giving a system with enough degrees of freedom to display chaotic dynamics (Shinbrot, Grebogi, Wisdom, & Yorke, 1992). If the experimental limitations of the data are minor enough to not interfere

with the analysis, then approximate entropy should be able to distinguish between data from these two mechanical systems. Thus mechanical pendulums can act as model systems to investigate the effect of the experimental noise on the analysis of system dynamics.

The approximate entropy algorithm has been described in detail elsewhere (Pincus, 1991; Pincus & Goldberger, 1994). As implemented (Kaplan & Staffin, 1996), the algorithm creates vectors of length m, and length m+1. It then counts vectors of time series data of length m that are similar to each of the vectors of length m, and then counts how many of those similar m length vectors are also similar at length m+1. Approximate entropy is then calculated as the logarithm of the sum of the count of similar m length vectors minus the logarithm of the sum of the count of similar m+1 length vectors, normalized by N, the number of data points. The difference between logarithms can be rewritten as the logarithm of the ratio of the count of similar vectors of length m divided by the count of similar vectors of length m+1. Thus repeated patterns in the data give rise to lower approximate entropy values, because two vectors similar at length m will also be similar at length m+1 due to the repeating pattern, resulting in a ratio near 1, the log of which is then near zero. For this reason, time series with repeated patterns have approximate entropy near zero.

An important aspect of the approximate entropy calculation is determining how similar vectors are defined. The approximate entropy algorithm uses a parameter r to define similar vectors. If each point in a vector is within a distance r of the corresponding point in the other vector, then the two vectors are counted as similar. If r is too large, vectors are counted as being similar when they are not; if r is too small, then vectors that

should be considered as similar are not counted as being similar. The time series data will have some measurement error, as is typical of experimentally derived data, and the r parameter allows for two vectors to be counted as similar, even if the experimental noise results in the values not being identical. A value for "R" is selected for all the time series in the analysis, and this value is multiplied times the standard deviation of each individual time series data in order to define the r for that time series; r_i=R*std($Data_i$) for each time series i. While a range of 0.1 to 0.25 for R is suggested in early work (Pincus & Goldberger, 1994), recent work suggests that R be set at 0.2 for biological applications; i.e. r_i=0.2*std($Data_i$) (Veldhuis, Keenan, & Pincus, 2008). While the r parameter may serve to filter experimental noise, it also filters the biological signal, and thus serves to select the length scale of the system dynamics that is being probed by the approximate entropy analysis. It is not clear whether the most important function of the r parameter is simply to reduce the sensitivity of the analysis to experimental noise, or if it has a more important function relevant to the length scale of the dynamics of biological system.

If the function of the r value is simply to reduce the sensitivity of the analysis to experimental noise, then basing the r value on the noise, r_i=R*std($Noise_i$), might be preferred. Pincus and Goldberger (1994) suggest that r must be chosen to be larger than the noise, but fail to give exact guidelines other than to suggest a value of three times the estimated mean noise has work well in their clinical studies. Thus one might expect that selecting the r value based on some estimation of the noise in the data might be a useful approach. Alternatively, other authors have suggested that r should be selected to maximize the entropy result (Castiglioni & Di Rienzo, 2008; Lu, Chen, Kanters, Soloman, & Chon, 2008). Both of these possibilities were investigated in this work.

Understanding the impact of experimental noise (i.e. measurement error) on results is often difficult, since the actual signal and noise are not known a priori. One method to address this is to use the measurement technique on a known system, i.e. on a model system with know dynamics. Because we are making mechanical measurements on the infant postural sway, we used mechanical systems with known dynamics to test the analysis. Two such mechanical systems were used, 1) the single pendulum, which exhibits simple limit-cycle dynamics, and 2) the double pendulum, which exhibits chaotic dynamics when launched from appropriate initial conditions.

The purpose of this work is to examine the impact of the parameters in the approximate entropy analysis to better understand dynamics of infant sitting postural sway, and we utilized COP data from single and double pendulums, in order to guide us in analysis of the infant sitting data. The long-term goal of the work is to discover differences between postural sway of infants with typical development and infants with delayed development that might be useful in a clinical setting to help assess alterations in infants motor control skills due to pathologies such as cerebral palsy, and to assess progress due to various therapeutic interventions.

2. Methods

2.1. Infant Participants

Thirty infants with 30 developmental delay (age=14.05 months, std=5.33 months, for early sitting and age=18.06 months, std=5.09 months, for advanced sitting) and 33 infants with typical development (age=4.92 months, std=0.57 months, for early sitting, and age = 7.92 months, std=0.60 months, for advanced sitting) participated in the study.

Recruitment was done through newsletters, flyers, and pediatric physical therapists employed at the University. Infants in the developmentally delayed group were diagnosed with cerebral palsy, or else were developmentally delayed and at risk for cerebral palsy. Obtaining a firm diagnosis of cerebral palsy at this young age is often not possible. Because a definitive diagnosis of cerebral palsy had not been made, we refer to these infants as developmentally delayed, because all scored below 1.5 standard deviations below the mean for their corrected age on the Peabody Gross Motor Scale (Folio & Fewell, 2000). However, the development is likely not just delayed, but also atypical (Chen & Wollacott, 2007). A consent form was signed by a parent or guardian of all infant participants, and all procedures were approved by the University of Nebraska Medical Center Institutional Review Board.

Inclusion criteria for entry into the study for the typically developing infants were: a score on the Peabody Gross Motor Scale of greater than 0.5 SD below the mean, age of five months at the time of initial data collection, and sitting skills as described below in beginning sitting. Exclusion criteria for the sample of infants who are typically developing were: a score on the Peabody Gross Motor Scales less than 0.5 SD below the mean, diagnosed visual deficits, or diagnosed musculoskeletal problems. If a typically developing infant was found to be less than 0.5 SD below the mean, and did not qualify for the study, the parents were informed of the score, the possibility of error in the measurement, and advised to have the infant re-evaluated within the next 3 months. Operational definitions of beginning sitting were used to determine the child's readiness for entry into the study. Beginning sitting was defined as (a) head control such that when trunk is supported at the mid-trunk, head is maintained for over one minute without

bobbing; (b) infant can track an object across midline without losing head control; (c) infant may prop hands on floor or legs to lean on arms, but should not be able to reach and maintain balance in the prop sit position; (d) when supported in sitting can reach for toy; (e) can prop on elbows in the prone position for at least 30 seconds. Each infant was tested when they entered into the study based on the ability to sit for about 10 sec, and then again 3-4 months later.

For the infants with developmental delay the inclusion and exclusion criteria were as follows. Inclusion criteria were: age from five months to two years, score less than 1.5 SD below the mean for their corrected age on the Peabody Gross Motor Scales, and sitting skills as described above for beginning sitting. Exclusion criteria were: age over two years, a score greater than 1.5 SD below the mean for their corrected age on the Peabody Gross Motor Scale, a diagnosed visual impairment, or a diagnosed hip dislocation or subluxation greater than 50%.

Note that “early” and “advanced” sitting are labels indicating that the sitting was either close to the time the infant was able to achieve about 10 seconds of upright sitting (early), or the sitting behavior that was displayed 3-4 months later (advanced). For the infants with typical development, the advanced sitting was also well controlled sitting. For the infants with developmental delay, the sitting behavior studied as advanced sitting was not necessarily well controlled sitting behavior, especially in infants who were more severely affected. The comparison between “early” and “advanced” should be understood as advancement in behavior with time, and not that the skill level had improved equally between the two groups. Thus the change in the measures of posture control might be expected to change less for the infants with delayed development than for those with

typical development.

2.2. Pendulums

Two pendulums were used in the study (Figure 4.1). The first was a single pendulum, constructed from steel bar (1" x .125" x 3') and mounted to swing freely on a rigid structure, using Bones Reds 608 Precision Skate Bearings (Bones Bearings, Santa Barbara, CA) to reduce friction as the pendulum swings. The pendulum arm length was selected to give the pendulum a frequency of approximately 0.7 Hz, because maximum power in the power spectra of the infant sitting was of a similar frequency. Weights were clamped on the pendulum arm to simulate the weight of an infant. Amplitude of the pendulum swing was varied from trial to trial. The second pendulum was a double pendulum, purchased commercially (http://www.chaoticpendulums.com), and could be mounted on the same mounting structure as the single pendulum. The double pendulum also had metal bearings to reduce friction.

2.3. Data Collections

Data collections for both infants and pendulums were performed with the same equipment, using all the same data acquisition parameters. For data acquisition (Figure 4.1), a pendulum or infant was placed on an AMTI force plate (Watertown, MA), interfaced to a computer system running Vicon data acquisition software (Lake Forest, CA). Markers can be seen on the infant in Figure 4.1, and kinematic data was also collected, but is not discussed in this paper. The time series data collected is center of pressure (COP) data, which is the position of the resultant vector where it intersects the surface of the force plate. Thus the time series data is position data, although it is derived

from the forces measured by the force plate. The COP time series were acquired through the Vicon software at 240 Hz, in order to have a sampling frequency 10 times above the highest frequency found the time series from in a pilot study.

For all data collection sessions, the infants were allowed time to get used to the laboratory setting, and were at their parent's side or on their lap for preparation and data collection. Infants were provided with a standard set of infant toys for distraction and comfort. All attempts were made to maintain a calm, alert state by allowing the infant to eat if hungry, be held by a parent for comforting, or adapting the temperature of the room to the infant's comfort level. Testing was only proceeded when the infant was in a calm and relaxed state, not crying or otherwise making extended vocalization. A soft cloth was placed over the plate for warmth and was securely adhered with tape on the force plate. The investigator and the parent remained at one side and in front of the infant respectively during all data collection, to assure the infant did not fall or became insecure. The child was held at the trunk for support, and gradually the infant was guided into a prop sitting position while being distracted by toys presented by the parent. Once the examiner could completely let go of the infant, data were collected for 10 seconds while the child attempted to maintain sitting postural control. Trials were performed until we had collected three trials that are acceptable for our criteria, or until the infant was indicating that they were done. At any time the child became irritated; the session was halted for comforting by the parent or a chance for feeding, and then resumed only when the child was again in a calm state. In some cases, if the infant was crying for a long period of time, then data was not collected at that session. Infants came to the lab twice within a single week, and we attempted to get three trials in each of the two sessions.

Segments of usable (described below) data were analyzed using custom MatLab software (MathWorks, Nantick, MA). No filtering was performed on the data in order to not alter the nonlinear results (Rapp, Albano, Schmah, & Farwell, 1993). Trials were recorded including force plate data and video data from the back and side views. Afterwards segments were selected by viewing the corresponding video. Segments of data with 2000 time steps (8.3 seconds at 240 Hz) were selected from these trials by examination of the video. Acceptable segments were required to have no crying or long vocalization, no extraneous items (e.g. toys) on the force platform, neither the assistant nor the mother were touching the infant, the infant was not engaged in rhythmic behavior (e.g. flapping arms), and the infant had to be sitting and could not be in the process of falling.

For the single pendulum, long time series could be collected (limited by the storage capacity of the computer), and then these were divided into 2000 time step segments (i.e. N=2001) to match the infant sitting data. Segments matching the infant sitting based on signal-to-noise (discussed below) were selected for analysis. For the data collection with the double pendulum, to ensure initial conditions that would lead to chaotic motion, the double pendulum was restarted before each data collection. The first 8.3 seconds of data (2000 time steps, N=2001) were selected for analysis.

2.4. Data Analysis

Signal-to-noise: During the course of data analysis, it became apparent that some time series had better signal-to-noise than other time series, and that this was affecting the approximate entropy analysis. For the single pendulum, the equation of motion can be solved using the small angle approximation, resulting in a sin function for the solution to

the equation of motion. As expected, the COP data obtained from the single pendulum appeared to be a sine function for small amplitudes of displacement, but appeared to have a noise component in addition to the expected sine wave. Based on this observation, a method was developed to estimate the signal-to-noise for our time series data. Here "signal" refers to the true data if no experimental noise were present in the time series data. Signal-to-noise is defined as the ratio of the variances of the signal and noise (Manolakis, Ingle, & Kogon, 2005); signal-to-noise = s_s^2/s_n^2 , where s_s indicates the standard deviation calculated from the smoothed time series (estimated signal), and s_n is the standard deviation of the difference between the unsmoothed time series and smoothed time series (estimated noise).

Because we wanted to estimate the signal-to-noise in both periodic data and chaotic data, we used a sine function and a numerical solution to the Lorenz attractor, each with different levels of added random noise, as test pseudo-data sets, where "pseudo-" indicates data was generated in MatLab, not acquired with the force plate. By generating pseudo-signal and pseudo-noise separately before adding them to make pseudo-data, time series pseudo-data were generated with known signal-to-noise, allowing the result of the signal-to-noise detection algorithm to be verified. Sampling rate, spectral frequencies, and apparent signal-to-noise of the pseudo-data were chosen to be similar to the infant sitting data. An estimate of the signal in each of the pseudo-data sets was made by smoothing the noisy data, and then the noise was estimated by the difference of the pseudo-data and the estimated signal. Two smoothing methods were used, Savisky-Golay polynomial smooth and a low-pass Butterworth filter smooth. It was felt that the critical measure of signal-to-noise was at poor signal-to-noise conditions,

so the parameters for the Savisky-Golay (polynomial order and window size) and for the low-pass filter (filter order and cut-off frequency), were optimized for matching the measured signal-to-noise with the actual signal-to-noise for the pseudo-data at poorer signal-to-noise levels. Then, comparing the measured with actual signal-to-noise at better signal to noise values, the Savistsky-Golay method was found to be better, so that method was adopted as the standard method, using the parameters of a polynomial order = 8, and window size = 121 (0.5 sec). The double pendulum has much higher signal-to-noise than the other data types, and these parameters for estimation of signal-to-noise did not appear to work for the double pendulum data. Application of this method to single pendulum data and infant sitting data appeared to give reasonable results (Figure 4.2), and the result from the single pendulum is especially encouraging because the solution to the equation of motion is expected to be a sine function, and the estimated signal, i.e. the smoothed data, closely resembles a sine function.

Approximate entropy: The approximate entropy calculation was described in the introduction, and Pincus (1991) and Pincus and Goldberger (1994) are good resources for additional discussion of the method. The MatLab code used to calculate approximate entropy was accessed online (Kaplan & Staffin, 1996). Approximate entropy, and all other calculations for this work, were done using MatLab (version R2007a).

Spectral analysis: Periodograms were calculated using MatLab to estimate the power spectrum for each trial using a Hann window function. Periodograms were averaged for all trials in each of 4 categories, 2 subject types (infants with typical or delayed development), at 2 sitting ages (early or advanced sitting). Sharp peaks were observed at 30 Hz, 60 Hz, and 90 Hz, the largest of which was at 60 Hz, and were

thought to be related to power transmission at 60 Hz, and not features of the infant sitting postural sway.

Statistical analysis: A statistic of interest in this analysis is the effect size in comparing two populations. Many estimators of effect size assume a normally distributed data, but the approximate entropy values in this study were observed to have a non-symmetric distribution, and the distribution was skewed to high side. Thus we used the nonparametric Wilcoxon rank sum test (Mann-Whitney U test) to perform comparisons. This has the advantage of being easy to calculate using MatLab, and allowed comparison of the p value obtained to a critical p value to assess if the approximate entropy analysis were likely significant ($p<p_{critical}$), or if the difference in approximate entropy values were likely not significant ($p>p_{critical}$). We also performed a paired t-test, again using the built-in MatLab function.

The reported p values are for three different comparisons: 1) comparisons of the n=30 infants with developmental delay compared with the n=33 infants with typical development, for approximate entropy analysis of postural sway in the anterior-posterior (front-to-back) axis, 2) comparisons of the n=30 infants with developmental delay compared with the n=33 infants with typical development, for approximate entropy analysis of postural sway in the medial-lateral (side-to-side) axis, and 3) comparisons of n=100 trials of single pendulum with n=100 trials of double pendulum. For comparisons 1 and 2 (infant sitting) up to 3 trials for each infant were averaged (sometimes the infant was crying, and fewer than 3 trials were collected). Hundreds of comparisons were made using different parameters for the approximate entropy calculation, but these are not independent comparisons, e.g. the ApEn (m=2, r=1, N=2001) are correlated with ApEn

(m=2, r=1, N=1001). Thus in correcting our significance level for multiple comparisons, we used a Bonferroni type correction considering three independent comparisons (infant sitting anterior-posterior axis, infant sitting medial-lateral axis, and pendulum comparisons), and set the significance level at alpha=0.05/3=0.017. Repeated measures ANOVA analysis, comparing sitting postural sway for infants with typical development and delayed development, for early sitting and advanced sitting was performed using SPSS Statistics (GradPack 17.0).

Results

Typical parameters used in many studies for calculating approximate entropy are m=2, r= .2* std(data), and lag=1, so we used these parameters as our starting point. To see the effect of noise on the approximate entropy result, we examined the relationship between approximate entropy using standard parameters ApEn(m=2, r=.2*std(data), N=8.33 sec acquired at 240 Hz, lag=1), and estimated signal-to-noise (Figure 4.3), and found that approximate entropy is systematically higher for poor signal-to-noise for single pendulum data, as well as infant sitting in both anterior-posterior (front-to-back) and medial-lateral (side-to-side) directions. Compensating for the effect of poor signal-to-noise is critical, because most of the variability in the approximate entropy is due to signal-to-noise.

Looking at the approximate entropy as a function of lag in data from the single pendulum (Figure 4.4), we found that for time series with poor signal-to-noise, the approximate entropy varies considerably with lag, but that for the time series with the best signal-to-noise, lag is not as important. We expect the approximate entropy for a

single pendulum to be near zero, due to the limit cycle dynamics of the single pendulum. The lowest approximate entropy value for the poor signal-to-noise time series was at lag=4. Spectral analysis of the time series data finds a small peak at 60 Hz, and even smaller peaks at 30 Hz and 90 Hz, presumably contamination from the 60 Hz frequency used for power delivery. Our data was acquired at 240 Hz, so the 60 Hz noise repeats every 4 data points in our data, explaining the utility of using lag=4 in the approximate entropy calculation. Alternatively, down-sampling the data to 60 Hz would be another way to reduce the impact of 60 Hz noise contamination on the approximate entropy result, so we included this in our subsequent data analysis.

Proper selection of the r parameter would be expected to improve the performance of the algorithm on data contaminated by experimental noise, since this parameter is thought to act as a filter parameter (Pincus, 1991; Pincus & Goldberger, 1994). Conceptually, if the r parameter is larger than the experimental noise, then the effect of the experimental noise on the analysis should be reduced. Thus we investigated the performance of the approximate entropy algorithm as a function of the r parameter. Typically, r is defined for each time series as some multiple of the standard deviation of the time series data, r_i=R*std($data_i$), where R is constant for a given analysis, but r varies for each time series i in the analysis because the standard deviation of each time series is different. Some authors have suggested that the best choice for the r parameter is to select one that maximizes the entropy calculated (Castiglioni & Di Rienzo, 2008; Lu, Chen, Kanters, Solomon, and Chon, 2008). Using r=R*std(data) for each time series, and varying R, we found that infant sitting and single pendulum data have maximum entropy with lowest values of r (Figure 4.5). For these data, there is no maximum in entropy with

changes in R, so that selecting R based on maximizing the time series is not feasible. The maximum in entropy for the double pendulum data down-sampled to 60 Hz, lag=1, occurs at R=0.25 (Lower left plot) and at R=0.15 for the 240 Hz data, lag=4. Perhaps the reason that the double pendulum has a maximum other than at the lowest R value is because the double pendulum data had better signal-to-noise than the infant sitting data and better than the single pendulum data, since trials of single pendulum data were chosen to match the infant sitting data in signal-to-noise. If maximizing the entropy were the best criteria, then the standard selection of R=0.2 appears to be near optimal for this better signal-to-noise data of the double pendulum.

However, the goal of the approximate entropy analysis on the infant postural sway data is to distinguish between infants with delayed motor development and the infants with typical development, with the notion that pathologic development could lead to more regularity in postural sway (Goldberger, Peng, & Lipsitz, 2002; Stergiou, Harbourne, & Cavanaugh, 2006). The corresponding goal of the pendulum analysis is to take a system with known high regularity (the single pendulum), and a system with known chaotic behavior (the double pendulum), and see how well the approximate entropy algorithm can be tuned to distinguish between these two systems. Thus the measure of interest is a measure of comparison between two groups, and we have used the p value from a Wilcoxon rank sum comparison. To investigate the effect of the r parameter on the analysis, three types of comparisons were made: 1) infant sitting anterior-posterior postural sway (delayed development versus typical development), 2) infant sitting medial-lateral postural sway (delayed development versus typical development), and 3) pendulum reaction forces (single versus double pendulums). These

3 comparisons were repeated for various R values in the approximate entropy calculation, and for the data sampled at 240 Hz using lag=1, data sampled at 240 Hz using lag=4, and the 240 Hz down-sampled to 60 Hz using lag=1 (Figure 4.6a). The comparison of single and double pendulum data showed that the dynamics are significantly different between these two systems, and that for the pendulum comparison, the difference is statistically significant for a wide range of parameters. For the comparisons of infant sitting postural sway data, choice of analysis parameters was more critical, with the data acquired at 240 Hz and analyzed at lag=1 (Black symbols in Figure 4.6 and 4.6b), no value of R was successful in producing a significant p value for the comparisons of infants with typical development and infants with delayed development. For the infant sitting postural sway comparisons, no comparisons in the medial-lateral axis (squares) were significant. For the postural sway in the anterior-posterior axis (circles), and for the time series data down-sampled to 60 Hz (white symbols) and for the 240 Hz data analyzed using lag=4 (grey symbols), the comparison was statistically significant, with minimum p values in the range R=1 to R=1.5.

Since it has been suggested that the function of the r parameter is to act as a noise filter (Pincus, 1991; Pincus & Goldberger, 1994), and since we have an estimate of the noise for each time series in our analysis, we investigated the use of the noise estimate to calculate the r parameter for each analysis. In this analysis, $r_i=R*std(Noise_i)$, where $Noise_i$ is the estimated noise time series based on subtracting the Savitsky-Golay fit to the data, as described in "signal-to-noise" methods section. Comparisons were again made using the infant sitting postural sway data (Figure 4.6c), but even thought the result can be considered significant for the anterior-posterior sway (circles) for the 240 Hz data

using lag=4 analysis, the p values obtained were an order of magnitude higher than for the analysis based on r_i=R*std($Data_i$). Thus even though one function of the r parameter is to act as filter parameter and reduce the sensitivity of the analysis to experimental noise, basing the value of the r parameter on the estimated experimental noise does not work as well as basing the r parameter on the standard deviation of the time series data. This result shows the importance of the r parameter as length scale for the system dynamics, not merely a filter for experimental noise. Based on these results, we have chosen to use r_i=R*std($Data_i$) where R=1, for the rest of our analyses.

While the r parameter is related to the y axis of the time series (amplitude of data), several parameters affect the approximate entropy analysis in the x axis (time axis of data). The length of data acquisition, sampling rate, and length of the comparison vectors (m parameter) all potentially interact to affect the results of the analysis. The data were all acquired at 240 Hz, but down-sampling the data allows emulation of data acquired at high frequencies. For example, by creating a time series using every tenth data point in the 240 Hz time series, a time series with the effective sampling rate of 24 Hz is created. Comparing sitting postural sway in the anterior-posterior axis of infants with typical versus delayed development, and single and double pendulums, a plot of Wilcoxon rank-sum p value versus effective sampling frequency was made for m values of 1, 2, 3, and 4 (Figure 4.7a). The comparison of single and double pendulums resulted in statistically significant differences regardless of the sampling frequency or m value used, consistent with the dynamics of these two systems being very different. For infant sitting, the minimum in p values occurred at 20-30 Hz (Figure 4.7a and expanded in Figure 4.7b), for which the time between data points is 33-50 msec. The m=4 data is

significant all the way to 120 Hz or .0083 sec, but m=4 means vectors of length 4 and 5 are used. Considering that 4*.0083=33 msec is still in that range of 33-50 msec. Similar results were obtained by using the lag parameter to generate comparison vectors with different time lengths, with lag = 8 to 12 giving the lowest p values (Figure 4.7c), and having similar p values to those obtained by simply down-sampling the data and using lag=1 for the analysis (Figure 4.7a and b). In general there is a good correlation between the p values obtained using a lag value to achieve a specific time between data points in the times series, and using down-sampling to achieve that same time lag (Figure 4.8). However, at the best p-values, there is slight advantage to using the lag method rather than down-sampling. Repeating this analysis for infant postural sway in the medial-lateral axis did not find any significant differences for infants with typical development versus infants with delayed development.

While the approximate entropy algorithm is considered to be more robust to short time series than many other methods of nonlinear analysis, length of the time series still must be adequate to sample the system dynamics. Thus we investigated shortening the time series data to see if we could establish a minimal length requirement for future studies. To compare time series of different lengths, we calculated ApEn(m, r=std(Data), t @ 240 Hz, lag=8), where t@240Hz means N=t*240 and t is the length in time of the time series used in this analysis. We used the first t seconds of the anterior-posterior COP time series data, and then plotted the p value from the Wilcoxon rank sum comparisons. For the comparison of single and double pendulum, just one second of data was sufficient to distinguish between the single and double pendulum (Figure 4.9a), again consistent with the dynamics being very different between the single and double pendulum. For the

infant sitting, p values were slightly below the p=0.017 level that had been set as the critical value for determining statistical significance with as little as 3 seconds of time series data (Figure 4.9a). However, the best p values were with t=8.33 seconds of data, and we did not have longer time series to determine if longer time series would be beneficial. To determine the effect of time series length on the approximate entropy values, and on the distribution of approximate entropy values, we also examined those values as a function of length of the time series (Figures 4.9b and 4.9c, respectively). The values have leveled off substantially by 8.33 seconds, so major improvements in the analysis with longer times series seem unlikely, but without actually having longer time series, this result is speculative.

Repeated measures ANOVA analysis was performed on the infant sitting data using ApEn(m=1, r=std(Data), t=8.33sec@240Hz, lag=8) with data from the early sitting and developed sitting. In the anterior-posterior axis, the development comparison was significant ($F=15.623$, $p<.001$), the group difference was significant ($F=6.908$, $p=.034$), and the interaction was significant ($F=4.723$, $p=.011$). Approximate entropy of anterior-posterior sitting postural sway decreases significantly with development for infants with typical development, while the change with development for infants with delayed development is not significant (Figure 4.10). The comparisons for postural sway in the medial-lateral axis were not significant.

The approximate entropy results indicating that down-sampling to 10 to 30 Hz range allows differences to be seen between postural sway in the anterior-posterior axis suggests that spectral differences in this region should be observed. To investigate this, spectral analysis was performed on the same time series data as the approximate entropy

analyses, and the spectral analysis confirms there are differences in the 10-30 Hz range, especially in the anterior-posterior axis data (Figure 4.11). The broad features seen in the power spectra from early sitting postural sway of infants with typical development in the 10-30 Hz region (Figure 4.11 c) are greatly reduced in intensity in the advanced sitting of these infants (Figure 4.11d), and are not seen in the power spectra of postural sway from infants with delayed development, for either early (Figure 4.11a) or advanced (Figure 4.11b) sitting. The 10-30 Hz features are much lower intensity in the medial-lateral axis (Figure 4.12). The narrow peak at 30 Hz in these spectra is an artifact related to the 60 Hz power, as a larger narrow peak is seen at 60 Hz. Note that the power spectra are plotted on a semilog axis, so the intensity in these high frequency features is small compared to the intensity of the lower frequency features.

Discussion

The use of measures of nonlinear dynamics in medicine and physiology research is appealing because there are pathologies that alter system dynamics (Goldberger, Peng, & Lipsitz, 2002; Stergiou, Harbourne & Cavanaugh, 2006), and these measures have the capability to quantify the changes in dynamics. Approximate entropy was developed to be robust when applied to experimental data, but appropriate choice of parameters used in the algorithm need to be made. Methods for selection of the r parameter based on experimental noise and on maximizing the approximate entropy value did not prove to be useful in our analysis. Use of a single and double pendulum as model systems provided to be of limited benefit, as the difference in the dynamics between these systems was so large, that the analysis was not sensitive to the choice of parameters used in the approximate entropy analysis. The analysis of infant postural sway, on the other hand, did

depend on the choice of parameters. The discussion below is in two sections, one on the implementation of the approximate entropy algorithm, followed by a discussion infant sitting postural sway.

Discussion of implementation of the approximate entropy algorithm

For comparing systems with vastly different dynamics, such as the single and double pendulum, approximate entropy is not terribly sensitive to the choice of analysis parameters. Statistically significant differences between the single pendulum, a strictly periodic system, and the double pendulum, a known chaotic system, were found for a wide variety of parameters. However, for comparing systems with similar dynamics, such as infants with typical development and infants with motor development delay, the analysis benefits from more careful attention to the parameters used. Based on our results, we make some practical recommends for performing approximate entropy analysis on flow data:

1. The r parameter in the approximate entropy algorithm is designed to compensate for experimental noise in the measured time series data, and many authors set the r parameter as r=0.2 * std(Data), i.e. 0.2 times the standard deviation of the time series. With our data set, use of the standard parameters ApEn(m=2, r=.2*std(Data), t @ 240 Hz, lag=1) leads to the erroneous conclusion that there is no significant difference between these two groups of infants, and use of ApEn(m=1, r=1.0*std(Data), t @ 240 Hz, lag=8) showed significant differences in infants with delayed versus typical development in early sitting in the anterior-posterior axis. In previous work (Deffeyes, Harbourne, DeJong, Kyvelidou, Stuberg, & Stergiou, 2009) we found that ApEn(m=2, r=3.0*std(Data), t @ 240 Hz, lag=4) showed significant differences in infants with

delayed versus typical development in developed sitting in the medial-lateral axis, although at the time that study was completed, not all the subjects had completed the data collections, so only n=22 infants with developmental delay and n=19 infants with typical development were included in that study. Perhaps because larger swings in postural sway are more difficult to control, larger movements are more sensitive to the differences in motor control between these populations, so the use of the smaller value of r= 0.2*std(Data) is not appropriate for finding these differences. The r parameter is not simply a filter for experimental noise, but also adjusts the analysis to be sensitive to the magnitude of changes that are characteristic of the dynamics of the system. An a priori prediction of the most useful r value is difficult, and we suggest exploring the effect of this parameter on the analysis. Using the standard approach of .2*std(Data) may not be the best choice for certain types of data, such as our infant sitting postural sway data, but for systems with large differences in the dynamics, such as the periodic single pendulum and the chaotic double pendulum, the standard choice of r may be appropriate.

2. The sampling frequency and lag are two ways to adjust the time constant to which the analysis is sensitive. For our analysis, 33-50 milliseconds between data points had the best sensitivity to differences between the infants with typical versus delayed development. A lag value of 1 is often used, and this may be a good choice for many data sets. However, for our postural sway data, the adjustment of the lag parameter can improve the analysis. Selection of the sampling frequency for spectral analysis is well understood, and the Nyquest criterion of sampling at twice the rate of the highest frequency feature in the data is a well known requirement. Sampling at higher than the Nyquist frequency for spectral analysis helps to give better definition to the spectral

features, and so oversampling by a factor of 5 to 10 is not uncommon. The penalty for oversampling in spectral analysis is minimal, with extra storage for the data and an increase in computational time for the power spectrum being two main disadvantages. However, with inexpensive data storage and the very highly optimized fast Fourier transform algorithms available, in most situations these are not significant disadvantages, so oversampling is a common practice. Oversampling the time series data for approximate entropy analysis means that the system does not evolve enough between data points for the system dynamics to be captured. Under-sampling means that the system has evolved too much between data points so the functional relationship between adjacent points is lost, and just as with spectral analysis, under-sampling leads to incorrect results. Thus there is an optimum sampling rate, and that sampling rate is related to a time scale of the system dynamics. We suggest over sampling for data acquisition to be sure fast system dynamics are captured, and then either down-sampling the data, or use of a lag value >1, in order to put the time between samples at a value that is appropriate for the system dynamics improves the approximate entropy analysis. If analysis time is a limiting factor (e.g. a very large data set), down-sampling the data and using a lag=1 is almost as good as using the lag to match the frequency of interest, and down-sampling the data reduces the time required for the approximate entropy analysis.

If periodic noise is present, then selection of the lag value based on the repeat of the periodic noise may be beneficial. For example, we sampled at 240 Hz, and have 60 Hz noise from the power distribution frequency, which means the 60 Hz noise repeats every 4 data points. Thus selecting a lag value of 4, 8, 12, 16, etc. results in all the points in the comparison vector being acquired at the same point in the noise cycle, to help

reduce the impact of the periodic noise on the analysis. Spectral analysis can be done first to help determine frequencies at which there are differences between populations of interest, and lag values of interest can be determined. Averaging spectra from multiple trials improves the analysis. Also, spectral analysis will show any periodic noise that might be present, and if present, may guide the choice of lag value. For example, our data acquired at 240 Hz with 30 Hz and 60 Hz noise, means that lags of 8 or 4 should be considered (240 Hz/30Hz=8; 240 Hz/60Hz=4) so that all the points in comparison vectors are acquired at the same phase in the noise contamination.

3. The m parameter is the length of the comparison vectors formed from the time series data. A comparison vector length of m=2 is commonly used, meaning that similar vectors of length 2 are tested to see if they are still similar at length 3. For more intricate patterns, longer comparison vectors may be beneficial to include in the analysis, but for our analysis, the m value was less critical than some of the other parameters. One reason to choose a smaller m value is that approximate entropy analysis with larger m values takes more time to run.

4. The length of the time series is important to the analysis, but verification that the length of the time series is appropriate is not as easy as we might have assumed at the outset. A commonly used criteria for the length of the time series data for approximate entropy analysis is that N, the number of data points in the time series, needs to be $N> 10^m$, or $N>30^m$ if possible (Pincus, 1991; Pincus & Goldberger, 1994). For our choice of m=1, we in theory would only need 10 to 30 data points. One issue is that N does not give the complete answer about the necessary length of the time series because sampling rate also needs to be considered. For example, with our sampling at 240 Hz, we could

have met the $N > 30^m$ criteria with a data collection of 125 msec. However, we found that at least 3 seconds of data was needed to find significant differences between infants with typical versus delayed development, and that the analysis improved for even longer data sets. Thus the length of the time series needs to be set based on sampling the complete dynamics of the system, and not set based on getting a certain number of data points. One way to examine if the time series is long enough is to perform the analysis on increasingly longer lengths of time series data, and see if increasing the length of the time series used in the analysis changes the results.

5. Specify the parameters used in the analysis in discussing the results. The parameters that were selected for calculation of the approximate entropy in this study were based on maximizing the p value for a rank sum test involving early infant sitting. In this study, we found no significant effect in the data from the medial-lateral direction, only in the anterior-posterior direction, based on ApEn(m=1, r=1.0*std(Data), t @ 240 Hz, lag=8), parameters optimized for comparing the early sitting. A somewhat similar approximate entropy analysis was performed using a subset of this data, but the parameters were optimized used the data from developed sitting (Deffeyes, Harbourne, DeJong, Kyvelidou, Stuberg, & Stergiou, 2009), which found a significant difference between ApEn(m=2, r=3*std(Data), t=8.33sec@240Hz, lag=4) sitting postural sway for infants with developmental delay and infants with typical development, but in the medial-lateral direction and not in the anterior-posterior direction. A third study with a subset of this data used nearly standard parameters ApEn(m=2, r=0.2*std(Data), t=8.33sec@240Hz, lag=4) and found no significant difference between postural sway of infants with delayed development and infants with typical development (Deffeyes,

Harbourne, Kyvelidou, Stuberg, & Stergiou, 2009). Thus it is not correct to say that the approximate entropy of one condition/group is different than another condition/group, but rather the parameters must be specified, i.e. that the ApEn(r,m,t @ Hz, lag) is different for the condition/group. Pincus (1991) has described the approximate entropy as a family of statistics, with members varying by r and m values. We point out that different family members may on occasion arrive at different conclusions.

6. A model system can give an indication that the approximate entropy result is being predominately influenced by noise. Using a single pendulum model of periodic motion, noise was found to be the main source of variability in approximate entropy calculated with the standard parameters. Consider whether the equipment used for data acquisition is suitable for the measurements, as approximate entropy analysis is sensitive to the dynamics in the noise.

Discussion of the infant sitting postural sway results

An important result from this work is that using a lag value of 8 or 12 in the approximate entropy analysis gave the best separation of early sitting between infants with typical development and infants with delayed development, and that the difference was only for postural sway in the anterior-posterior direction. ANOVA analysis of the ApEn(m=1, r=std(Data), t=8.33sec@240Hz, lag=8) results found a significant interaction between sitting development and subject group being found only for the anterior-posterior axis. A lag value of 8 corresponds to a time lag of 33 msec, or a frequency of 30 Hz; a lag value of 12 corresponds to a time lag of 50 msec, or a frequency of 20 Hz. Spectral analysis confirmed that there are features in the 20-30 Hz range in the early

sitting of infants with typical development that are greatly reduced in mature sitting, and these features are not seen in either early or developed sitting of infants with delayed development. These features are apparent in the anterior-posterior data, but not in the medial-lateral data. The importance of these 20-30 Hz features is not that they are the largest features in the power spectra, but rather that they are more prominent for postural sway in the anterior-posterior axis in infants with typical development in early sitting, the same group/condition where the ApEn(m=1, r=std(Data), t=8.33sec@240Hz, lag=8) was higher. As discussed in more detail below, our results suggest a contribution from a fast acting (20-30 Hz) mechanism in early (~4.9 months of age) sitting of typical infants, such as a stretch reflex. This fast mechanism is greatly reduced in their postural control in advanced (~7.9 months) sitting, presumably because better control from other mechanisms has become active.

Our sitting postural sway results in typically developing infants fit well with results reported of infant sitting by Hadders-Algra (2005), as she reports a change in postural variability that occurs at about 6 months of age, so that our early sitting is before the transition and the developed sitting is after the transition. The transition that occurs at 6 months of age (Hadders-Algra, 2005) is a transition from “primary variability” in postural activity characterized by high variability and only poorly adapted to environmental constraints, to a more well-coordinated “secondary variability.” The “secondary variability” that emerges in infants at about age 6 months Hadders-Algra (2005) describes as being related to the infants refining the ability to successfully incorporate multiple sensory systems, such as somatosensory, visual, and vestibular, into the postural control. In our study, higher frequency postural sway perhaps due to stretch

reflex in early sitting corresponds to the more poorly controlled “primary variability” described by Hadders-Algra (2005) (REF). As the ability to incorporate more types of sensory information into the postural control improves, the apparent stretch reflex contribution to postural sway declines and the advanced sitting with the lower contribution from the apparent stretch reflex corresponds to the “secondary variability” described by Hadders-Algra (2005)(REF).

In the vocabulary of dynamic systems theory, as a control parameter changes, the attractor changes, resulting in the emergence of a new behavior, such as the emergence of sitting. While we have not elucidated the control parameter for the transition in infant sitting, candidates include neurological maturation, physical growth, muscle strength gains, or learning due to interaction with the environment that alters central nervous system connectivity based on neural plasticity mechanisms. While certainly neural myelination is an ongoing process during infancy, and physical growth and strength gains are apparent, Hadders-Aldra (2005) describes the emergence of the secondary variability from primary variability in infant sitting as being related to motor learning, and the increased use of appropriate motor synergies, while acknowledging that some of the other control parameters may also be contributing. If an important control parameter is increased experience, how is that translated into more appropriate motor synergies? What is it that an infant learns when learning to sit? One possibility is that the internal model of the infant is refined to the point that correct control decisions can be made, allowing the emergence of the new behavior (Chen, Metcalfe, Jeka, & Clark, 2007). The description of an improved internal model is somewhat of a mechanistic description of the changing attractor landscape, where the internal model is thought to be associated with cerebellar

function (Ebner & Pasalar, 2008). Hadders-Algra (2005) studied the response to postural perturbations to arrive at these conclusions that the transition allows better response to external perturbations with "secondary variability" in postural control than with the "primary variability" found in younger infants. Our study did not include perturbations in the protocol, but internal perturbations, such as breathing movements, are present. If the infant's internal model of their body is not well refined, then response to a perturbation, even if it is simply the breathing of the infants, will not be as well controlled as it would be with a better internal model. Sitting postural sway in infants has been shown to increase with the acquisition of walking skills, which was interpreted as being due to changes of the infant's internal model of their body with walking (Chen, Metcalfe, Jeka, & Clark, 2007), showing that infants are actively refining their internal model, and that sitting postural sway can change based on changes in the internal model. To the extent that the younger infant's internal model of their own body is not yet well developed, the movement of any part of their body may act as an unexpected perturbation to sitting posture. The infants in our study at age 7.9 months likely have not only a better ability to deal with unexpected perturbations than the infants at age 4.9 months as Hadders-Algra (2005) data on response to external perturbations would suggest, but also a more refined internal model of their body so that they would be expected to encounter fewer unexpected internal perturbations.

Our data comparing sitting behavior of infants with typical development to infants with delayed development also fits well with other reported entropy results. We found differences between early sitting postural sway of infants with typical development compared to infants with delayed development, with the ApEn(m=1, r=std(Data),

t=8.33sec@240Hz, lag=8) being lower in the postural sway of infants with cerebral palsy. Our result of higher approximate entropy for postural sway of infants with typical development is consistent with the results of Donker, Ledebt, Roerdink, Savelsbergh & Beek (2008) who find lower sample entropy, a measure very similar to approximate entropy, for standing postural sway in infants with cerebral palsy. Approximate entropy has been described as a measure of complexity (Pincus, 1991). Infants with typical development have been described as having more complex movements than infants with cerebral palsy, perhaps due to impaired cerebral connectivity (Hadders-Algra, 2008). If approximate entropy is a measure of complexity, then the higher ApEn(m=1, r=std(Data), t=8.33sec@240Hz, lag=8) values we found for postural sway of infants with typical development are consistent with the reported higher complexity. We see the high values for ApEn(m=1, r=std(Data), t=8.33sec@240Hz, lag=8) decrease with development, whereas Hadders-Algra (2008) hypothesizes that complexity should always be higher for infants with typical development, regardless of age. However, Hadders-Algra (2007) reports different types of movement complexity, including “pre-term”, “writhing”, and “fidgety”, depending upon the age of the infant. Our particular analysis may only be sensitive to one particular type of movement complexity that is prevalent in infants when they are 5 months old, i.e. the early sitting in our study. Infants with cerebral palsy may have inappropriate muscle sequencing, even in older children (Wollacott & Shumway-Cook, 2005; van der Heide & Hadders-Algra, 2005).

The development of motor skills has also been considered from a developmental psychology perspective, where the development of locomotion has been described as initiating a psychological reorganization that is wide ranging and impacts perception,

spatial cognition, and social and emotional development (Campos, Anderson, Barbu-Roth, Hubbard, Hertenstein, & Witherington, 2000). While locomotor development may occur in synchrony with cognitive performance, the unilateral focus of Campos, Anderson, Barbu-Roth, Hubbard, Hertenstein, and Witherington (2000) on motor skills as the cause of cognitive change is unfortunate given that cognitive change is likely driving motor skill acquisition just as much as motor skill acquisition is driving cognitive change (Bushnell, 2000). However, Campos, Anderson, Barbu-Roth, Hubbard, Hertenstein, and Witherington (2000) make an interesting point that locomotion allows the infant to explore the environment by moving to and exploring objects of interest, thereby engaging cognitive function that might not otherwise be active. Relating this speculation to our study, sitting likely affords some of the same cognitive benefits as locomotion because the visual exploration of the environment is enabled by a stable sitting posture, and reaching to nearby objects is enabled by a stable sitting posture. From the perspective of Campos, Anderson, Barbu-Roth, Hubbard, Hertenstein, & Witherington, (2000), one might speculate infants development of upright sitting skills would enhance cognitive development, and from this perspective the higher incidence of mental retardation in infants with cerebral palsy (Odding, Roebroeck, & Stam, 2006) would be attributed to poor development of motor skills. However, from the perspective of bidirectionality of causation of Bushnell (2000), the cognitive interest in surrounding environment is also likely important in development of the motor skill. From this perspective the high incidence of mental retardation in infants with cerebral palsy (Odding, Roebroeck, & Stam, 2006), may contribute to the delay of motor skill acquisition, as the intellectual curiosity motivating the infant to explore the environment may be lower in infants with

mental retardation. However, one cannot neglect the possibility that the correlation between mental retardation and cerebral palsy is only partially one of cause and effect, and that both are substantially mediated by the severity of the original brain injury.

The cultural influence on motor development is an intriguing aspect of development as it supports the notion that experience influences motor development, as the different experiences that infants have in different cultures result in differences in motor development. In African societies where early sitting is encouraged by parents' manipulating of infants' posture, the infants develop sitting at an earlier age and spend more time in an unsupported sitting posture than American infants, and it is hypothesized that experiencing a greater number of postural positions influences motor learning of postural control (Bril & Sabatier, 1986). The development of postural control is not entirely a matter of maturation of biological control systems, but also is influenced by the environment in which the infant develops. However, there is no culture in which infants develop independent sitting skills at age 1 month, as the neuromuscular system apparently cannot control sitting at that age regardless of environmental influences. The development of postural control is not entirely a matter of the environment in which the infant develops, but also depends on the maturation of the biological control systems. It is the interaction of the biological system and the environment in which it develops that determines the outcome of the infant's motor development, not simply biology or environment acting alone.

The postural positions that an infant experiences without external intervention, such as those performed by the parents in the African societies (Bril & Sabatier, 1986) discussed above, are a result of movements the infant makes itself. If more positions are

beneficial for motor learning of postural control, then there would be a benefit for infants to move more, but what benefit is there to moving in a random manner? Fractal movements, such as Levy flights, are more random than periodic movements, and are a good search method. For example, Levy flights are used by animals for searching an area for food or mates (Reynolds & Rhodes, 2009). Infants sitting postural sway has been shown to be fractal (Deffeyes, Kochi, Harbourne, Kyvelidou, Stuberg, & Stergiou, 2009). Thus the higher entropy postural sway may be an adaptive method for exploring various postural positions. It seems counterintuitive that a young infant with poor postural control skills would attempt to use a wide range of different postures, as adopting new challenging postures may result in falls. However, unlike falling in adults that may cause injury, infants' falling is typically inconsequential from an injury standpoint, and is instead part of the exploratory behavior of an infant as they learn new motor skills such as sitting, crawling, cruising, and walking, and learn to use these skills in novel environments (Adolph, 2008). The biological interpretation of the large value of the r parameter used in the analysis is that large excursions of the COP are required to be counted as non-matches by the approximate entropy algorithm. Near fall events, where the infant nearly falls but then recovers balance, might give rise to large excursions in the COP. Actual falling events were not included in the data, the infant must be sitting in order for the trial to be used. Higher entropy for early sitting infants with typical development might then reflect more near fall events, as compared to more developed and thus more skilled sitting. Higher entropy for infants with typical development as compared to infants with delayed development may indict an increased willingness to engage in behaviors that result in near fall events as they explore various control

strategies.

Adults have difficulty in producing random movement patterns even when requested to do so (Newell, Deutsch, & Morrision, 2000), so it is perhaps not surprising that the typical infants sitting behavior loses much, but not all, of its random quality in becoming more adult-like. Optimal variability theory (Stergiou, Harbourne, & Cavanaugh, 2006) suggests that there is an optimal randomness in human movement variability, and early sitting in infants with typical development may have too high a randomness compared to optimal adult values, with a subsequent loss of variability with development. However, this study only assesses infant sitting at two points in time, and there is no reason to believe that the development of infant sitting is linear progression towards adult sitting (Adolph, Young, Robinson, Gill-Alvarez, 2008; Harbourne & Stergiou, 2003). While some authors suggest daily evaluation of a motor skill in order to assess developmental nuances (Adolph, Young, Robinson, Gill-Alvarez, 2008), a major goal of this work was to understand the parameters necessary for the approximate entropy analysis, rather than mapping out the shape of the developmental trajectory.

An interesting aspect of the postural sway features that we found are the high frequencies of the COP movements. The features in the 20-30 Hz range are at a higher frequency than is typically found in postural sway data, or even in other types of human movement data. Human clapping can be maintained as fast as 7 to 8 Hz (Morrison, Hong, & Newell, 2009), and the world's fastest drummer can perform tapping movements no faster than 10 Hz (Fujii, Kudo, Ohtsuki, & Oda, 2009). Because of their high frequency, these COP movements are not thought to be related to any type of voluntary movement of the infants, and trials with observable repetitive movements, such as clapping or

flapping the arms, were excluded from our analysis. Faster movements may be accomplished by reflexes, in particular the short latency reflexes that result from stretch reflex mechanism. Although different authors adopt different definitions of short latency, one definition is a latency less than 60 msec is short latency (Taube, Schubert, Gruber, Beck, Faist, & Gollhofer, 2006), and we would classify the features 33 to 50 msec as being short latency, if they are in fact due to reflex activity. For comparison, in adult sitting the stretch reflex of the paraspinal muscles, which help stabilize the spine in upright sitting, has a mean latency of 30.7 (21.3) msec in response to external perturbations (Granata, Slota, & Bennett, 2004). The response latency is the time from the perturbation until electromyography detects activation of the muscle. It does not include time for the muscle to reach full activation, which in adults was an additional 71.3 (27.7) msec (Granata, Slota, & Bennett, 2004). Thus the fastest reflex response might be fast enough to contribute to the 20-30 Hz, 50-33 msec features that we find in the anterior-posterior sitting postural sway of typically developing infant. As a comparison, normal finger tremor includes a 20-25 Hz component that is produced by the stretch reflex loop (Deutsch & Newell, 2006). However, for this tremor the frequency depends on the inertial properties and the stiffness properties of the limb, and to the best of our knowledge, the frequency for infant trunk movements has not been reported, but might be considerably different than the reported 20-25 Hz range for finger movement. Perhaps the near-fall events, where the infant nearly falls but recovers (discussed above), result in high frequency components of the COP either by exciting a stretch reflex, or from high accelerations associated with the fall and/or recovery result in tissue vibrations in the high frequency range. The features in the 20 to 30 Hz range of the power spectra

of sitting postural sway of typically developing infants may be stretch reflex associated movement, but it is not clear that this is the case.

Is it reasonable to propose stretch reflexes are active in unperturbed infant sitting? Historically, reflexes were thought to be the main posture control mechanism, but more recent work has shown posture control is a more complex sensory motor integration problem (Horak, 2006). Additionally, the small movements in well-controlled postural balance do not seem capable of exciting a stretch reflex. Proposing stretch reflexes in a sitting posture study seems unlikely from this perspective, but sitting in young infants is not as well controlled as in adults. Postural control in adult standing has been much more widely studied than infant sitting, and one might hypothesize that similar control mechanisms are operative in infant sitting. Because stretch reflexes likely play only a small role in unperturbed adult standing postural control (Bove, Trompetto, Abbruzzese, & Schieppati, 2006), it might be argued that stretch reflexes are not active in early infant sitting. However, while stretch reflexes are not the main mechanism for control of sitting posture, evidence for stretch reflexes making some contribution to infant sitting postural sway has also been reported by Hadders-Algra, Brogren, and Forsserberg (1996). Stretch reflexes are certainly important in generating a quick response to an external perturbation in adult sitting (Granata, Slota, & Bennett, 2004), but may not be activated in unperturbed sitting in adults. There are some important differences between adult postural control and young infants postural control. Adult postural control can potentially use information from a wide array of different sensory modalities, including visual information, vestibular information, joint proprioceptive information, cutaneous information from the plantar surface of the feet, as well as sensory information from the muscles. Some of these

sensory modalities are not as well developed in the infant compared to adults or even older infants, and sensory integration capabilities are not as well developed. Children do not achieve fully adult-like sensory integration until they are 12 years old (Peterson, Christou, Rosengren, 2006). Using an oscillating moving-room experimental paradigm, infants' sitting postural sway was found to become more strongly entrained to the visual stimuli as they reached the age where they learned to sit (Bertenthal, Rose, & Bai, 1997), and infant sensitivity to optic flow in contraction (meaning the image appears to be moving away from the infant) increased from 2 to 8 months, but still had not attained adult values (Brosseau-Lachaine, Casanova, & Faubert, 2008). The vestibular-ocular reflex matures as infants learn to walk (Wiener-Vacher, Toupet, & Narcy, 1996). Thus the younger, typically developing infants in our study did not have the full spectrum of sensory information to use for posture control. One might speculate that, as a result of not having fully developed sensory input to the postural control, postural sway carries the body to more extreme positions, sufficient to trigger stretch reflexes. Additionally, infants in early sitting more often adopt a "prop sitting" posture where they lean forward and place their hands on the ground or on their legs, and support some of their upper body weight with their arms. Perhaps because of the forward leaning, the hamstring muscles are closer to being stretched to the threshold that can trigger a stretch reflex, and thus smaller amounts of postural sway in the anterior direction may be capable of triggering a stretch reflex. The differences found in our study were only significant in the anterior-posterior direction, not in the medial lateral direction, consistent with a stretch reflex of the hamstring muscles being triggered more often from a forward leaning posture. These results do not indicate that stretch reflexes are the main control mechanism for the infant

controlling postural sway, but merely that the differences between the infants with developmental delay and those with typical development are more pronounced on time scales that are associated with reflex control.

If the features are related to a stretch reflex, why then would higher ApEn(m=1, r=std(Data), t=8.33sec@240Hz, lag=8) values be associated with the movement? The stretch reflex in adults is well tuned, with the muscle stretch inducing contraction in the muscle that was stretched, and inhibition of the antagonist muscle. However, in infants the stretch reflex sensory neurons project to a number of different motor muscles, as the connections have not yet been optimally tuned (Myklebust & Gottlieb, 1993; Lichtman & Colman, 2000). Thus when any given muscle is stretched, a variety of muscles contract, generating movement in a direction that is not entirely appropriate. Thus the higher entropy values in postural sway of early sitting of typically developing infants are consistent with the occasional occurrence of a movement that triggers a stretch reflex, in conjunction with the poorly organized postural sway as result of reflex irradiation that is present in these younger infants. ApEn(m=1, r=std(Data), t=8.33sec@240Hz, lag=8) decreases as the infants develop, consistent with better coordinated reflex activity.

If the features we observe in the early sitting postural sway data from infants with typical development are indeed due to a stretch reflex, then why do the infants with delayed development not have these features in their postural sway data? One potential reason for not seeing stretch reflexes in the data from infants with delayed development is that if the infant moves enough to trigger a stretch reflex, the reflex may be poorly coordinated and cause the infant to lose balance and fall, and we did not use data in our analysis where the infant was falling, which may have resulted in not including data

where stretch reflex was activated in infants with delayed development.

A second potential reason is that the emergent behavior in infants with cerebral palsy is different that in infants with typical development because the neuromuscular control constraints are different, and the optimal behavior for each system is different. For example, muscle firing patterns in walking that emerge in infants with Down's syndrome are longer than in infants with typical development, and this emergent pattern is thought to be adaptive in these infants in order to help stabilize lax joints (Chang, Kubo, & Ulrich, 2009). Children with cerebral palsy have hyperactive stretch reflexes (Poon & Hui-Chan, 2009), although the functional implications of the altered reflexes are not entirely clear (Matiello & Wollacott, 1997). In some cases, spasticity in limbs associated with cerebral palsy may be a result of an altered stretch reflex (van Doornik, Kukke, & Sanger, 2009). The infants with delayed development also use a prop sitting posture in early sitting, and unlike the infants with typical development, some maintain this posture in developed sitting. It may be that these high frequency features are not seen in the sitting postural of infants with delayed development because the infants with developmental delay do not exhibit as much movement as those with typical development, and therefore are less likely to trigger a stretch reflex. A previous analysis of this data set, minus a few subjects who had not yet finished the study, found the infants with typical development had slightly more postural sway than infants with delayed development, although the difference was not statistically significant (Deffeyes, Harbourne, Kyvelidou, Stuberg, & Stergiou, 2009). Given the nonlinear response of the stretch reflex, that small difference measured in amount of movement may be more important than the linear statistical analysis used in that study would indicate.

Additionally, if the infant has learned through experience that certain behavior triggers a stretch reflex, and if that poorly coordinated stretch reflex results in a fall, the infant may adapt their behavior to avoid triggering a stretch reflex. Sitting still may be an adaptive response to an altered stretch reflex in these infants. Children with CP are reported to use more top-down postural control (van der Heide & Hadders-Algra, 2005), perhaps because reflexive control is less functional in these children.

A third potential reason for not seeing a stretch reflex response in the postural sway data is that it may be related to some unknown parameter that changes with normal development of the infants, rather than to typical or delayed developmental. A weakness of the experimental design is that, even though both the infants with typical development and the infants with delayed development were just learning to sit, the infants with delayed development were necessarily older than the infants with typical development. Thus any normal developmental change, such as height gain, change in body adipose mass, change in lean mass lean mass, could account for the differences we observed. Changes in anthropometric features in infants can have unexpected consequences. As an example, the stepping reflex seen in young infants appears to disappear with development. If young infants are held over a moving treadmill, their feet will make stepping motions on the treadmill surface (Thelen, Fisher, & Ridley-Johnson, 1984). As the infants developed, they no longer make these stepping movements. Thelen, Fisher, and Ridley-Johnson (1984) found the reflex had not disappeared, but rather the infants had gained mass due to growth, and the muscle strength had not yet caught up, and if the infants' legs were submerged in water, such that the buoyancy force helped support the infant's mass, the stepping movements were again observed. Similarly, as the typically

developing infants in our study developed from age 4.9 months at early sitting to age 7.9 months at advanced sitting, weight gain may prevent small contributions from reflex activity from moving the mass of the infant enough to be detected by the force plate. The high frequency features were not observed in the infants with delayed development, at any time early or advanced sitting. These infants were age 14.1 months at early sitting and 18.1 months at advanced sitting. While these infants were delayed in their development, they were also older than the typically developing infants, and thus may have different anthropometric characteristics than the typically developing infants.

There is also the possibility that the high frequency features are due to some cause other than a stretch reflex. While stretch reflexes are fast for control of movement, the fast movements we see in our study may not be controlled movements. Often gait data is low pass filtered in order to remove high frequency contributions from tissue vibrations that occur on impact of foot with the ground. There is a possibility that the high frequency features found in this study are some type of tissue vibration. Perhaps a rapid change of direction might be able to cause enough vibration of soft tissue for the vibration to be detectable. However, in sitting there are no impacts with the ground to excite tissue vibrations. Vibrations could be excited by quick movements in the anterior-posterior axis, accounting for the high frequency features in the anterior-posterior COP data. However, root-mean-square and range of movement did not differ significantly between infants with developmental delay and infants with typical development in the anterior-posterior axis (Deffeyes, Harbourne, Kyvelidou, Stuberg, & Stergiou, 2009), so differences in vibration would perhaps be due to differences in mass distribution or tissue elasticity between the two groups. Infants with cerebral palsy may have eating difficulties

(Sleigh, Sullivan, & Thomas, 2004), prevented adequate nutrient intake during development and thereby reducing the adipose tissue compared to infants with typical development (Kuzawa, 1998).

Opportunities for further work

One area that was not investigated was the use of filtering to remove noise. Filtering data for linear analysis or spectral analysis is a well developed area of signal processing, but filtering for nonlinear analysis is not as well developed. Use of filters designed for linear or spectral analysis prior to nonlinear analysis may be problematic (Rapp, Albano, Schmah, & Farwell, 1993; Schreiber & Katz, 1995; Theiler & Eubank, 1993) as the filters have been designed to preserve certain linear and spectral aspects of the data, and may not preserve nonlinear features that are of interest in nonlinear analysis. However, many researchers use standard filter techniques on standing postural sway data, such as a low pass Butterworth filter (Donker, Ledebt, Roerdink, Savelsbergh, & Beek, 2008; Hong, James, & Newell, 2008; Stins, Michielson, Roerdink, & Beek, 2009;), Savitsky-Golay smoothing (Hong, Manor, & Li, (2007), and some authors use detrending methods which effectively serve as filters for the data (Costa, Priplata, Lipsitz, Wu, Huang, Goldberger, & Peng, 2007). Our results suggest that down-sampling or appropriate choice of a lag value may be a good alternative to filtering noisy data, but we did not investigate filtering, so a test of this hypothesis is needed. Another approach to removing noise from the data is to use equipment for data collection that gives high signal-to-noise data, so that the dynamics of the system under study can be more readily quantified without filtering. Future studies from this lab on infant sitting will use force plate equipment with a dynamic range selected specifically for infant sitting postural

analysis.

There are a number opportunities for further exploration of the approximate entropy algorithm and related measures. Attempting to select the one best set of parameters for approximate entropy misses the opportunity to use multiple sets of parameters to characterize a data set. For example, values of approximate entropy both using low and high values for the r parameter may provide a useful contrast, if the data has different dynamics at different length scales, such as our data that has differences with r=1*std(Data) versus r=3*std(Data). Similarly, differences could exist on different time scales, and multiscale entropy could be used to more rigorously investigate the entropy of dynamics that occur on multiple time scales (Costa, Goldberger, & Peng, 2002; Costa, Priplata, Lipsitz, Wu, Huang, Goldberger, & Peng, 2007). Postural sway data is not necessarily stationary (Schumann, Redfern, Furman, el-Jaroudi, Chaparro, 1995), and these high frequency features are likely not occurring all the time, but may be occurring only sporadically in the sitting position. Time frequency analysis (Schumann, Redfern, Furman, el-Jaroudi, Chaparro, 1995) or wavelet analysis might give more insight into the occurrence of these features. Additionally, using techniques such as electromyography to monitor muscle activity after perturbation of sitting, and accelerometers to monitor tissue vibration, might shed light on the origins of the 20-30 Hz spectral features.

SUMMARY:

The use of standard parameters, ApEn(r=.2*std(Data),m=2, N, lag=1) , for the approximate entropy analysis may work well for comparing systems with very different

dynamics, but to detect more subtle differences, the standard parameters may not be optimal. A useful pragmatic finding of this work for researchers who use nonlinear measures is that spectral analysis can be used as a guide to select lag parameters for approximate entropy analysis. From a clinical perspective, this work is of interest because the design of an infant postural analysis system, coupled with computer for data analysis, may one day bring this technology to the clinical setting for a more sensitive analysis of postural control than is currently available. From a developmental neuroscience perspective, this work is of interest because it suggests the possibility that a short latency reflex for control of sitting posture is operative, perhaps triggered by near-falls. The stretch reflex does not disappear with development, so the disappearance of the measured short latency reflex contribution to postural sway may be a result of not being activated in older infants as other sensory modalities develop and postural control improves. More work is needed to elucidate the important of the stretch reflex in early sitting postural control, and to understand the differences in postural control between infants with developmental delay and those with typical development.

References

Adolph, K.E. (2008). Learning to move. *Current Directions in Psychological Science*, 17(3), 213-218.

Adolph, K.E., Young, J.W., Robinson, S.R., Gill-Alvarez, F., (2008). What is the shape of developmental change? *Psychological Review*, 115(3), 527-543.

Bertenthal, B.I., Rose, J.L., & Bai, D.L. (1997). Perception-action coupling in the development of visual control of posture. *Journal of Experimental Psychology Human Perception and Performance*, 23(6), 1631-1643.

Blauw-Hospers, C.H., de Graaf-Peters, V.B., Dirks, T., Bos, A.F., Hadders-Algra, M., 2007. Does early intervention in infants at high risk for a developmental motor disorder improve motor and cognitive development? *Neuroscience and Biobehavioral Reviews*, 31(8), 1201-1212.

Blauw-Hospers, C.H., Hadders-Algra, M., 2005. A systematic review of the effects of early intervention on motor development. *Developmental Medicine and Child Neurology*, 47 (6), 421–432.

Bove, M., Trompetto, C., Abbruzzese, G., Schieppati, M. (2006). The posture-related interaction between Ia-afferent and descending input on the spinal reflex excitability in humans. *Neuroscience Letters*, 397(3), 301-306.

Bril, B. & Sabatier, C. (1986). The cultural context of motor development: postural manipulations in the daily life of Bambara babies (Mali). *International Journal of Behavioral Development*, 9, 439-453.

Brosseau-Lachaine O, Casanova C, Faubert J. (2008). Infant sensitivity to radial optic flow fields during the first months of life. *Journal of Vision*, 8(4), 5.

Bushnell, E.W. (2000). Two steps forward, one step back. *Infancy*, 1(2), 225-230.

Campos, J.J., Anderson, D.I., Barbu-Roth, M.A., Hubbard, E.M., Hertenstein, M.J., Witherington, D. (2000). Travel broadens the mind. *Infancy*, 1(2), 149-219.

Castiglioni, P. and Di Rienzo, M. (2008). How the threshold "r" influences approximate entropy analysis of heart-rate variability. *Computers in Cardiology*, 35, 561-564.

Cavanaugh, J.T., Guskiewicz, K.M., Giuliani, C., Marshall S., Mercer V.S., & Stergiou, N. (2006). Recovery of postural control after cerebral concussion: new insights using approximate entropy. *Journal of Athletic Training*, 41(3), 305-313.

Cavanaugh, J.T., Guskiewicz, K.M., Giuliani, C., Marshall, S., Mercer, V., & Stergiou, N., (2005). Detecting altered postural control after cerebral concussion in athletes with normal postural stability. *British Journal of Sports Medicine,* 39(11), 805-11.

Chang, C.L., Kubo, M., & Ulrich, B.D. (2009). Emergence of neuromuscular patterns during walking in toddlers with typical development and with Down syndrome. *Human Movement Science*, 28, 283-296.

Chen, J. & Wollacott, M.H. (2007). Lower extremity kinetics for balance control in children with cerebral palsy. *Journal of Motor Behavior*, 39(4), 306-316.

Chen, L.C., Metcalfe, J.S., Jeka, J.J., & Clark, J.E., (2007). Two steps forward and one back: learning to walk affects infants' sitting posture. *Infant Behavior and Development*, 30(1), 16-25.

Costa, M., Goldberger, A.L., Peng, C.K. (2002). Multiscale entropy analysis of complex physiologic time series. *Physical Review Letters*, 89(6), 068102.

Costa, M., Priplata, A.A., Lipsitz, L.A., Wu, Z., Huang, N.E., Goldberger, A.L., & Peng, C.K., (2007). Noise and poise: enhancement of postural complexity in the elderly

with a stochastic-resonance-based therapy. *Europhysics Letters*, 77, 68008.

de Graaf-Peters, V.B., Blauw-Hospers, C.H., Dirks, T., Bakker, H., Bos, A.F., Hadders-Algra, M., 2007. Development of postural control in typically developing children and children with cerebral palsy: possibilities for intervention? *Neuroscience and Biobehavioral Reviews*, 31(8), 1191-1200.

Deffeyes, J.E., Harbourne, R.T., DeJong, S.L., Kyvelidou, A., Stuberg, W.A. & Stergiou, N. (2009). Use of information entropy measures of sitting postural sway to quantify developmental delay in infants. *Journal of Neurological Engineering and Rehabilitation*, 6(1), 34.

Deffeyes, J.E., Harbourne, R.T., Kyvelidou, A., Stuberg, W.A., & Stergiou, N., (2009). Nonlinear analysis of sitting postural sway indicates developmental delay in infants. *Clinical Biomechanics*, 24(7), 564-70.

Deffeyes, J. E., Kochi, N., Harbourne, R. T., Kyvelidou, A., Stuberg, W. A., & Stergiou, N. (2009). Nonlinear detrended fluctuation analysis of sitting center-of- pressure data as an early measure of motor development pathology in infants. *Nonlinear Dynamics, Psychology and Life Sciences*, 13(4), 351-368.

Deutsch, K.M., & Newell, K.M., (2006). Age-related changes in the frequency profile of children's finger tremor. Neuroscience Letters, 404(1-2), 191-5.

Donker, S.F., Ledebt, A., Roerdink, M., Savelsbergh, G.J., & Beek, P.J., (2008). Children with cerebral palsy exhibit greater and more regular postural sway than typically developing children. *Experimental Brain Research*, 184(3), 363-70.

Ebner, T.J. & Pasalar, S. (2008). Cerebellum predicts the future motor state. Cerebellum,

7(4), 583-588.

Folio, M.R. & Fewell, R.R. (2000). *Peabody development motor scale (2nd ed.).* Austin, TX: PRO-ED, Inc.

Fujii, S., Kudo, K., Ohtsuki, T., & Oda, S., (2009). Tapping performance and underlying wrist muscle activity of non-drummers, drummers, and the world's fastest drummer. *Neuroscience Letters*, 459(2), 69-73.

Georgoulis, A.D., Moraiti, C., Ristanis, S., & Stergiou, N. (2006). A novel approach to measure variability in the anterior cruciate ligament deficient knee during walking: the use of the approximate entropy in orthopaedics. *Journal of Clinical Monitoring and Computing*, 20(1), 11-18.

Goldberger AL, Peng CK, Lipsitz LA. (2002). What is physiologic complexity and how does it change with aging and disease? *Neurobiology of Aging*, 23(1), 23-26.

Granata, K.P., Slota, G.P., & Bennett, B.C., (2004). Paraspinal muscle reflex dynamics. *Journal of Biomechanics*, 37(2), 241-247.

Hadders-Algra, M., (2004). General movements: a window for early identification of children at high risk for developmental disorders. *The Journal of Pediatrics*, 145(2 Suppl), S12-8.

Hadders-Algra, M., (2005). Development of postural control during the first 18 months of life. *Neural Plasticity*, 12(2-3), 99-108.

Hadders-Algra, M., (2007). Putative neural substrate of normal and abnormal general movements. *Neuroscience and Biobehavioral Reviews*, 31(8), 1181-90.

Hadders-Algra, M., (2008). Reduced variability in motor behaviour: an indicator of impaired cerebral connectivity? *Early Human Development*, 84(12), 787-9.

Hadders-Algra, M., Brogren, E., & Forssberg, H., (1996). Ontogeny of postural adjustments during sitting in infancy: variation, selection and modulation. *The Journal of Physiology*, 493 (Pt 1), 273-288.

Harbourne, R.T. & Stergiou, N. (2003). Nonlinear analysis of the development of sitting postural control. *Developmental Psychobiology*, 42, 368-77.

Hong, S.L., James, E.G., & Newell, K.M., (2008). Age-related complexity and coupling of children's sitting posture. *Developmental Psychobiology*, 50(5), 502-10.

Hong, S.L., Manor, B., & Li, L., (2007). Stance and sensory feedback influence on postural dynamics. *Neuroscience Letters*, 423(2), 104-8.

Horak, F.B., (2006). Postural orientation and equilibrium: what do we need to know about neural control of balance to prevent falls? *Age and Ageing*, 35 Suppl 2, ii7-ii11.

Kaplan, D.T., Furman, M.I., Pincus, S.M., Ryan, S.M., Lipsitz, L.A., & Goldberger, A.L., (1991). Aging and the complexity of cardiovascular dynamics. *Biophysical Journal*, 59(4), 945-949.

Kaplan, D. & Staffin, P. (1996). Software for heart rate variability. Retrieved from http://www.macalester.edu/~kaplan/hrv/doc/

Kumar, A., Anand, S., Chari, P., Yaddanapudi, L.N., & Srivastava, A., (2007). A set of EEG parameters to predict clinically anaesthetized state in humans for halothane anaesthesia. *Journal of Medical Engineering & Technology*, 31(1), 46-53.

Kuzawa, C.W., (1998). Adipose tissue in human infancy and childhood: an evolutionary perspective. *American Journal of Physical Anthropology*, Suppl 27, 177-209.

Lichtman, J.W. and Colman, H. (2000). Synapse elimination and indelible memory.

Neuron, 25(2), 269-78.

Liu, P.Y., Iranmanesh, A., Keenan, D.M., Pincus, S.M., & Veldhuis, J.D., (2007). A noninvasive measure of negative-feedback strength, approximate entropy, unmasks strong diurnal variations in the regularity of LH secretion. *American Journal of Physiology*. Endocrinology and Metabolism, 293(5), E1409-15.

Lu, S. Chen, X., Kanters, J.K., Solomon, I.C., and Chon, K.H. (2008). Automatic selection of the threshold value r for approximate entropy. *IEEE Transactions on Biomedical Engineering*, 55(8), 1966-1972.

Manolakis, D.G., Ingle, V.K. & Kogon, S.M. (2005). *Statistical and adaptive signal processing: Spectral estimation, signal modeling, adaptive filtering, and array processing*. Norwood, MA: Artech House.

Matiello, D. and Wollacott, M. (1997). Postural control in children: Development in typical populations and in children with cerebral palsy and Down's syndrome. In K.J. Connolly and H. Forssberg, Neurophysiology and neuropsychology of motor development. *Clinics in Developmental Medicine*, Volume 143-144, pp 68-69. London: Mac Keith Press.

Morrison, S., Hong, S.L. & Newell, K. (2009). Upper frequency limits of bilateral coordination patterns. *Neuroscience Letters*, 454, 233-238.

Morrison, S., Kerr, G., Newell, K.M., & Silburn, P.A., (2008). Differential time- and frequency-dependent structure of postural sway and finger tremor in Parkinson's disease. *Neuroscience Letters*, 443(3), 123-128.

Newell, K.M., Deutsch, K.M., & Morrison, S. (2000). On learning to move randomly. *Journal of Motor Behavior*, 32(3), 314-320.

Myklebust, B.M., Gottlieb, G.L. (1993).Development of the stretch reflex in the newborn: reciprocal excitation and reflex irradiation. *Child Development*, 64(4), 1036-1045.

Odding, E., Roebroeck, M.E., & Stam, H.J. (2006). The epidemiology of cerebral palsy: Incidence, impairments and risk factors. *Disability and Rehabilitation*, 28(4), 183 – 191.

Peterson, M.L., Christou, E., & Rosengren, K.S., (2006). Children achieve adult-like sensory integration during stance at 12-years-old. *Gait and Posture*, 23(4), 455-63.

Pincus S.M. (1991). Approximate entropy as a measure of system complexity. Proceedings of the National Academy of Sciences of the United States of America, 88, 2297-2301.

Pincus, S.M. & Goldberger, A.L. (1994). Physiological time-series analysis: what does regularity quantify? *American Journal of Physiology – Heart and Circulatory Physiology*, 266(4), H1643-H1656.

Poon, D.M. and Hui-Chan, C.W. (2009). Hyperactive stretch reflexes, co-contraction, and muscle weakness in children with cerebral palsy. *Developmental Medicine and Child Neurology*, 51(2), 128-135.

Rapp, P.E., Albano, A.M., Schmah, T.I., & Farwell, L.A. (1993). Filtered noise can mimic low-dimensional chaotic attractors. *Physical Review E, Statistical Physics, Plasmas, Fluids, and Related Interdisciplinary Topics*, 47(4), 2289-2297.

Reynolds, A.M. & Rhodes, C.J. (2009).The Levy flight paradigm: random search patterns and mechanisms. *Ecology*, 90(4), 877-887.

Schreiber, T. & Katz, H. (1995). Noise in chaotic data: diagnosis and treatment. *Chaos*, 5, 133.

Schumann, T., Redfern, M.S., Furman, J.M., el-Jaroudi, A., Chaparro, L.F. (1995). Time-frequency analysis of postural sway. *Journal of Biomechanics*, 28(5), 603-607.

Shinbrot, T., Grebogi, C., Wisdom, J., and Yorke, J.A. (1992). Chaos in a double penduum. *American Journal of Physics*, 60(6), 491-499.

Sleigh, G., Sullivan, P.B., & Thomas, A.G., (2004). Gastrostomy feeding versus oral feeding alone for children with cerebral palsy. *Cochrane Database of Systematic Reviews*, (2), CD003943.

Stergiou, N., Harbourne, R.T., & Cavanaugh, J.T. (2006). Optimal movement variability: a new theoretical perspective for neurologic physical therapy. *Journal of Neurologic Physical Therapy*, 30(3), 120-129.

Stins, J.F., Michielsen, M.E., Roerdink, M., & Beek, P.J., (2009). Sway regularity reflects attentional involvement in postural control: effects of expertise, vision and cognition. *Gait and Posture*, 30(1), 106-9.

Taube W, Schubert M, Gruber M, Beck S, Faist M, Gollhofer A. (2006). Direct corticospinal pathways contribute to neuromuscular control of perturbed stance. *Journal of Applied Physiology*, 101(2), 420-9.

Theiler, J. & Eubank, S. (1993). Don't Bleach Chaotic Data. *Chaos*, 771, 782.

Thelen, E., Fisher, D. M., & Ridley-Johnson, R. (1984). The relationship between physical growth and a newborn reflex. *Infant Behavior and Development*, 7, 479–493.

van der Heide, J.C., & Hadders-Algra, M., (2005). Postural muscle dyscoordination in

children with cerebral palsy. *Neural Plasticity*, 12(2-3), 197-203.

van Doornik, J., Kukke, S., & Sanger, T.D., (2009). Hypertonia in childhood secondary dystonia due to cerebral palsy is associated with reflex muscle activation. *Movement Disorders*, 24(7), 965-71.

Veldhuis, J.D., Keenan, D.M., & Pincus, S.M., (2008). Motivations and methods for analyzing pulsatile hormone secretion. *Endocrine Reviews*, 29(7), 823-64.

Wiener-Vacher, S.R., Toupet, F., & Narcy, P., (1996). Canal and otolith vestibulo-ocular reflexes to vertical and off vertical axis rotations in children learning to walk. *Acta Oto-Laryngologica*, 116(5), 657-65.

Woollacott, M.H., & Shumway-Cook, A., (2005). Postural dysfunction during standing and walking in children with cerebral palsy: what are the underlying problems and what new therapies might improve balance? *Neural Plasticity*, 12(2-3), 211-219.

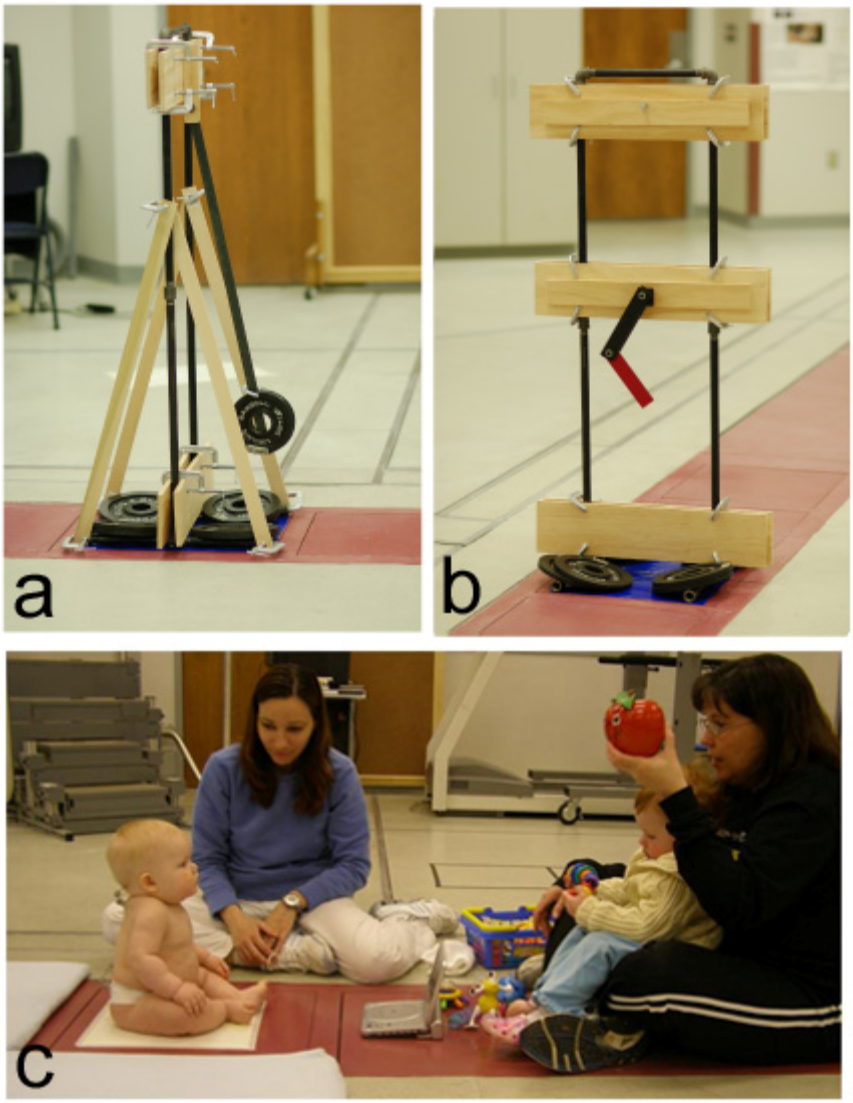

Figure 4.1. All data acquisition used the same force plate, which is built into the floor as is typical in a gait laboratory. a. single pendulum, b. double pendulum, c. infant sitting.

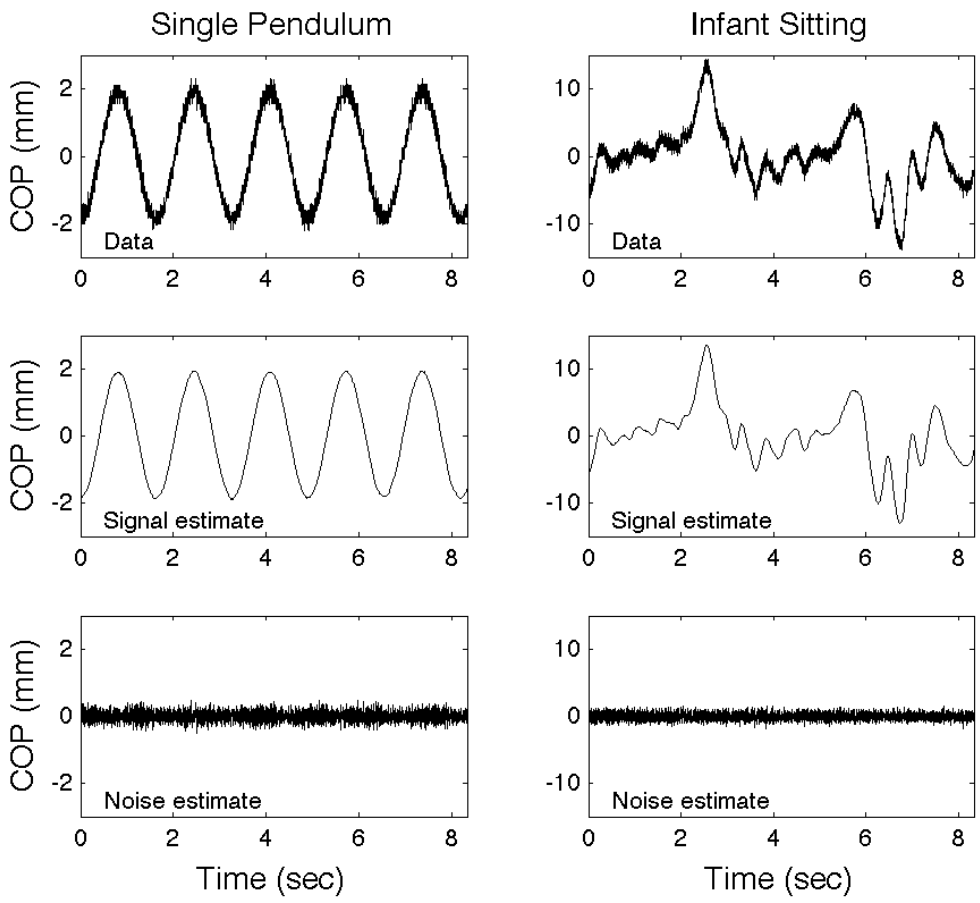

Figure 4.2. COP time series data acquired at 240 Hz from single pendulum (top left) and infant with delayed development (top right), with decomposition of each into signal (middle) and noise (bottom) using a Savitsky-Golay smooth to estimate the signal, and subtracting the signal from the data to estimate the noise.

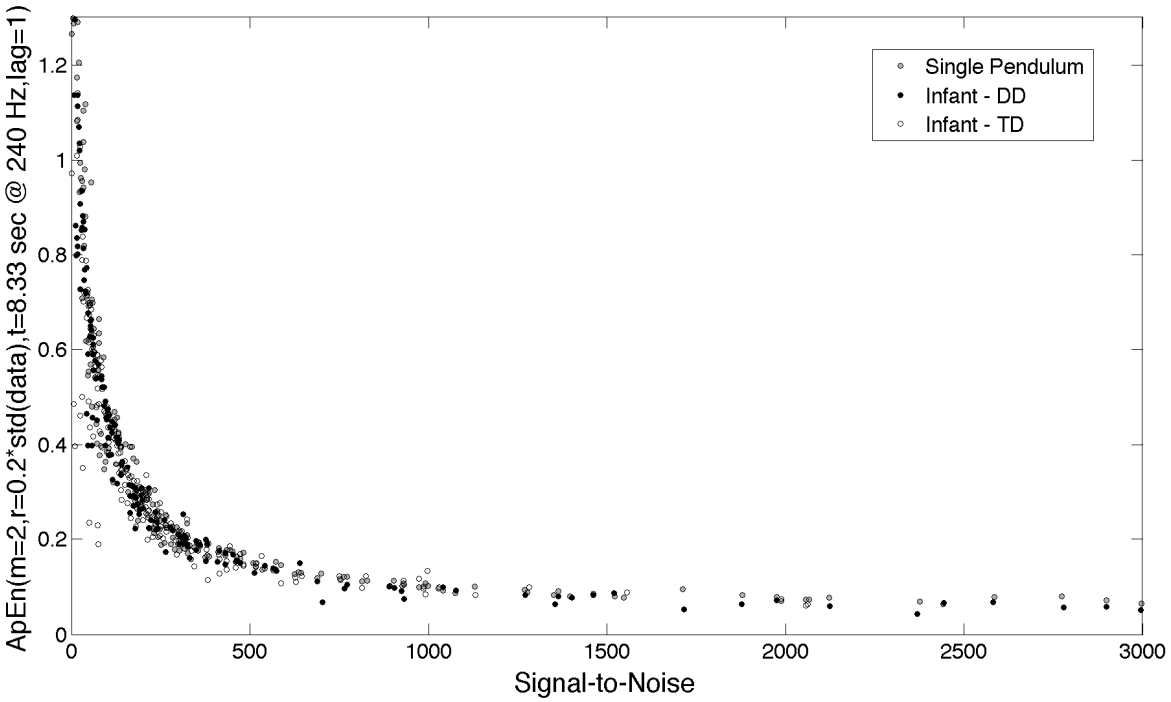

Figure 4.3. Plot of approximate entropy using "standard" parameters (m=2, r=0.2*std(Data), N=8.3 sec @240 Hz , lag=1) versus estimated signal-to-noise. Signal-to-noise is the ratio of the variances of the estimated signal and estimated noise (σ_s^2/σ_n^2).

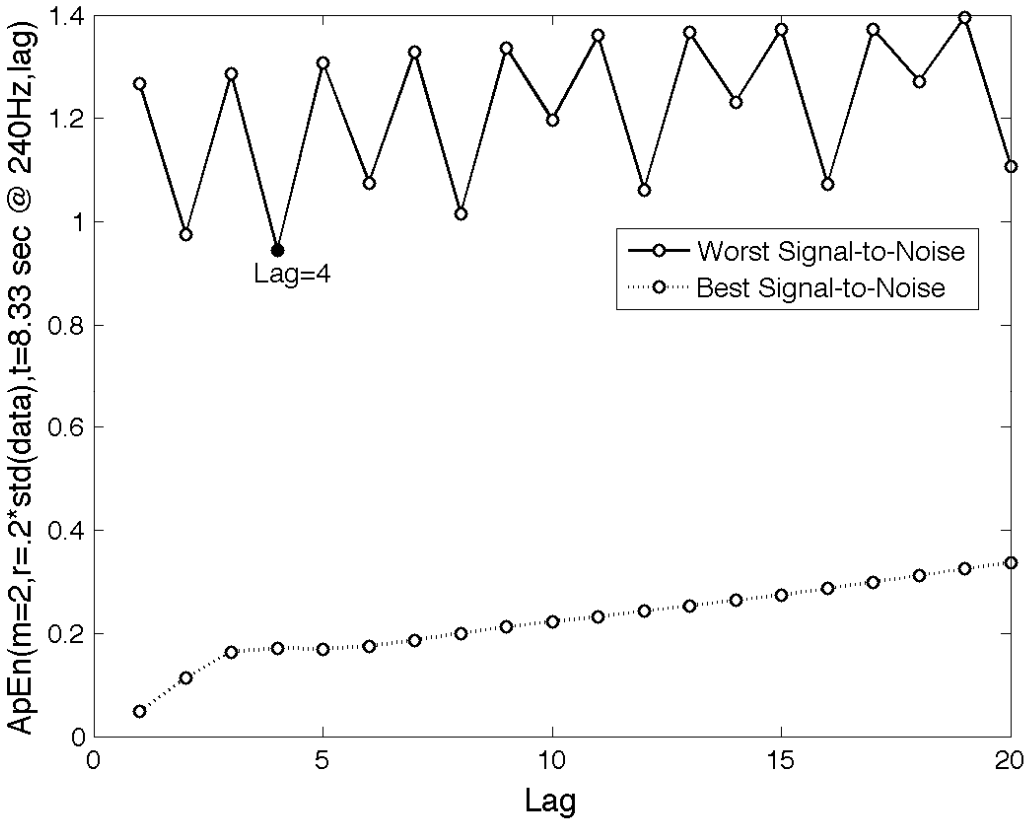

Figure 4.4. Average of approximate entropy(m=2, r=0.2*std(Data), N=8.3 sec @240 Hz , lag=1) from single pendulum COP data for the five time series with the worst signal-to-noise (solid line) and the five time series with the best signal-to-noise (dashed line), plotted versus lag. Contamination of data acquired at 240 Hz with 60 Hz noise leads to a dependence on lag for low signal-to-noise data. Note that for the lag=4 (filled circle) the approximate entropy of the worse signal-to-noise data is lowest (240 Hz/60 Hz = 4).

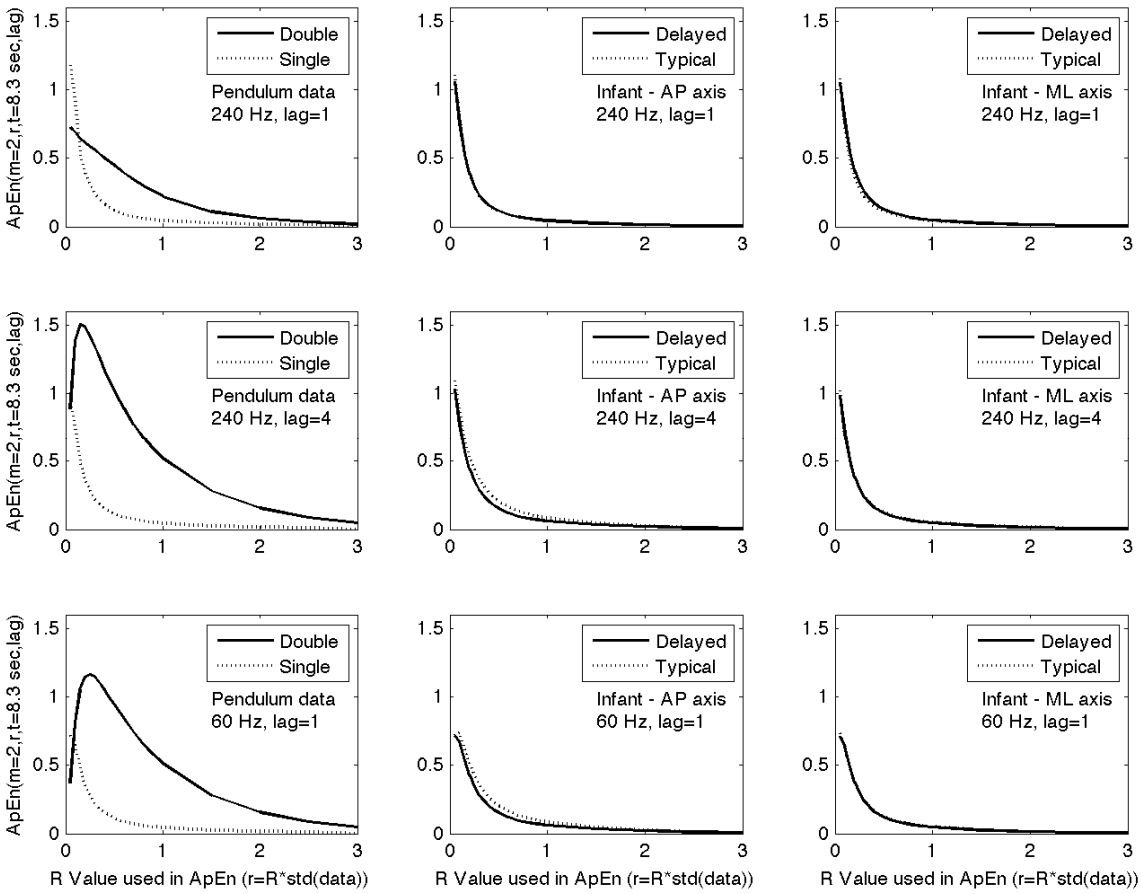

Figure 4.5. Plots of approximate entropy(m=2,r,t=8.3 sec, lag) versus R value used in approximate entropy calculation (r = R*std(Data)), for pendulum data (left column), infant sitting anterior-posterior axis (middle column) and infant sitting medial-lateral axis (right column). Data was sampled at 240 Hz and analyzed at lag=1 (top row), or lag=4 (middle row), or down sampled to 60 Hz and analyzed at lag=1 (bottom row).

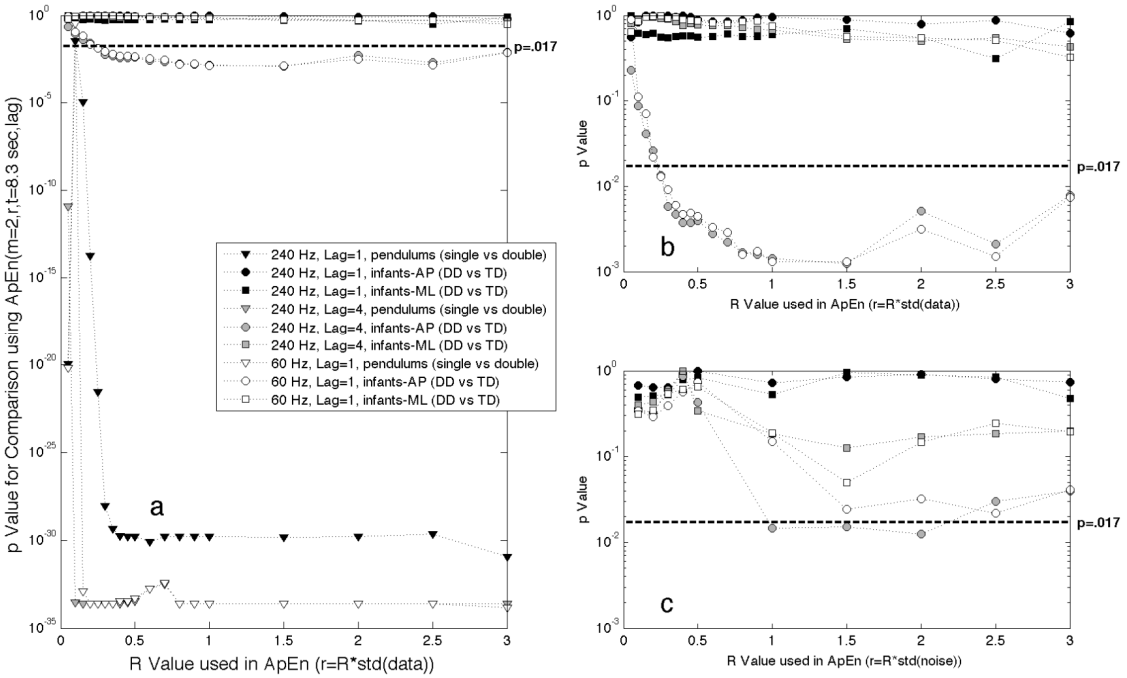

Figure 4.6. Effect of R-parameter. Wilcoxon rank sum (Mann-Whitney U test) p values for comparison of approximate entropy(m=2,r,t=8.3 sec, lag) for single versus double pendulums (triangles), infants with cerebral palsy versus typical development in anterior-posterior axis (circles) and in medial-lateral axis (squares), plotted versus R value used in the calculation of approximate entropy. Similarity of points in comparison vectors r is determined by R*std(Data) in plots a and b, and by R*std(estimated noise) in plot c. Plot b is an expanded plot of the infant sitting data in a, for comparison with plot c using the same y axis scale as plot c, but note x axes differ between plots b and c.

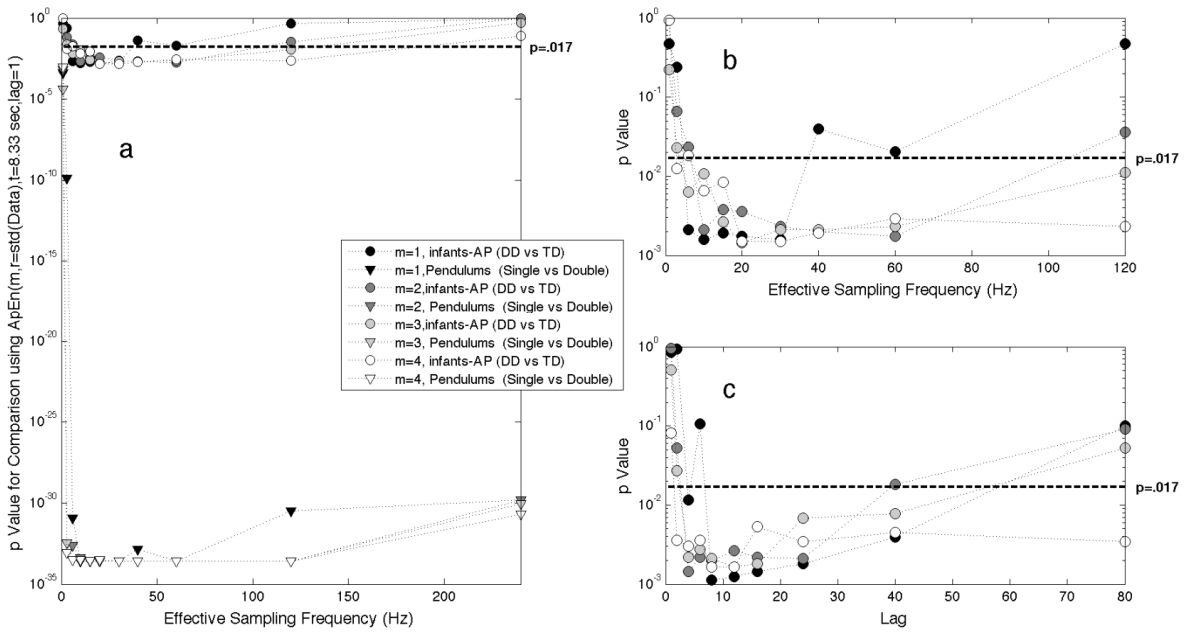

Figure 4.7. Effect of sampling frequency and lag. Wilcoxon rank sum (Mann-Whitney U test) p values for comparison of approximate entropy(m, r=std(Data), t=8.3 sec, lag) for single versus double pendulums (triangles, plot a), infants with cerebral palsy versus typical development in anterior-posterior axis (circles, plots a and b), plotted versus frequency obtained by down-sampling the 240 Hz data using lag=1 (plots a and b), and versus lag value using 240 Hz data (plot c). Plot b is an expanded plot of the infant sitting data in a, for comparison with plot c using the same y axis scale as plot c, but note x axes differ between plots b and c. Legend symbols apply to all three plots.

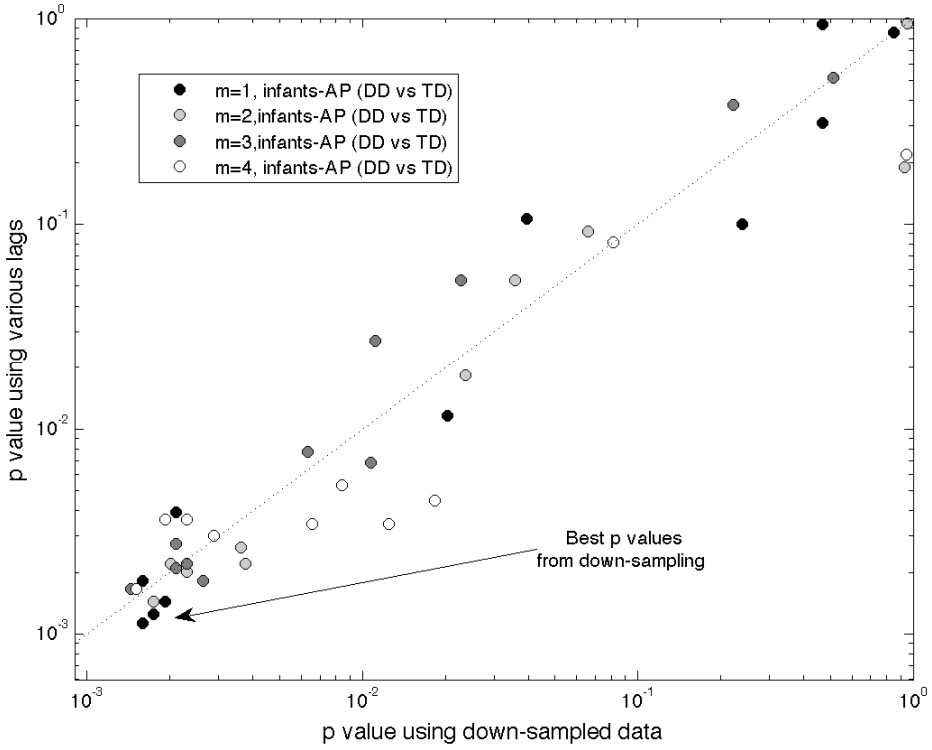

Figure 4.8. Wilcoxon rank sum (Mann-Whitney U test) p values from comparison of infant sitting postural sway in the anterior-posterior axis, based on the analysis presented in Figure 4.7b and 4.7c. The vertical axis is p values from comparison of approximate entropy(m, r=std(Data), t=8.3 sec @ 240 Hz, lag) using various lags (see Figure 4.7c) corresponding to down-sampled frequency, plotted versus Wilcoxon rank sum (Mann-Whitney U test) p values for comparison of down-sampled approximate entropy(m, r=std(Data), t=8.3 sec, lag=1) (see Figure 4.7b). Corresponding frequency means 60 Hz down-sampled p-value is paired with 240 Hz data using lag 4 p-value, for example.

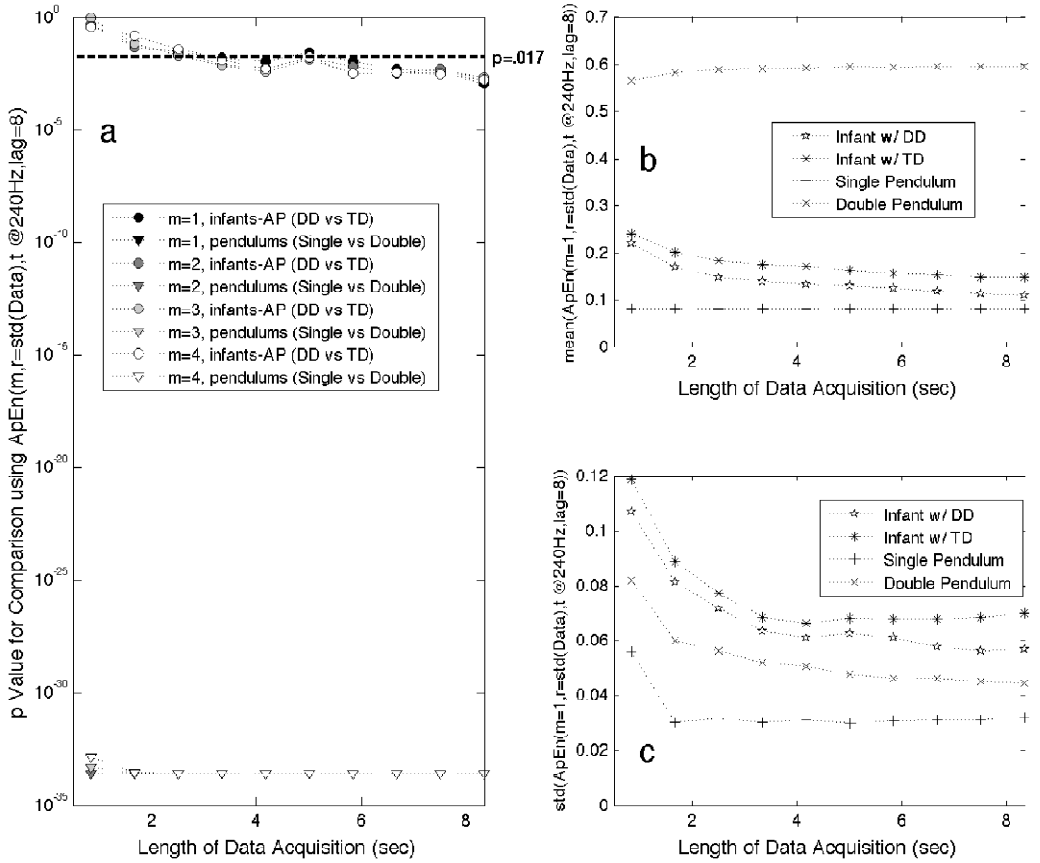

Figure 4.9. Effect of length of time series on the analysis. 4.9a. Wilcoxon rank sum (Mann-Whitney U test) p values for comparison of approximate entropy(m, r=std(Data), t @ 240Hz, lag=8) for single versus double pendulums (triangles), infants with cerebral palsy versus typical development in anterior-posterior axis (circles), plotted versus length of data acquisition in seconds. 4.9b. Mean values of ApEn(m=1, r=std(Data), t @ 240 Hz, lag=8) plotted versus length of time series used in the analysis. 4.9c. Standard deviation of ApEn(m=1, r=std(Data), t @ 240 Hz, lag=8) plotted versus length of time series used in the analysis.

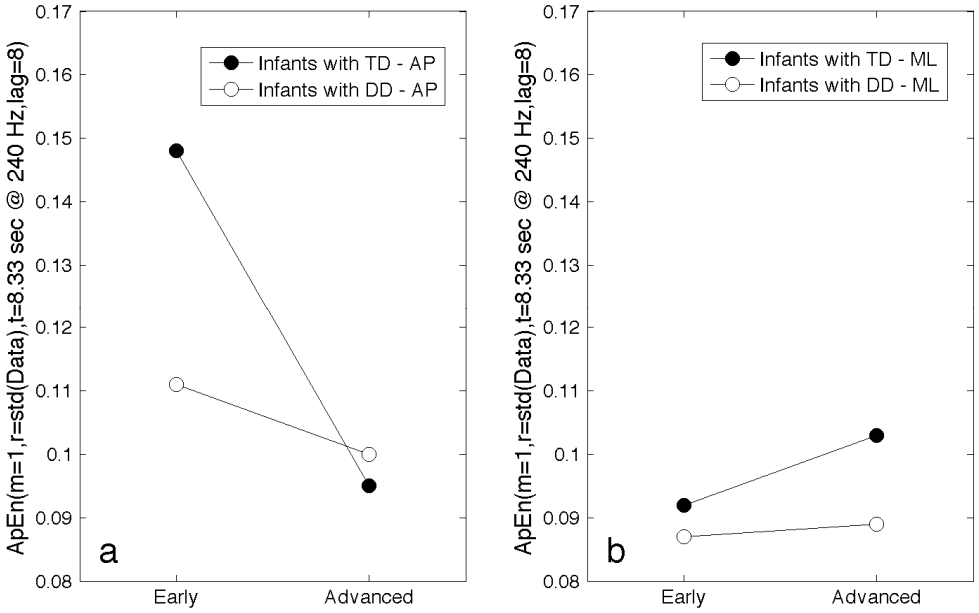

Figure 4.10. Mean values of ApEn(m=1, r=std(Data), t=8.33sec@240Hz, lag=8) for postural sway of early and advanced infant sitting in the anterior-posterior(AP) axis (a) and in the medial-lateral(ML) axis (b). Groups were infants with typical development (TD) and infants with delayed development (DD).

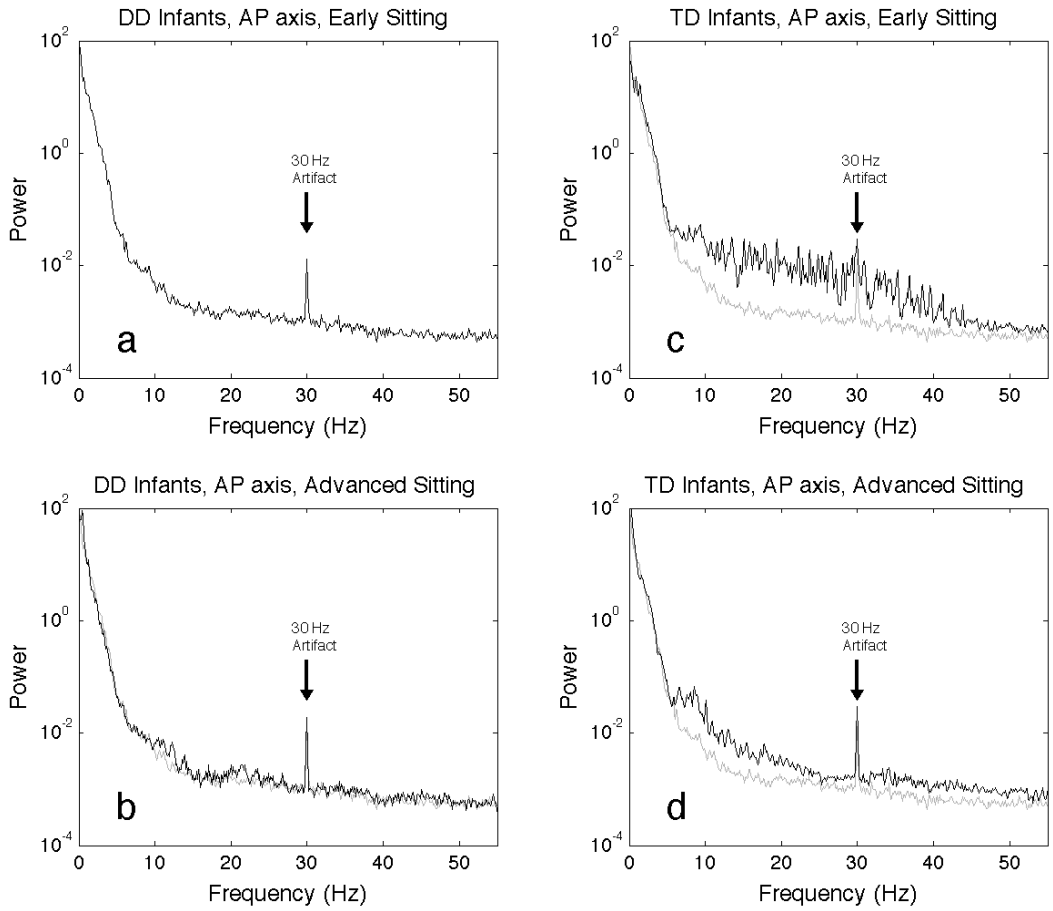

Figure 4.11. Spectral analysis of infant sitting postural sway in the anterior-posterior axis. Plotted in black is the average periodogram for all trials for infants with developmental delay, early sitting (a), advanced sitting (b), and infants with typical development, early sitting (c) and advanced sitting (d). To aid in visual comparison, plotted in grey on all four plots is the average periodogram for all trials of the developmentally delayed, early sitting. Artifacts seen at 30 Hz are due to electrical power distribution, and are not related to infant sitting.

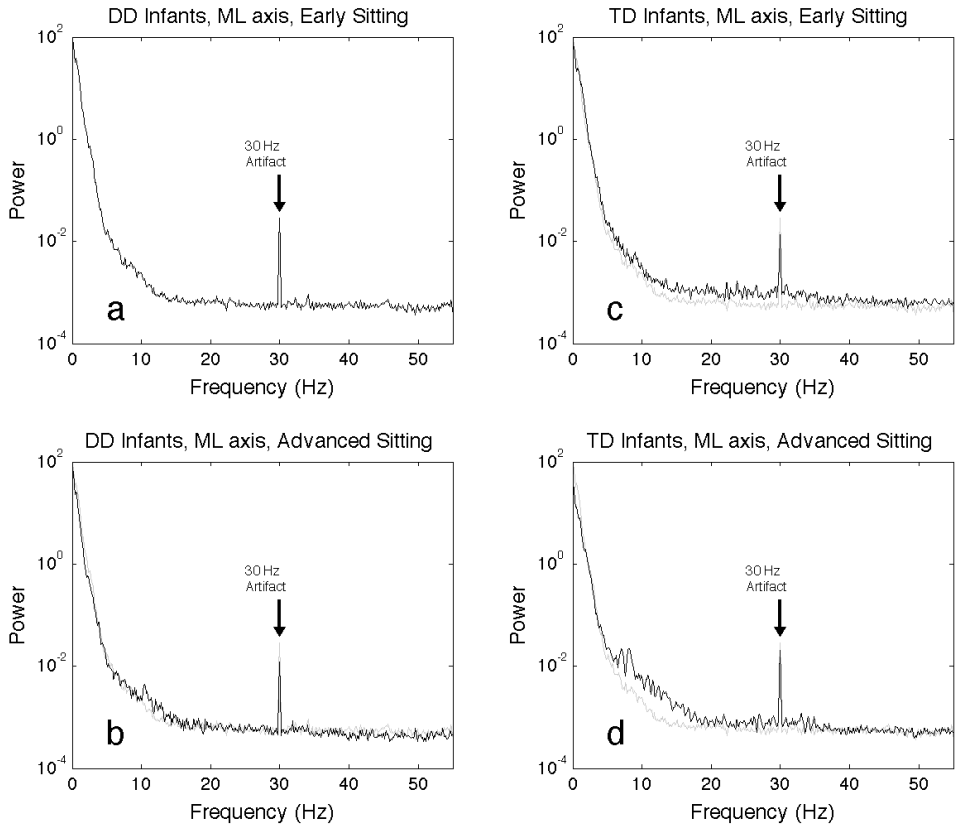

Figure 4.12. Spectral analysis of infant sitting postural sway in the medial-lateral axis. Plotted in black is the average periodogram for all trials for infants with developmental delay, early sitting (a), advanced sitting (b), and infants with typical development, early sitting (c) and advanced sitting (d). To aid in visual comparison, plotted in grey on all four plots is the average periodogram for all trials of the developmentally delayed, early sitting. Artifacts seen at 30 Hz are due to electrical power distribution, and are not related to infant sitting.

CHAPTER 5

NONLINEAR DETRENDED FLUCTUATION ANALYSIS OF SITTING CENTER-OF-PRESSURE DATA AS AN EARLY MEASURE OF MOTOR DEVELOPMENT PATHOLOGY IN INFANTS

Abstract: Upright sitting is one of the first motor skills an infant learns, and thus sitting postural control provides an early window into the infant's motor development. Early identification of infants with motor developmental delay, such as infants with cerebral palsy, allows for early therapeutic intervention by physical therapists. Early intervention is thought to produce better outcomes, due to greater neural plasticity in younger infants. Postural sway, as measured by a force plate, can be used to objectively and quantitatively characterize infant motor control during sitting. Pathology, such as cerebral palsy, may alter the fractal properties of motor function. Often physiologic time series data, including infant sitting postural sway data, is mathematically non-stationary. Detrended Fluctuation Analysis (DFA) is useful to characterize the fractal nature of time series data because it is does not assume stationarity of the data. In this study we found that suitable selection of the order of the detrending function improves the performance of the DFA algorithm, with a higher order polynomial detrending better able to distinguish infant sitting posture time series data from Brown noise (random walk), and first order detrending better able to distinguish infants with motor delay (cerebral palsy) from infants with typical development.

INTRODUCTION

Cerebral palsy is a result of brain injury that occurs early in life, before, during or shortly after birth, and occurs in 1.5 to 2.5 per 1000 live births (Paneth, Hong, & Korzeniewski, 2006). Many areas of the brain can be involved, including the motor cortex, periventricular area, or basal ganglia, which subsequently affects the control of movement (i.e. motor control). The injury may be due to many causes, such as placental lesions and/or umbilical cord obstruction (Redline, 2008), exposure of the mother to certain chemicals during gestation (Kenyon, Brocklehurst, Jones, Marlow, Salt, & Taylor, 2008), and is often associated with premature birth (Hemming, Colver, Hutton, Kurinczuk, & Pharoah, 2008). While the injury occurs early in life, the effects of the injury impact the individual for the rest of their lives (Krakovsky, Huth, Lin, & Levin, 2007). Abnormal movement due to cerebral palsy can result in abnormal bone development sometimes requiring corrective surgery, especially at the hip joint (O'Sullivan, Walsh, Hewart, Jenkinson, Ross, O'Brien, 2006). If the infant does not learn to sit by age 2, there is a good chance that they will never learn to walk (da Paz Junior, Burnett, & Braga, 1994; Fedrizzi, et al., 2000). Physical therapy for these children may be most beneficial if started early in life, when the brain is better able to learn and adapt (Blauw-Hospers, de Graaf-Peters, Dirks, Bos, Hadders-Algra, 2007). A reliable, quantitative measure is needed to assess infant motor control early in infancy to (a) help clinicians identify infants who might benefit from interventions, and (b) help physical therapists assess the effectiveness of the intervention. Current methods of assessment are inadequate (Heineman & Hadders-Algra, 2008).

Upright sitting is one of the first developmental motor milestones that an infant achieves. Attainment of the ability to sit upright is important as it indicates healthy development of the infant, and also because the upright sitting posture will allow the infant to explore the environment from a stable upright posture (Harbourne & Stergiou, 2003). Additionally, sitting is an early indicator of motor development, and identifying infants with motor development delays early in life, when therapeutic intervention may be most effective, is desirable (de Graaf-Peters, Blauw-Hospers, Dirks, Bakker, Bos, & Hadders-Algra, 2007). Thus using sitting posture as a window into an infant's motor control development has the potential to identify infants with motor dysfunction, such as that caused by cerebral palsy, as opposed to a transient motor delay. Identification of this dysfunction early in life when therapy may be most effective has the potential to be a sensitive indicator of progress being made in therapy.

Motor control in infants is typically judged in a clinical setting by observing specific behaviors, such as rolling to the appropriate side if a toy is presented on one side. To quantify motor development, tests such as the Peabody Gross Motor Skill Test (Folio & Fewell, 2000), are used which assign points based on the behaviors that can be elicited by the clinician, such as rolling towards the toy, and comparing with standards for infants of that age. While some of these tests may have high reliability, they are lacking in ability to discriminate between healthy and pathologic infants (Spittle, Doyle, & Boyd, 2008), and thus would likely not be useful in monitoring progress of the infant receiving physical therapy intervention. New tests are being developed to try and improve the results (Heineman, Bos, Hadders-Algra, 2008). Because the standard tests are based on what can be visually observed by the clinician, they require significant training of the

clinician to produce consistent results. Developing a new test with objective measures of motor control that can be administered by an untrained individual has the potential to improve clinical identification of infants who have motor control pathology, such as cerebral palsy, and may be useful in assessing progress in therapy. Additionally, a new test that is based on highly sensitive measurements, coupled with suitable data analysis techniques, may allow sensitivity and selectivity above and beyond what even the best-trained clinician is able to observe visually.

The use of a force plate to objectively measure postural sway is a potentially useful technique to quantify sitting behavior. A force plate is a rigid plate instrumented with force transducers to measure force applied to the plate in all directions. From this data, the center of pressure (COP) can be calculated for both the anterior-posterior (front-to-back) postural sway and the medial-lateral (side-to-side) postural sway, and then stored on a computer for analysis. The COP is the point at which the resultant force vector from the infant's body contacting the force plate intersects the plane of the force plate. Thus the COP is a time series that captures the subtle sway associated with posture control that is not evident visually to an observer. COP analysis has been used to examine standing posture of children with cerebral palsy (Donker, Ledebt, Roerdink, Savelsbergh, & Beek, 2008), making it a logical candidate technique to explore sitting posture of children with cerebral palsy. The force plate can quantify subtle shifts in posture that a human observer would not be able to notice, and add valuable information to the data collected during a movement evaluation. Analysis of force plate data from infant sitting thus has the potential to be increase the accuracy and objectivity of currently available methods for assessment of motor control in young infants. Traditional statistical measures

such as variance, range, etc. can be used to quantify the variability in COP time series data. However, these measures ignore an important feature of time series data, in that the time aspect of the data is ignored. For example, if the time series data were to be randomly shuffled, the variance would be the same. In order to probe the dynamics of the system, a different type of measure is needed. Methods from nonlinear dynamics may provide the sensitivity to motor control system dynamics (Guastello, 2006) that is needed to probe clinically relevant aspects of postural sway in infant sitting (Harbourne & Stergiou, 2003; Stergiou, Harbourne & Cavanaugh, 2006).

Fractal properties of the human neuromuscular system can be seen in electroencephalogram (EEG) recordings of brain waves (Nikulin & Brismar, 2005; Hwa & Ferree, 2002), as well as in recordings of human movement, such as walking gait (Jordan, Challis, & Newell, 2007), running gait (Jordan, Challis, & Newell, 2006), standing posture (Kim, Nussbaum, & Madigan, 2008), and eye movements (Shelhamer, 2005). Fractal properties are an emergent property of the system dynamics, and to the extent that a given pathology disrupts those dynamics, the resulting fractal properties will be altered. For example, the fractal properties of EEG are seen to be altered in Alzheimer's disease (Abasolo, Hornero, Escudero, & Espino, 2008), in stroke (Hwa, He, & Ferree, 2003), and in depression (Lee, Yang, Lee, Choi, Choi, & Kim, 2007). In Huntington's disease, the fractal dynamics of walking gait are found to be altered compared to healthy controls (Hausdorff, Mitchell, Firtion, Peng, Cudkowicz, Wei, & Goldberger, 1997). In searching for a measure of postural sway of infant sitting that we would anticipate would be altered in cerebral palsy, fractal measures are good candidates.

The COP time series from postural control studies are considered to be nonstationary (Carol & Freedman, 1993; Loughlin, Redfern, & Furman, 2003). Nonstationarity in the mathematical sense means that the mean, variance, and/or higher moments are different for different segments of the time series data. Compared to other nonlinear measures, detrended fluctuation analysis (DFA) is thought to be more robust to nonstationarity (Peng, Havlin, Stanley & Goldberger, 1995), and thus might prove to be a useful tool for infant sitting COP data analysis. Traditionally, DFA analysis is performed by repeatedly dividing the time series data into segments of different lengths, and then measuring the average error (sum of the residuals squared divided by segment length) after performing a linear least squares analysis on the data in that segment. A log-log plot is made of the average error versus segment length. The DFA parameter of interest is alpha, the slope of this plot. For a pure random walk alpha is 1.5, and for white noise alpha is 0.5 (Peng, Havlin, Stanley & Goldberger, 1995).

DFA has been applied in a number of studies of medical pathology. For example, DFA has been applied to fetal heart rate to detect pathology (Ferrario, Signorini, & Magenes, 2007) and adult heart rate (Peng, Havlin, Hausdorff, Mietus, Stanley, Goldberger, 1995; Goldberger, Amaral, Hausdorff, Ivanov, Peng, & Stanley, 2002). DFA has also been used to characterize gender and aging effects on respiration (Peng, Mietus, Liu, Lee, Hausdorff, Stanley, Goldberger, & Lipsitz, 2002) and analysis of brain activity from fMRI data (Lee, Hu, Gao, Crosson, Peck, Wierenga, McGregor, Zhao, & White 2008; Hu, Lee, Gao, White, & Crosson, 2008). One of the first applications to motor control time series analysis was the investigation of long-range correlations in stride interval in unperturbed walking (Hausdorff, Peng, Ladin, Wei, & Goldberger, 1995).

Other motor control applications of DFA include finger tapping at different speeds (Kadota, Kudo, & Ohtsuki, 2004), gait with development and aging (Hausdorff, Ashkenazy, Peng, Ivanov, Stanley, & Goldberger, 2001), gait with metronome beat (Hausdorff, Purdon, Peng, Ladin, Wei, & Goldberger,1996), gait at different speeds (Hausdorff, Purdon, Peng, Ladin, Wei, & Goldberger,1996; Jordan, Challis, Newell, 2007), and gait in Huntington's disease (Hausdorff, Mitchell, Firtion, Peng, Cudkowicz, Wei, & Goldberger, 1997). Thus DFA has wide-ranging applications in the medical sciences, due at least in part to its applicability to analysis of non-stationary time series. DFA has been found to be a relatively reliable measure of adult standing COP (Lin, Seol, Nussbaum, & Madigan, 2008). DFA analysis of standing posture in elderly may be useful in identifying individuals who are at risk of injury from falling (Amoud, Abadi, Hewson, Michel-Pellegrino, Doussot, & Duchene, 2007). DFA analysis of infant sitting postural sway data has not yet been reported.

Because DFA is an analysis of the goodness of fit of a linear polynomial, or more accurately the "badness" of fit since it is the residuals of the fit that are used in the calculation, any linear trend due to nonstationarity will be removed. Thus DFA is thought to be robust to nonstationarity. However, there is no reason to believe that the nonstationarity will be linear. In fact, given the prevalence of nonlinear processes in physiologic control systems (Mackey & Glass, 1977), including human motor control (Guastello, 2006; Schoner & Kelso, 1988), it would instead be surprising if the nonstationarity were found to be linear. Nonlinear DFA can be performed, which involves using higher order polynomials to perform the detrending (Hu, Ivanov, Chen, Carpena, & Stanley, 2001; Munoz-Diosdado & del Rio Correa, 2006). In this paper, we

investigated the use of nonlinear DFA as a method to quantify clinically relevant features from COP data from infant sitting. In order to determine if the nonlinear DFA is capturing clinically relevant information, we compared data from two sets of infants, one with typical development, and the other with delayed development, where the delay in development is likely due to cerebral palsy. We hypothesized that DFA will be able to detect a difference between the two groups of infants, and that the dynamics of infant sitting will be significantly different from Brown noise.

EXPERIMENTAL METHODS AND DATA ANALYSIS

Subjects

Infants were recruited into the study when they were just developing the ability to sit upright. Recruitment was done through newsletters, flyers, and pediatric physical therapists employed at the University. Subjects included 18 developmentally delayed infants, with an average age of 13.22 months (std = 2.96); and 23 typically developing infants, with an average age of 5.08 months (std = 0.68). Infants in the developmentally delayed group were diagnosed with cerebral palsy, or else were developmentally delayed and at risk for cerebral palsy. Some of the infants in this group may not actually have cerebral palsy because definitive diagnosis at this age is difficult. At risk infants met one or more of the following conditions: premature delivery, brain bleeding (of any level of severity), diagnosis of periventricular leukomalacia, or significantly delayed gross motor development as measured on standardized testing. While a definitive diagnosis of cerebral palsy had not been made, these infants were all developmentally delayed, and all scored below 1.5 standard deviations below the mean for their corrected age on the

Peabody Gross Motor Scale (Folio & Fewell, 2000). Thus it is possible that a small number of these infants did not have cerebral palsy, and that the developmental delay is due to another cause, such as early medical problems. Exclusion criteria included having an untreated, diagnosed visual impairment, a diagnosed hip dislocation or subluxation greater than 50%, or an age outside the range of 5 months to two years. Typically developing infants were screened for normal development by a physical therapist prior to admission into the study, being excluded if they failed to score above 0.5 standard deviations below the mean on the Peabody Gross Motor Scale, had a diagnosed visual impairment, a diagnosed musculoskeletal problem, or were older than five months at the start of the study. A consent form was signed by a parent/caregiver of all infant participants, and all procedures were approved by the University of Nebraska Medical Center Institutional Review Board.

Data Collection Methods

For data acquisition, infants were seated on an AMTI force plate (Watertown, MA), interfaced to a computer system running Vicon data acquisition software (Lake Forest, CA). COP data were acquired through the Vicon software at 240 Hz, in order to be above a factor of ten higher than the highest frequency that might contain relevant signal. Trunk and pelvis markers were also placed on the infant, but the marker data was not analyzed for this study. An assistant sat to the left side of the infant during data acquisition, and a parent or relative (typically the mother) sat in front of the infant, for comfort and support, as well as to keep the attention of the infants focused on toys held in front of them.

Trials were recorded including force plate and video data from the back and side views. Afterwards segments were selected by viewing the corresponding video. Segments of data with 2000 time steps (8.3 seconds at 240 Hz) were selected from these trials by examination of the video. Acceptable segments were required to (a) have no crying or long vocalization, (b) no extraneous items (e.g. toys) on the force platform, (c) neither the assistant nor the mother were touching the infant, (d) the infant was not engaged in rhythmic behavior (e.g. flapping arms), and (e) the infant had to be sitting and could not be in the process of falling. Both anterior-posterior (front-to-back) and medial-lateral (side-to-side) center of pressure data was used for the analysis.

Data Analysis Methods

COP data was analyzed using custom software developed using MatLab (Nantick, MA). The 2000 time step data was analyzed as is, then divided into sub-segments, first into two segments each half the length of the time series, then into four segments each one quarter the length of the time series, etc., until segments were no shorter than eight time steps (0.0333 sec). Each sub-segment was fit with a polynomial (Figure 5.1), and then F was calculated as the average of the absolute values of the residuals. Alpha is the slope of least squares fit from a log-log plot of F versus segment length. This procedure was repeated four times, first for a first order polynomial, then for a second order, then a third order polynomial and finally, for a fourth order polynomial (Munoz-Diosdado & del Rio Correa, 2006).

One way to calculate the DFA alpha value is to perform a least-square fit to the log F versus log n plot, and this was one of the two methods we used. For very small

window sizes, the slope of the log-log plot of F versus window size is sampling the dynamics of the system on short time scales, and thus is likely contaminated by experimental noise. For very long window sizes, the slope of the log-log plot of F versus window size is altered because the window size is on the order of the length of the data time series. Thus a plot of experimentally acquired log-log plot of F versus window size may not be linear at very high and/or very low values of n. One approach to calculating a slope from this non-linear relationship is to restrict the window size to some arbitrary range of lengths that includes the region in the center that appears to be linear. We used a somewhat different approach which we felt was more objective. We fit the log-log plot of F versus window size to a third order polynomial, because a third order polynomial allows for two inflection points that would allow the curve to fit the two expected bends in the curve, one at short window sizes, and the other at long window sizes. We then analytically calculated the slope of the polynomial, evaluating the derivative at the middle of the window size range.

Fit of ln(F) versus ln(n): $y= ax^3 + bx^2 + cx +d$

Slope (DFA alpha): $dy/dx = 3ax^2 + 2bx +c$; evaluated at $x= n_{middle}$

This appears to give a better estimate of the slope for some trials where the log-log plot of F versus window size was not linear (Figure 5.2).

In order to compare the infant sitting data to results from Brown noise, DFA was performed on 25 trials of pseudo-data. The “randn” function in MatLab was used to generate Gaussian white noise time series the same length as the infant sitting COP data (2000 time steps), which was then integrated with the “cumsum” function to create Brown noise. DFA was performed using the same methodology described for the infant

sitting COP data. These results were compared to DFA results for infants sitting, to test whether time series from infant sitting is different than Brown noise.

Statistical Methods

Independent t-tests were used to compare the DFA alpha values from COP data for infants with typical development with DFA alpha values from COP data for infants with delayed development. Independent t-tests were also performed to compare DFA alpha values from infant sitting with brown noise, both for infants with typical development and infants with delayed development. A significance level of $\alpha < 0.001$ was used to make comparisons (note the statistical alpha is a different concept from the DFA alpha). There were 48 t-tests performed, and by correcting for multiple comparisons the α level was set to .001 (.05/48 = .001).

RESULTS

DFA alpha values for COP data from medial-lateral postural sway from sitting infants (Table 5.1), and for COP data from anterior-posterior postural sway (Table 5.2), were not too far off of the value of 1.5 with first order detrending, which would be expected for Brownian noise. Use of our analysis algorithm on computer generated Brown noise results in values very near the theoretically expected result of 1.5 (Table 5.3). However, t-tests showed that there are significant differences between infant sitting postural sway and Brown noise, especially for higher order detrending (Tables 5.4 and 5.5). Note that an analysis performed only with the standard method of first order detrending would have concluded that postural sway for the medial-lateral axis is not

significantly different than Brown noise, but the higher order detrending found a significant difference (Table 5.4). In the case of anterior-posterior postural sway (Table 5.5), using only the standard linear detrending would have lead to the conclusion that postural sway of the infants with delayed development/cerebral palsy was not significantly different than Brown noise, whereas postural sway of those with typical development was found to be significantly different than Brown noise. The analysis with higher order detrending found that both populations have postural sway significantly different than Brown noise.

The method of evaluating the first derivative of the plot of ln(F) versus ln(n) at the center, rather than simply evaluating the slope of a linear fit to all the data, did not have a significant impact in comparison of the DFA alpha values for medial-lateral postural sway (Table 5.4, compare asterisks indicating significant differences in top and bottom sections of the table). However, it did have an impact in comparison to the DFA alpha values for postural sway in the anterior-posterior axis (Table 5.5), where the difference between Brown noise and postural sway for typical developing infants is significant for third and fourth order detrending. This was evident using the derivative method for evaluating slope, but not for the slope of the linear fit. Thus, we believe this method to be somewhat superior, and we have used results from this method in creating Figure 5.3.

One goal of this work was to distinguish between infants with typical development and infants with delayed development, where the developmental delay was likely due to cerebral palsy. DFA alpha values for sitting COP from infants with delayed development are compared to DFA alpha values for sitting COP from infants with typical

development for the anterior-posterior axis, and are found to be significantly different for first and second order polynomials, but only in the anterior-posterior axis (Table 5.5). The analysis of Brown noise was relatively insensitive to the order of the polynomial used for detrending, compared to the infant sitting COP. For Brown noise, the DFA alpha value is close to 1.5 regardless of the order of the polynomial used for detrending (Figure 5.3 and Table 5.3). For infant sitting COP data in the medial-lateral direction (Figure 5.3a), the DFA alpha values were similar for infants with typical development and infants with delayed development, regardless of the order of the polynomial used for detrending. However, for infant sitting COP data in the anterior-posterior direction (Figure 5.3b), the separation was least when the forth order polynomial was used for detrending, with a first order polynomial giving the best separation ($p = 0.0004$; Table 5.5).

DISCUSSION

The theoretical DFA alpha value from Brown noise is 1.5 (Peng, Havlin, Stanley & Goldberger, 1995) and the algorithm we used reproduced this result. Postural sway time series data visually appeared very similar to Brown noise, and the results of this study agreed with other published DFA results for adult standing where DFA results for postural sway were similar to Brown noise with linear (i.e. first order) detrending. Amound et al. (2007) used the DFA algorithm with linear detrending to evaluate postural sway from elderly and young adults. However, they subtracted 1 from the DFA alpha values that they report. Taking their reported values and adding back 1 to compare with our values, we get DFA alpha values in the range of 1.25 to 1.55. This range compares well to the results that we found for infant sitting of 1.22 to 1.52, with the DFA alpha

values calculated using linear detrending. In another study of adult standing, Kim, Nussbaum, and Madigan (2008) reported DFA alpha values between 1.31 and 1.48, also within the range of our results. Thus our results are in good agreement with both theoretical values and experimental values for adult standing from the literature. DFA alpha values for infants sitting have not been reported.

DFA is considered a measure of the fractal properties of a time series because the scaling behavior is probed by using different segment lengths of the data. Brown noise is integrated white noise, and thus the value at one point in time affects values at other points in time –i.e. long range correlations. While white noise has no long range correlations and a correspondingly low DFA alpha value of 0.5, Brown noise has a higher value of 1.5 (Peng, Havlin, Stanley & Goldberger, 1995). One way to interpret the results is in terms of long range correlations, as has been done in DNA sequences (Peng, Buldyrev, Havlin, Simons, Stanley, & Goldberger, 1993) and heart rate analysis (Peng, Havlin, Stanley & Goldberger, 1995). DFA results from gait data have also been interpreted as being descriptive of long range correlations (Hausdorff, Purdon, Peng, Ladin, Wei, & Goldberger, 1996). By examining the DFA alpha values calculated with the linear detrending, as it has been done in other studies, we found that infants with typical development have less long-range correlations (lower alpha values) than do infants with developmental delay/cerebral palsy, for postural sway in the anterior-posterior direction. Pink noise (e.g. $1/f^1$) is intermediate between white noise ($1/f^0$) and Brown noise ($1/f^2$), and has a DFA alpha value between that of white noise and Brown noise. Pink noise dynamics has been associated with healthy dynamics, as opposed to pathologic dynamics (Goldberger, Amaral , Hausdorff, Ivanov, Peng, & Stanley, 2002).

This is consistent with our findings that pathologic infant sitting was not statistically different from Brown noise using DFA analysis with linear detrending, whereas typically developing infants were closer to pink noise.

However, this interpretation should be treated with caution. Interpretation of DFA results in terms of the presence or absence of long range correlations may not be straight forward in all cases, due to limited length of the time series data (Maraun, Rust, & Timmer, 2004). One weakness of this study is the time series of 2000 time steps is only 8.3 seconds. This is a practical limitation of working with infants who may not be willing or able to sit for longer data acquisitions. Postural control mechanisms that operate with characteristic time scales longer than 8.3 seconds will not be found in our analysis. Importantly, we found that DFA analysis using higher order polynomial detrending, rather than linear detrending, resulted in significant differences between Brown noise and postural sway of both the infants with typical development and the infants with delayed development/cerebral palsy. In fact, the infant sitting postural sway was quite different from Brown noise, both for infants with typical development and infants with delayed development. The variance of Brown noise increases with increasing length of the time series without bound. The variance of postural sway cannot increase without bounds, because the result would be a fall. Thus one would expect to find differences between postural sway data and Brown noise, and the fact that detrending with higher order polynomials was sensitive to that difference shows the strength of this technique. Any analysis technique that cannot distinguish between infant sitting postural sway and Brown noise is lacking sensitivity to a fundamental aspect of motor control. A significant result of this study is that detrending with polynomials of different orders

when performing DFA analysis can provide additional insight that the linear detrending by itself can not provide.

Another way to interpret these results is to note that the detrending was reported to remove nonstationarity (Peng, Havlin, Stanley, & Goldberger, 1995), and thus one could describe the infants with delayed development/cerebral palsy as having different characteristics of the nonstationarity, as compared to infants with typical development. Often nonstationarity is conceived of as a drift in the measurement over time that is not part of the system dynamics that one is attempting to characterize. However, there was not a drift in the experimental apparatus giving rise to nonstationarity in these results. Any "nonstationarity" that the detrending is removing, is a biological nonstationarity. It was influencing the infant's motor control system, or was part of the motor control system, and thus may have been affected by the underlying pathology in the motor control system. For example, we may speculate that the infant's attention may shift from one object to another, impacting motor function, and this shifting of attention may be different between the two populations. A cognitive task has been shown to influence posture control in adults and even more so in younger children (Reilly, van Donkelaar, Saavedra, Woollacott, 2008). An interesting topic for future research is the impact of cognitive function on infant motor control. The use of polynomials of different order for detrending has discovered interesting differences in the system dynamics of infants sitting, but further work is necessary to fully interpret the results.

One goal of this work was to develop a clinically useful methodology to objectively distinguish between infants with cerebral palsy and infants who are unaffected. We would like to develop a methodology that is sensitive enough to provide

early identification of infants with cerebral palsy, and to assist physical therapists with evaluation of the effectiveness of specific interventions. Here we have reported that DFA has shown statistically significant differences between the two populations that we analyzed. However, the differences between the two populations are not wide enough to be used for clinical identification of pathology. In other words, there is quite a bit of overlap between the DFA alpha values for the two populations studied. Future work will include other data analysis methods capable of probing nonlinear dynamics of infant sitting, as well as the application of more sophisticated classification methods based on the results of multiple data analysis methods.

In summary, this work has demonstrated that DFA analysis of infant sitting postural sway is sensitive to differences in developmental delay. A major finding was that the use of higher order polynomials for the detrending step in the DFA algorithm helps to distinguish infant sitting posture COP from Brown noise. Another major finding was that DFA analysis using the standard linear detrending method is the most sensitive to differences between sitting postural sway of infants with delayed development/cerebral palsy as compared to infants with typical development. Future work is needed to increase the sensitivity, specificity, and reliability of the measures used for analysis of postural control, in order to make this approach clinically useful for identification of infants with developmental delay, and for characterization of effectiveness of therapeutic interventions.

REFERENCES

Abasolo, D., Hornero, R., Escudero, J., & Espino, P. (2008). A study on the possible usefulness of detrended fluctuation analysis of the electroencephalogram background activity in Alzheimer's disease. IEEE Transactions on Bio-medical Engineering, 55, 2171-2179.

Amoud, H., Abadi, M., Hewson, D.J., Michel-Pellegrino, V., Doussot, M., & Duchêne, J. (2007). Fractal time series analysis of postural stability in elderly and control subjects. Journal of Neuroengineering and Rehabilitation, 4, 12.

Blauw-Hospers, C.H., de Graaf-Peters, V.B., Dirks, T., Bos, A.F., & Hadders-Algra, M. (2007). Does early intervention in infants at high risk for a developmental motor disorder improve motor and cognitive development? Neuroscience and Biobehavioral Reviews, 31, 1201-1212.

Carroll, J.P., & Freedman, W. (1993). Nonstationarity properties of postural sway, Journal of Biomechanics, 26, 409-416.

da Paz Junior, A.C., Burnett, S.M., & Braga, L.W. (1994). Walking prognosis in cerebral palsy: a 22-year retrospective analysis. Developmental Medicine and Child Neurology, 36, 130-134.

de Graaf-Peters, V.B., Blauw-Hospers, C.H., Dirks, T., Bakker, H., Bos, A.F., & Hadders-Algra, M. (2008). Development of postural control in typically developing children and children with cerebral palsy: Possibilities for intervention? Neuroscience and Biobehavioral Reviews, 31, 1191-1200.

Donker, S.F., Ledebt, A., Roerdink, M., Savelsbergh, G.J., & Beek, P.J. (2008). Children with cerebral palsy exhibit greater and more regular postural sway than typically

developing children. Experimental Brain Research, 184, 363-70.

Fedrizzi, E., Facchin, P., Marzaroli, M., Pagliano, E., Botteon, G., Percivalle, L., & Fazzi, E. (2000). Predictors of independent walking in children with spastic diplegia. Journal of Child Neurology, 15, 228-234.

Ferrario, M., Signorini, M.G., & Magenes, G. (2007). Estimation of long-term correlations from fetal heart rate variability signal for the identification of pathological fetuses. Conference Proceedings of the IEEE Engineering in Medicine and Biology Society, 2007, 295-298.

Folio, M.R. & Fewell, R.R.(2000). Peabody Developmental Motor Scales (2nd ed.). Austin, TX : Pro-ed, Inc.

Goldberger, A.L., Amaral, L.A.N., Hausdorff, J.M., Ivanov, P.C., Peng, C.-K., & Stanley, H.E. (2002). Fractal dynamics in physiology: Alterations with disease and aging. Proceedings of the National Academy of Sciences of the United States of America, 99, 2466-2472.

Guastello, S.J. (2006). Motor control research requires nonlinear dynamics. American Psychologist, 61, 77-78.

Harbourne, R.T. & Stergiou, N. (2003). Nonlinear analysis of the development of sitting postural control. Developmental Psychobiology, 42, 368-77.

Hausdorff, J.M., Ashkenazy, Y., Peng, C.K., Ivanov, P.C., Stanley, H.E., Goldberger, A.L. (2001). When human walking becomes random walking: fractal analysis and modeling of gait rhythm fluctuations. Physica A, 302, 138-47.

Hausdorff, J.M., Mitchell, S.L., Firtion, R., Peng, C.-K., Cudkowicz, M.E., Wei, J.Y., & Goldberger, A.L. (1997). Altered fractal dynamics of gait: reduced stride-interval

correlations with aging and Huntington's disease. Journal of Applied Physiology, 82, 262-269.

Hausdorff, J.M., Peng, C.K., Ladin, Z., Wei, J.Y., & Goldberger, A.L. (1995) Is walking a random walk? Evidence for long-range correlations in stride interval of human gait. Journal of Applied Physiology, 78, 349-58.

Hausdorff, J.M., Purdon, P.L., Peng, C.-K., Ladin, Z., Wei, J.Y., & Goldberger, A.L. (1996). Fractal dynamics of human gait: stability of long-range correlations in stride interval fluctuations. Journal of Applied Physiology, 80,1448-1457.

Heineman, K.R., Bos, A.F., & Hadders-Algra, M. (2008). The Infant Motor Profile: a standardized and qualitative method to assess motor behaviour in infancy. Developmental Medicine and Child Neurology, 50, 275-282.

Heineman, K.R. & Hadders-Algra, M. (2008). Evaluation of neuromotor function in infancy-A systematic review of available methods. Journal of Developmental and Behavioral Pediatrics, 29, 315-323.

Hemming, K., Colver, A., Hutton, J.L., Kurinczuk, J.J., & Pharoah, P.O. (2008). The influence of gestational age on severity of impairment in spastic cerebral palsy. Journal of Pediatrics, 153, 203-8.

Hu, J., Lee, J.M., Gao, J., White, K.D., & Crosson, B. (2008). Assessing a signal model and identifying brain activity from fMRI data by a detrending-based fractal analysis. Brain Structure and Function, 212, 417-26.

Hu, K., Ivanov, P.C., Chen, Z., Carpena, P., & Stanley, H.E. (2001). Effect of trends on detrended fluctuation analysis. Physical Review, E. Statistical, Nonlinear and Soft Matter Physics, 64, 011114.

Hwa, R.C. & Ferree, T.C. (2002). Scaling properties of fluctuations in the human electroencephalogram. Physical Review E, 66, 021901.

Hwa, R.C., He, W., & Ferree, T.C. (2003). The global effects of stroke on the human electroencephalogram. Journal of Integrative Neuroscience, 2, 45-53.

Jordan, K., Challis, J.H., & Newell, K.M. (2006). Long range correlations in the stride interval of running. Gait and Posture, 24, 120-125.

Jordan, K., Challis, J.H., & Newell, K.M. (2007). Walking speed influences on gait cycle variability. Gait and Posture, 26, 128-34.

Kadota, H., Kudo, K., & Ohtsuki, T. (2004). Time-series pattern changes related to movement rate in synchronized human tapping. Neuroscience Letters, 370, 97-101.

Kenyon, S., Brocklehurst, P. Jones, D., Marlow, N., Salt, A. & Taylor, D. (2008). MRC ORACLE Children Study. Long term outcomes following prescription of antibiotics to pregnant women with either spontaneous preterm labour or preterm rupture of the membranes. BMC Pregnancy and Childbirth, 8, 14.

Kim, S., Nussbaum, M.A., & Madigan, M.L. (2008). Direct parameterization of postural stability during quiet upright stance: Effects of age and altered sensory conditions. Journal of Biomechanics, 41, 406-411.

Krakovsky, G., Huth, M.M., Lin, L., & Levin, R.S. (2007). Functional changes in children, adolescents, and young adults with cerebral palsy. Research in Developmental Disabilities, 2, 331-340.

Lee, J.M., Hu, J., Gao, J., Crosson, B., Peck, K.K., Wierenga, C.E., McGregor, K., Zhao, Q., & White, K.D., (2008). Discriminating brain activity from task-related artifacts in

functional MRI: Fractal scaling analysis simulation and application. Neuroimage, 40, 197- 212.

Lee, J.S., Yang, B.H., Lee, J.H., Choi, J.H., Choi, I.G., & Kim, S.B. (2007). Detrended fluctuation analysis of resting EEG in depressed outpatients and healthy controls. Clinical Neurophysiology, 118, 2489-2496.

Lin, D., Seol, H., Nussbaum, M.A., Madigan, M.L. (2008). Reliability of COP-based postural sway measures and age-related differences. Gait and Posture, 28, 337-342.

Loughlin, P.J., Redfern, M.S., & Furman, J.M. (2003). Nonstationarities of postural sway. IEEE Engineering in Medicine and Biology Magazine, 22, 69-75.

Mackey, M.C. & Glass, L. (1977). Oscillation and chaos in physiological control systems. Science. 197, 287-289.

Maraun, D., Rust, H.W., & Timmer, J. (2004). Tempting long-memory – on the interpretation of DFA results. Nonlinear Processes in Geophysics, 11, 495-503.

Munoz-Diosdado, A. & del Rio Correa, J.L. (2006). Analysis of crossovers in the interbeat sequences of elderly individuals and heart failure patients. Medical Physics: Ninth Mexican Symposium on Medical Physics, 854, 215-217.

Nikulin, V.V. & Brismar, T. (2005). Long-range temporal correlations in electroencephalographic oscillations: Relation to topography, frequency band, age and gender. Neuroscience, 130, 549-558.

O'Sullivan, R., Walsh, M., Hewart, P., Jenkinson, A., Ross, L.A., & O'Brien, T. (2006). Factors associated with internal hip rotation gait in patients with cerebral palsy. Journal of Pediatric Orthopedics, 26, 537-541.

Paneth, N., Hong, T., & Korzeniewski, S. (2006). The descriptive epidemiology of cerebral palsy. Clinics in Perinatology, 33, 251-267.

Peng, C.-K., Mietus, J.E., Liu, Y., Lee, C., Hausdorff, J.M., Stanley, H.E., Goldberger, A.L., & Lipsitz, L.A. (2002). Quantifying fractal dynamics of human respiration: age and gender effects. Annals of Biomedical Engineering, 30, 683-692.

Peng, C.K., Buldyrev, S.V., Havlin, S., Simons, M., Stanley, H.E., & Goldberger, A.L. (1994). Mosaic organization of DNA nucleotides. Physical Review, E., 49, 1685-1689.

Peng, C.K., Havlin, S., Hausdorff, J.M., Mietus, J.E., Stanley, H.E., & Goldberger, A.L. (1995). Fractal mechanisms and heart rate dynamics. Long-range correlations and their breakdown with disease. Journal of Electrocardiology, 28 Suppl, 59-65.

Peng, C.K., Havlin, S., Stanley, H.E., & Goldberger, A.L. (1995).Quantification of scaling exponents and crossover phenomena in nonstationary heartbeat time series. Chaos, 5, 82-87.

Redline, R. (2008). Cerebral palsy in term infants: a clinicopathologic analysis of 158 medicolegal case reviews. Pediatric and Developmental Pathology, 10, 1.

Reilly, D.S., van Donkelaar, P., Saavedra, S., Woollacott, M.H. (2008). Interaction between the development of postural control and the executive function of attention. Journal of Motor Behavior, 40, 90-102.

Schoner, G. & Kelso, J.A. (1988). Dynamic pattern generation in behavioral and neural systems. Science, 239, 1513-1520.

Shelhamer, M. (2005). Sequences of predictive eye movements form a fractional Brownian series--implications for self-organized criticality in the oculomotor system. Biological Cybernetics, 93, 43-53.

Spittle, A.J., Doyle, L.W., Boyd, R.N. (2008). A systematic review of the clinimetric properties of neuromotor assessments for preterm infants during the first year of life. Developmental Medicine and Child Neurology, 50, 254-266.

Stergiou, N., Harbourne, R.T., & Cavanaugh, J.T. (2006). Optimal Movement Variability: A New Theoretical Perspective for Neurologic Physical Therapy. Journal of Neurological Physical Therapy, 30, 120-129.

Table 5.1. Alpha values for DFA analysis of infant sitting postural sway along the medial-lateral axis.

	Polynomial Order			
	1	2	3	4
DFA alpha values calculated from linear fit of ln(F) vs. ln(n)				
Typical Development (n=23)				
Mean	1.44	1.62	1.65	1.62
Standard Deviation	0.09	0.15	0.15	0.15
Delayed Development/Cerebral Palsy (n=18)				
Mean	1.47	1.66	1.69	1.65
Standard Deviation	0.11	0.16	0.18	0.17
DFA alpha values calculated from center of ln(F) vs. ln(n)				
Typical Development (n=23)				
Mean	1.42	1.95	2.19	2.24
Standard Deviation	0.18	0.25	0.25	0.25
Delayed Development/Cerebral Palsy (n=18)				
Mean	1.53	2.04	2.27	2.30
Standard Deviation	0.18	0.25	0.28	0.29

Table 5.2. Alpha values for DFA analysis of infant sitting postural sway along the anterior-posterior axis.

	Polynomial Order			
	1	2	3	4
DFA alpha values calculated from linear fit of ln(F) vs. ln(n)				
Typical Development (n=23)				
Mean	1.33	1.50	1.57	1.58
Standard Deviation	0.15	0.17	0.16	0.15
Delayed Development/Cerebral Palsy (n=18)				
Mean	1.47	1.64	1.67	1.64
Standard Deviation	0.12	0.14	0.18	0.20
DFA alpha values calculated from center of ln(F) vs. ln(n)				
Typical Development (n=23)				
Mean	1.22	1.59	1.89	2.08
Standard Deviation	0.23	0.32	0.33	0.33
Delayed Development/Cerebral Palsy (n=18)				
Mean	1.47	1.88	2.08	2.16
Standard Deviation	0.19	0.22	0.22	0.27

Table 5.3. Alpha values for DFA analysis of computer generated (synthetic) Brown noise.

	Polynomial Order			
	1	2	3	4
DFA alpha values calculated from linear fit of ln(F) vs. ln(n)				
Brown Noise (n=25)				
Mean	1.50	1.49	1.48	1.48
Standard Deviation	0.10	0.07	0.07	0.06
DFA alpha values calculated from center of ln(F) vs. ln(n)				
Brown Noise (n=25)				
Mean	1.52	1.52	1.47	1.48
Standard Deviation	0.13	0.12	0.13	0.10

Table 5.4. Results of independent t-tests comparing DFA alpha values for postural sway along the medial-lateral axis.

	Polynomial Order			
	1	2	3	4
Results using DFA alpha calculated from linear fit of ln(F) vs. ln(n)				
TD vs CP	-1.06	-0.87	-0.91	-0.57
Brown vs TD	2.10	-3.62*	-4.99*	-4.39*
Brown vs CP	1.70	-4.24*	-4.29*	-3.33
Results using DFA alpha calculated from center of ln(F) vs. ln(n)				
TD vs CP	-1.89	-1.17	-1.03	-0.72
Brown vs TD	2.49	-6.90*	-12.22*	-13.15*
Brown vs CP	-0.53	-7.95*	-10.78*	-11.13*

Note. *p < .001

Table 5.5. Results of independent t-tests comparing DFA alpha values for postural sway along the anterior-posterior axis.

	Polynomial Order			
	1	2	3	4
Results using DFA alpha calculated from linear fit of ln(F) vs. ln(n)				
TD vs CP	-3.27	-2.76	-1.82	-1.19
Brown vs TD	4.63*	-0.30	-2.63	-2.90
Brown vs CP 1	0.67	-4.14*	-3.81*	-2.95
Results using DFA alpha calculated from center of ln(F) vs. ln(n)				
TD vs CP	-3.85*	-3.26	-2.09	-0.85
Brown vs TD	5.86*	-0.73	-5.59*	-8.09*
Brown vs CP	0.51	-5.95*	-9.79*	-9.80*

Note. * $p < .001$

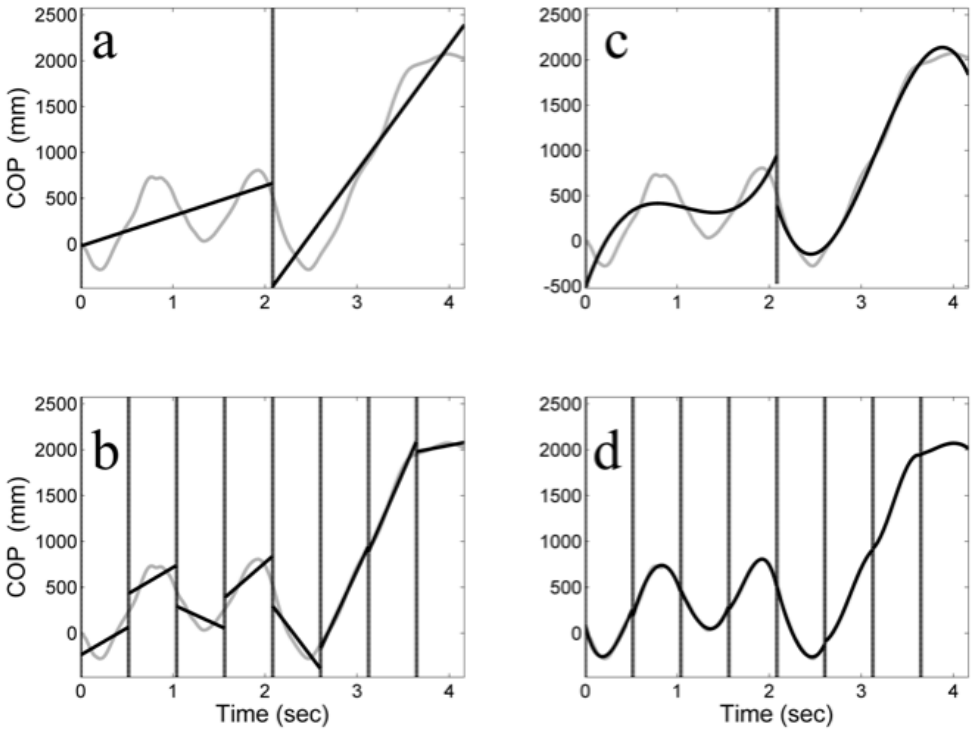

Figure 5.1. Plot of cumulative COP versus time, with first order fit (linear) fit (left side, a and b) and third order polynomial (cubic) fit (right side, c and d). Top panels (a and c) show a long window size, bottom panels (b and d) show a shorter window size. Windows are indicated by the vertical dashed lines, cumulative COP data in grey lines, and black lines indicate the fit to the data.

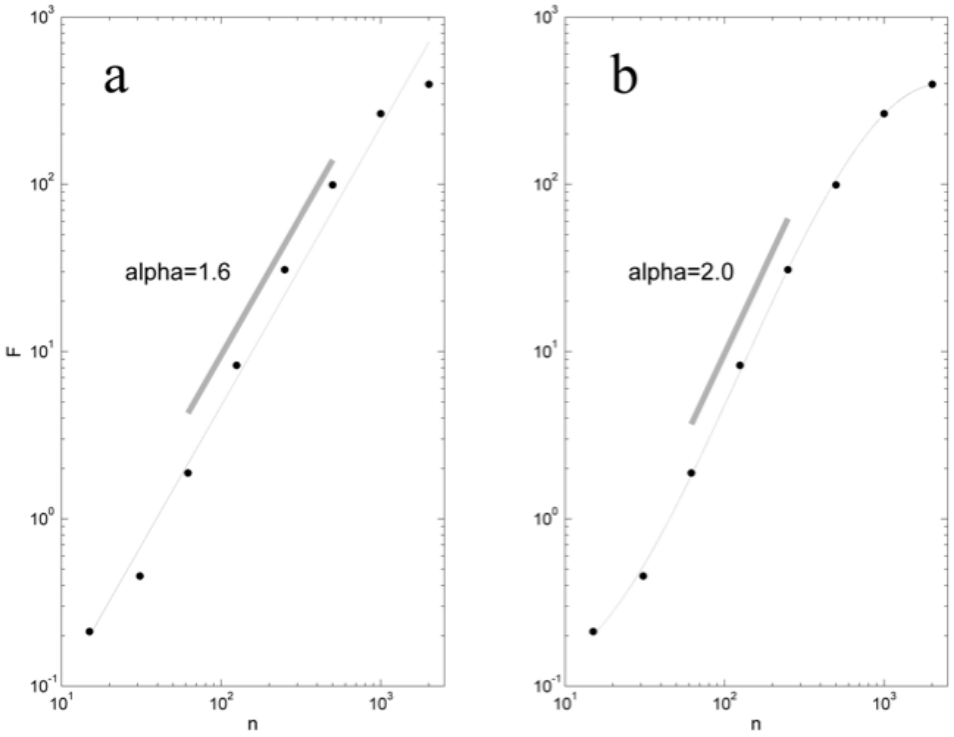

Figure 5.2. Plot of log mean error F(n) versus log window size (n). A linear fit (left) gives a lower slope than the derivative of a third order polynomial fit evaluated at the at the center (right). The slope of the F versus n plot is the DFA alpha value.

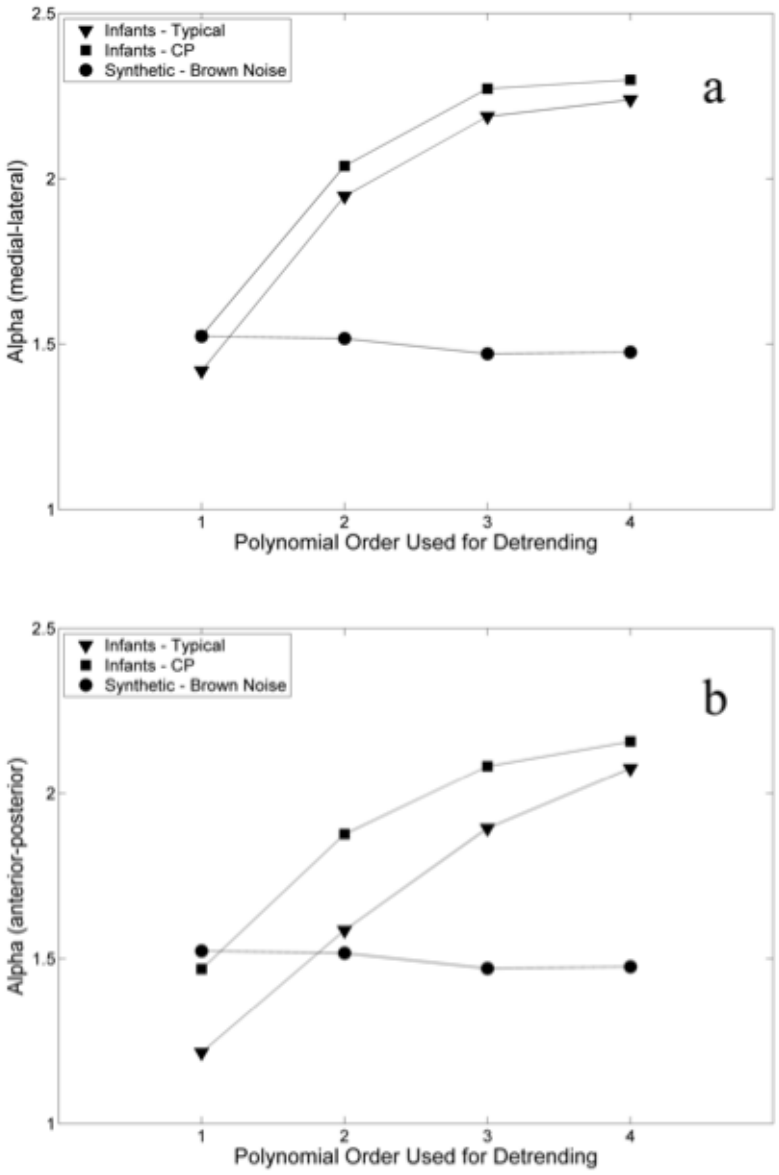

Figure 5.3. DFA alpha values from slope evaluated at the center of the F versus n plot. DFA was performed on COP data from infant sitting, for infants with typical development (triangles), infants with delayed development and at risk for cerebral palsy (squares), and synthetic Brown noise generated by integrating computer generated Gaussian-distributed white noise (circles). Top plot (a) shows medial-lateral results, bottom plot (b) shows anterior-posterior results.

CHAPTER 6

SENSORY INFORMATION UTILIZATION AND TIME DELAYS CHARACTERIZE MOTOR DEVELOPMENTAL PATHOLOGY IN INFANT SITTING POSTURAL CONTROL

Abstract:

Sitting is one of the first developmental milestones that an infant achieves. Thus measurements of sitting posture present an opportunity to assess sensorimotor development at a young age, in order to identify infants who might benefit from therapeutic intervention, and to monitor the efficacy of the intervention. Sitting postural sway data was collected using a force plate, and the data was used to train a neural network controller of a model of sitting posture. The network was trained with data from infants with cerebral palsy, and data from infants without cerebral palsy, both for early sitting (as soon as they could sit for about 10 sec), and late sitting (a few months later). The trained networks were then probed for sensitivity to position, velocity, and acceleration information. Late sitting for infants with typical development had a higher reliance on velocity information in control in the anterior-posterior axis, and utilized more types of information in control in the medial-lateral axis, perhaps indicative of lower stability along the medial-lateral axis. The use of velocity information for control in the anterior-posterior direction may emerge independently in both typical infant sitting and in typical adult standing, as an efficient means of control for those particular postures, given the anatomical and physiological constraints of each of those systems.

Infants with delayed development, where the developmental delay is due to cerebral palsy for most of the infants in the study, did not develop this reliance on velocity information. Infants with delayed development have less reliance on short latency control mechanisms compared to infants with typical development, apparently necessitating an adaptive switch to other longer latency control mechanisms in the infants with deleayed development.

Introduction

Cerebral palsy is due to a brain injury that occurs early in life, where "cerebral" indicates involvement of the cerebrum, and "palsy" indicates a movement disorder. Thus impairment in motor function is a hallmark of the disorder, but impairments in sensory function are also prevalent, perhaps as a result of injury to thalamocortical pathways (Hoon, et al., 2009). Sensory impairment can include proprioception (Goble, Hurvitz, & Brown, 2009) and cutaneous sensation (Lesny, Stehlik, Tomasek, Tomankova, & Havlicek, 1993; Sanger & Kukke, 2007), and sensory deficits and/or deficits in sensory integration likely contribute both to impairment in motor performance (Bumin & Kayihan, 2001; Bumin & Kavak, 2008; Hadders-Algra, van der Fits, Stremmelaar, & Touwen, 1999) and motor development (Wilke & Staudt, 2009). Sitting is an important motor control skill that infants learn early in life, at about age 6-8 months. Stable sitting allows the infant to reach for objects in his environment, and allows visual inspection of the environment. Additionally, sitting is a major developmental milestone. Infants who do not learn to sit by age 2 years, typically never learn to walk (Fedrizzi, et al., 2000). Thus sitting is not only important in itself, but can serve as a window into the

sensorimotor system of the developing infant, and provide insight into deficits in motor control in infants with developmental delay.

The control of sitting posture, like standing posture, requires maintaining the center of mass within the base of support. In order to achieve this goal both in sitting and standing, information from various sensory modalities, including visual information, vestibular information, proprioceptive information, and cutaneous information, is used to provide feedback for various postural control mechanisms (Horak, 2006). Much of the research on postural control in standing is focused on understanding the contributions of these different modes of sensory information, which is accomplished by blocking or altering various sensory modalities, such as closed eyes/open eyes to investigate the importance of vision in postural sway (Kiemel, Oie, Jeka, 2002), altering visual surround movement to provide false visual information (Peterka, 2002), using vibration to alter touch information to investigate the importance of cutaneous sensory input (Kiemel, Oie, Jeka, 2002), or use of galvanic stimulation to investigate vestibular function in postural sway (Ali, Rowen, & Iles, 2003). However, when one sensory modality is altered, the information from other modalities is used more for control; i.e. sensory reweighting occurs such that the control dynamics may not be representative of the control dynamics under more typical conditions. For example, in normal adult standing, about a third of the information used for control is from visual information (Peterka, 2002), but in the blindfolded condition used as an experimental manipulation of sensory input for postural control, vestibular information and proprioceptive information become more heavily weighted (Horak, 2006). A different strategy in the study of postural control is to apply mechanical perturbations to the subject, and characterize the response, to gain insight into

the postural control mechanism. Perturbation methods have been applied to adult sitting (Granata, Slota, & Bennett, 2004) and to infant sitting (Harbourne, Giuliani, & Neela, 1993; Hedberg, Carlberg, Forssberg, & Hadders-Algra, 2005; Hedberg, Forssberg, & Hadders-Algra, 2004; Hirschfeld, & Forssberg, 1994). These studies characterize the response to extreme events that may not represent typical control mechanisms in unperturbed sitting. For example, stretch reflexes might be triggered by a strong perturbation during sitting (Granata, Slota, & Bennett, 2004), but it is not clear from that result whether stretch reflexes are important in control of unperturbed sitting. While understanding sensory reweighting and response to external perturbations are important goals, it is also important to understand normal postural control, i.e. postural control without experimentally altered sensory input or external perturbations. Normal postural control serves as a baseline with which to compare experimental manipulations of postural control, and is relevant to postural control in many everyday situations. Thus it is desirable to develop methods to study normal postural control, and analysis of center of pressure (COP) data from unperturbed sitting with no sensory manipulation is one such method, and it is the method we have chosen to investigate infant sitting.

The mechanism for control of upright posture is not known, but a leading hypothesis is that a control parameter is the time to contact of the perimeter of the base of support (Slobounov, Cao, Jaiswal, & Newell, 2009). In order to calculate the time to contact parameter, position, velocity and acceleration information must be known. The various sensory modalities provide different types of sensory information. Visual information may include position, velocity and acceleration (Thiel, Greschner, Eurich, Ammermüller, & Kretzberg, 2007). The vestibular labyrinth is particularly suited to

sensing acceleration information (Kandel, Jessel, & Schwartz, 2000, p. 802-803). Proprioceptive feedback includes position, velocity and acceleration information (Schouten, de Vlugt, van Hilten, & van der Helm, 2008). Stretch receptors in the skin also contribute information for postural control (Kandel, Jessel, & Schwartz, 2000, p 443). These multiple modes of sensory information must be interpreted and integrated by the central nervous system in order for postural control mechanisms to maintain upright posture (Horak, 2006). While estimations of position information, velocity information, and acceleration information are all available from integrated sensory input, it is not known which information is actually used for infant sitting postural control. Velocity information is thought to be more accurately estimated than position or acceleration from sensory input, and that it is the predominate type of information used for standing postural control in healthy adults (Jeka, Kiemel, Creath, Horak, & Peterka, 2004). It is unclear if infant sitting postural control can benefit from relying more heavily on the more accurately estimated velocity information, compared to position or acceleration information, or if the time-to-contact calculation requires equal use of all three types of information. Additionally, it is not known if infants with developmental delay will use the same types of sensory information on a delayed developmental schedule, or if they will adaptively find alternate ways to use sensory information to compensate for sensorimotor deficits.

Postural control, just like any motor control task, is accomplished by contraction of the appropriate muscles at the appropriate time. If sensory information indicates an acceleration in a particular direction is needed, then a motor command is executed to provide that acceleration. At a given point in time, the sensory system may detect

position, velocity, and acceleration information, but there is a time lag before that information can be acted upon. The time lag is due to nerve conduction time for the sensory information to flow to the central nervous system (CNS), processing of the sensory signal by the CNS, motor command flow back to the muscle, and muscle activation time. There are a range of delay times that have been measured in adult postural control, including stretch reflex time delay with a latency on the order of about 30 msec and rise time of about 70 msec (Granata, Slota, & Bennett, 2004), vestibular control time delay on the order of 60-100 msec (Ali, Rowen, & Iles, 2003), and visual control time delay on the order of about 500 -750 msec (van den Heuvel, Balasubramaniam, Daffertshofer, Longtin, & Beek, 2009). Multiple postural control mechanisms exist (Horak, 2006), resulting in multiple time scales associated with postural control, as the various control mechanisms have different time delays associated with them. Thus time delay is a critical parameter in analysis of postural sway data. In investigating how infants utilize position, velocity, and acceleration information, it is necessary to also investigate the time delay associated with the utilization of that information.

Conceptually, to maintain upright sitting posture, a control signal is generated by biological neural networks within the central nervous system, with sensory information as the input. The output of the biological controller is a motor control signal that initiates muscle activation. Muscles produce forces and joint torques, which are proportional to accelerations via Newton's second law, often written as F=ma for a system of constant mass. Due to finite nerve conduction velocities and muscle activation response times, there is a time delay between the activation of sensory neurons, and the

acceleration of the body that occurs following the sensory input. Thus the biological system is has sensory input from which, after sensory integration, includes position, velocity and acceleration information, and the output is a muscle activation that causes an acceleration at time delay τ. As a model of the biological control system in this work, we will use a simple artificial neural network (ANN) controller. The input to the ANN is position, velocity and acceleration at time t, and the output is an acceleration at time $t+\tau$. By training the ANN with position, velocity, and acceleration information form experimental COP data from infant sitting, and then probing the response of the network with a sensitivity analysis, the importance of position, velocity and acceleration information to the postural control can be evaluated. We hypothesize that infants will utilize velocity information more than position or acceleration information for sitting postural control, based upon velocity information utilization in adult standing postural sway (Jeka, Kiemel, Creath, Horak, & Peterka, (2004) We also hypothesize infants with delayed development will utilize sensory information differently compared to infants with typical development, rather than simply being delayed in development. Thisd hypothesis is based on sensory deficits in infants with cerebral palsy, which compromise the majority of the sample with atypical development.

Methods

2.1. Infant participants and data collection

Thirty infants with 30 developmental delay (age=14.05 months, std=5.33 months, for early sitting and age=18.06 months, std=5.09 months, for late sitting) and 33 infants with typical development(age=4.92 months, std=0.57 months, for early sitting, and age =

7.92 months, std=0.60 months, for late sitting) participated in the study. Recruitment was done through newsletters, flyers, and pediatric physical therapists employed at the University. Infants in the developmentally delayed group were diagnosed with cerebral palsy, or else were developmentally delayed and at risk for cerebral palsy. Obtaining a firm diagnosis of cerebral palsy at this young age is often not possible. Because a definitive diagnosis of cerebral palsy had not been made, we refer to these infants as developmentally delayed, because all scored below 1.5 standard deviations below the mean for their corrected age on the Peabody Gross Motor Scale (Folio & Fewell, 2000). However, the development is likely not just delayed, but also atypical (Chen & Wollacott, 2007). A consent form was signed by a parent or guardian of all infant participants, and all procedures were approved by the University of Nebraska Medical Center Institutional Review Board.

Inclusion criteria for entry into the study for the typically developing infants were: a score on the Peabody Gross Motor Scale of greater than 0.5 SD below the mean, age of five months at the time of initial data collection, and sitting skills as described below in beginning sitting. Exclusion criteria for the sample of infants who are typically developing were: a score on the Peabody Gross Motor Scales less than 0.5 SD below the mean, diagnosed visual deficits, or diagnosed musculoskeletal problems. If a typically developing infant was found to be less than 0.5 SD below the mean, and did not qualify for the study, the parents were informed of the score, the possibility of error in the measurement, and advised to have the infant re-evaluated within the next 3 months. Operational definitions of beginning sitting were used to determine the child's readiness for entry into the study. Beginning sitting was defined as (a) head control such that when

trunk is supported at the mid-trunk, head is maintained for over one minute without bobbing; (b) infant can track an object across midline without losing head control; (c) infant may prop hands on floor or legs to lean on arms, but should not be able to reach and maintain balance in the prop sit position; (d) when supported in sitting can reach for toy; (e) can prop on elbows in the prone position for at least 30 seconds. Each infant was tested when they entered into the study based on the ability to sit for about 10 sec, and then again 3-4 months later.

For the infants with developmental delay the inclusion and exclusion criteria were as follows. Inclusion criteria were: age from five months to two years, score less than 1.5 SD below the mean for their corrected age on the Peabody Gross Motor Scales, and sitting skills as described above for beginning sitting. Exclusion criteria were: age over two years, a score greater than 1.5 SD below the mean for their corrected age on the Peabody Gross Motor Scale, a diagnosed visual impairment, or a diagnosed hip dislocation or subluxation greater than 50%.

For all data collection sessions, the infants were allowed time to get used to the laboratory setting, and were at their parent's side or on their lap for preparation and data collection. All attempts were made to maintain a calm, alert state by allowing the infant to eat if hungry, be held by a parent for comforting, or adapting the temperature of the room to the infant's comfort level. A blanket was placed over the plate for warmth and was securely adhered with double sided tape on the ground. The baby was held in the sitting position in the middle of the plate to start. Once the examiner could completely let go of the infant, data were collected for 10 seconds while the child attempted to maintain sitting postural control. Trials were performed until we had collected three trials, or until

the infant was no longer interested in sitting, i.e. was crying or agitated and could not be calmed. At any time the child became irritated; the session was halted for comforting by the parent or a chance for feeding, and then resumed only when the child was again in a calm state. We attempted to collect three trials at each of the two sessions, but could not always get that many, depending on the infant's behavior.

For data acquisition (Figure 6.1), infants sat on an AMTI force plate (Watertown, MA), interfaced to a computer system running Vicon data acquisition software (Lake Forest, CA). Center of pressure (COP) data were acquired at 240 Hz using the Vicon software. Trials were recorded including force plate data and video data from the back and side views. Afterwards segments were selected by viewing the corresponding video. Segments of data with 2000 time steps were selected from these trials by examination of the video. Acceptable segments were required to have no crying or long vocalization, no extraneous items (e.g. toys) on the force platform, neither the assistant nor the mother were touching the infant, the infant was not engaged in rhythmic behavior (e.g. flapping arms), and the infant had to be sitting and could not be in the process of falling.

Calculation of position, velocity and acceleration from COP data

The time delay in a sensory feedback system is an important parameter. Since the goal is to model actual infant sitting, the delay from one time step to the next should be appropriate for human motor control. The data in this study was acquired at 240 Hz, meaning there were 240 data points collected each second, or a time lag of 4.2 msec between points. In order to investigate time lags of different lengths, the time series data was sectioned into non-overlapping windows sized from 33 msec (8 data points) to 750 msec (180 data points). Position data for each window was calculated as the average

position for that window. Velocity data was calculated by differencing the position data in that window, and calculating the average, and similarly differencing the position data twice and averaging gave the acceleration for that window. For example, for a window of 33 msec, each COP position time series was broken into segments with length of 8 data points. Averaging these points gave an estimate of the position for that 33 msec time step. Differencing the 8 points and averaging the resulting 7 points gave the velocity estimation for that time step. Differencing twice and averaging the six points gave an estimation of the acceleration for that time step. Thus from the original time series, three time series were calculated: position time series, velocity time series, and acceleration time series.

Because the effect of the three different information types were to be compared, all of the input data to the model needed to be comparable in magnitude for the comparison to be meaningful. Each point of the position data was then normalized by subtracting the mean and dividing by the standard deviation for all position data. Likewise, all the velocity data was normalized using mean and standard deviation for velocity, and acceleration data normalized using mean and standard deviation for acceleration. The normalization process was used in order that each type of data had mean of zero and a standard deviation of 1, and thus the weights from the ANN would be related to the importance of that type of information, and not influenced by the different units on position, velocity and acceleration.

Neural network model

A simple neural network model was created with 3 neurons in the input layer, one each for position, velocity, and acceleration; a hidden layer with 6 neurons, and an output layer with one neuron (Figure 6.2). All neurons used a simple sigmoidal function for activation (Duda, Hart, & Stork, 2001), which has an output of [0, 1], so the acceleration for comparison with the model output was normalized to be in the range [0,1]. Each neuron in the model summed the input from the preceding layer, and then used the following sigmoidal function to compute the output:

$$f(net_j) = \frac{1}{1 + e^{-\sigma \cdot net_j}}$$

where σ is a steepness parameter, that was set equal to one for this model, and net_j is the summation of input to the neuron j. The output of a sigmoid neuron is between zero and one, so all the desired output calculated from the infant posture data was scaled to be between zero and one.

Back propagation of error was used to train the network, where error calculated in each time step was back-propagated based on the current weights of the network, allowing new weights to be calculated (Duda, Hart, & Stork, 2001). Initial weights were randomly generated. Iteration was terminated when the error reached below a threshold value, and if the algorithm did not converge, new random weights were chosen, and the training repeated. The network was trained using the inputs position, velocity and acceleration at time (t), and trained to calculate acceleration at the next time window (t+1). The contribution of position, velocity and acceleration were ascertained by propagating [p,v,a], through the trained network, where p is a position value, v is a velocity value, and a is an acceleration value. For example, propagation of [1,0,0]

through the trained network results in an output that indicates the response of to a positive position, and neutral velocity and acceleration, i.e. what acceleration would the infant's muscles and gravity provide if the infant were leaning 1 standard deviation away from the mean in the positive direction. The output of the network is in the range [0,1], where a value of 0.5 corresponds to no acceleration, an output close to 0 corresponds to a negative acceleration, and a value near 1 corresponds to a positive acceleration. In this manner, for each time series, the contribution of position, velocity, and acceleration were determined for each time series by propagation of [1,0,0], [0,1,0], and [0,0,1], respectively.

Statistical analysis

A repeated measures ANOVA analysis was performed with 2 levels of time (early and late sitting), two axes (anterior-posterior and medial-lateral), 3 levels of ANN input (position, velocity, and acceleration), and 11 window sizes (spanning 33.3 msec to 750 msec). The between subjects factor was the developmental group, delayed versus typical. The significance level for the ANOVA was set at alpha=0.05.

In order to evaluate whether a control effect was observed, the output of the network was compared to 0.5 for each group and condition combination. The output of the network is a value between 0 and 1, with a value of 0.5 being the neutral output of the network, i.e. 0.5 indicates no acceleration in the next time step. An output significantly above 0.5 indicates acceleration in the positive direction in the next time, and an output significantly below 0.5 indicates negative acceleration in the next time. For a perturbation, whether it is position, velocity, or acceleration, the correct response is acceleration in the opposite direction in order to correct for the perturbation. Since we

tested the network with a positive perturbation (either [1,0,0] for position, [0,1,0] for velocity, or [0,0,1] for acceleration), the correct response of the network is a value below 0.5, indicating that the acceleration in the next time step is in the opposite direction to the perturbation. Thus one-sided, independent t-tests were used test whether the output results were below 0.5. For each window size, infants with typical development and infants with delayed development, at early sitting and late sitting, in each of two axes (anterior-posterior and medial-lateral), are evaluated for the effect of three different types of posture control information (position, velocity and acceleration), resulting in 2 x 2 x 2 x 3 = 24 comparisons for each window size used. Because 11 window sizes were examined, 24*11= 264 conditions were tested. With so many conditions, using 0.05 as the critical alpha value for all these tests would likely result in reporting some effects as significant, when in fact they were due to chance. A conservative Bonferroni correction for multiple comparisons would require setting the $alpha_{critical}$=.05/264 = .000189, which is quite difficult to meet. If we had knowledge of the one best window size for posture control in infants sitting, then only 24 conditions would have been examined, and $alpha_{critical}$=.05/24 = .0021 would be used. Because of the exploratory nature of this work, we relaxed the criteria for significance from the Bonferroni standard, and we chose to examine two critical values, $alpha_{critical}$=0.01 and $alpha_{critical}$ =.0021. To get an idea of the effect of the relaxed criteria, using an $alpha_{critical}$ value of 0.01 means we expect to reject the null hypothesis when in fact it is true for 1% of the comparisons. For 264 comparisons, we expect about .01*264 = 2.64 comparisons to appear as significant, even if the results are actually random. Similarly, for $alpha_{critical}$ = 0.0021, we expect about 0.6 comparisons to be evaluated as significant when in fact they are not.

Results

The repeated measures ANOVA analysis did not reveal any significant differences for group, nor did it find a main effect for the repeated measures, day, axis, perturbation type, or window size. However, within subject contrasts found significant interactions in perturbation type x group (p=.044), window size x axis (p=.034), window size x day x axis (p=.041), window size x axis x perturbation type x group (p=.019), and window size x day x axis x perturbation type x group (p=.014), where the p value shown represents the best p value for each type of contrast (i.e., lowest among linear , quadratic, etc). Note that the last interaction with all 5 conditions and group is significant, and has the lowest p value, so there is no simple interpretation of these results, as all interactions must be considered.

To help interpret the interactions, there is an additional consideration about the results that will be helpful, namely that the comparison of the neural network output to the neutral value of 0.5 for each condition. The output of the network is a normalized acceleration, with a value ranging from 0 to 1, where a value of 0 indicates a maximum acceleration in the negative direction, a value of 1 indicates a maximum acceleration in the positive direction, and a value of 0.5 indicates no acceleration in response to the input. If the network is tested with a positive perturbation, the appropriate response is in the negative direction, i.e. in the opposite direction to the perturbation, which corresponds to an output significantly less than 0.5 If the output of the network for a positive perturbation is not significantly less than 0.5 for that time lag and input perturbation type (i.e. position, velocity, or acceleration), that indicates that the time lag/information type

combination is not contributing significantly to control. One-sample t-tests were used to compare the output for each condition to 0.5, for inputs designed to test the trained networks sensitivity to position [1,0,0], velocity [0,1,0], and acceleration [0,0,1] (Table 6.1). The tests were two-sided t-tests, but the mean values for all conditions that are significantly different than 0.5 are less than 0.5, consistent with the output of the network having useful control functionality. Using a criteria of statistical significance of 0.01, 44 conditions/group combinations were found to be significantly lower than 0.5, out of 264 tested, compared to only about 3 combinations would be expected to be significantly different if the results were random. Using a criteria of statistical significance of 0.0021, 11 conditions/group combinations were found to be significantly lower than 0.5, out of 264 tested, compared to only about 1 combination would be expected to be significantly different if the results were random.

The significant results (Table 6.1) were organized by group, day, and axis (Table 6.2) to facilitate comparisons. Typically developing infants have a wide range of time windows contributing to control in the medial-lateral axis. Additionally, position, velocity and acceleration are all contributing to control in the medial-lateral axis for infants with typical development. In contrast, the anterior-posterior axis for late sitting for infants with typical development is very dependent on velocity information. The infants with delayed development have no short time window contributions to control, as there are no significant contributions from time windows less that 100 msec for infants with delayed development, and for late sitting no significant contribution from a time window less that 250 msec. Additionally, infants with delayed development have more equal lag/information types contributing to control for the anterior-posterior axis and medial-

lateral axis, compared to the infants with delayed development who have more in the medial-lateral axis and fewer in the anterior-posterior axis.

Discussion

Our first hypothesis was that velocity information would be more heavily used in infant sitting posture control. We found this to be true, but only for infants with typical development, and then only for control in the anterior-posterior axis for late sitting. That late sitting should use velocity information more heavily is consistent with the sensory integration capabilities of the infants becoming more nearly adult like later in development. In adult standing posture control, Jeka, Kiemel, Creath, Horak, and Peterka (2004) find that velocity information is more heavily used than position or acceleration. They point out that the proprioceptive, cutaneous, and visual systems are all velocity sensitive, due to the sensor physiology being more sensitive to changes in position rather than absolute position. They mentioned that the vestibular system, a source of acceleration information, is relied on under conditions where sway referenced support has altered normal sensory input. They argue that under normal postural sway conditions, the vestibular system is likely not sensitive enough to contribute greatly to postural control. However, the study by Jeka, Kiemel, Creath, Horak, and Peterka (2004) only examined control in the anterior-posterior axis due to the sway platform being used allowing tilt in only one direction, and their study does not address control in the medial-lateral axis. Just because velocity is more heavily used for control of adult standing posture in the anterior-posterior axis, does not imply that the same is true in the medial-lateral axis, as sensory information is used differently for control in the two different axes. For example, a study by O'Conner and Kuo (2009) found that normal adult standing postural sway is more

influenced by visual perturbations in the anterior-posterior axis than in the medial-lateral axis, while the sensitivity is higher in the medial-lateral direction if the feet are placed in tandem rather than side-by-side. As infants learn to sit they must learn to appropriately use sensory information based on task demands.

Our second hypothesis was that infants with developmental delay use sensory information differently than infants with typical development. The infants with developmental delay were found to lack the short time delay contributions to posture control that the infants with typical development demonstrated. Infants with developmental delay were found to not simply be delayed in the development of sitting, but were less able to utilize short latency sensory information in postural control than infants with typical development, instead relying on longer delay time mechanisms for postural control. One short delay time control mechanism that might be used in postural control is the stretch reflex (Granata, Slota, & Bennett, 2004). Infants with spastic cerebral palsy have altered stretch reflex activity and greater stiffness of the musckuloskeletal system, and thus this mechanism may not be as useful for postural control for infants with cerebral palsy compared to infants with typical development. Perhaps an adaptive strategy for maintaining upright posture for infants with altered short latency control, possibly altered stretch reflexes, is a more complete reliance on higher level control mechanisms, which necessarily have a longer delay time. With a reduced number of postural control strategies available, the motor control system has fewer synergies to invoke, so the motor control development becomes atypical as well.

Children with cerebral palsy have been found to have an increased time to produce a given amount of force in lower extremity movements (Downing, Ganley, Fay,

& Abbas, 2009), and patients with dystonia have slower reaction times in a visual stimulus and button-pushing task (Jahanshahi, Rowe, & Fuller, 2001). The slow response time of the neuromuscular control system, and the necessary reliance on longer time lag control mechanisms, has important implications for postural control. One model of postural control is the inverted pendulum model, where a mass remains positioned above the ground on a vertical rod due to actuators controlled by a feed back controller. If the delay time of the feedback controller exceeds a critical time delay, then the upright position cannot be maintained. The critical time is given by: t_c= sqrt(2*L/3*g), where L is the distance from ground to the center of mass of the pendulum, and g is the acceleration of gravity, which works out to 260 msec for adult standing (Milton, Cabrera, Ohira, Tajima, Tonosaki, Eurich, & Campell, 2009) . From this formula, the critical delay time for control of an inverted pendulum depends on the size of the pendulum, with taller pendulums able to be controlled using slower response times. For an infant, with a center of mass about 20 cm above the ground, the critical control time is 117 msec. None of the significant control time delays for infants with delayed development meet this criterion (Table 6.2). While the inverted pendulum is a very crude model of infant sitting postural control (Kyvelidou, Stuberg, Harbourne, Deffeyes, Blanke, Stergiou, 2009), and ignores what are likely important contributions from the viscoelastic properties of the infant's body as well as the pelvis and spine joints, the inverted pendulum model suggests that an infant who is not able to use fast latency control mechanisms may have a more difficult control problem to solve than infants with typical development.

This study investigated control of normal postural sway, where no external mechanical perturbations are applied, and no sensory alteration is used. While an

important feature of this study is that the results apply to normal, unperturbed posture control with normal sensory weighting, a weakness of this study is that the specific sensory modalities involved in estimation of position, velocity, and acceleration can not be identified. This study used a very simple ANN to model postural control, which is a complicated control process with multiple control mechanisms interacting to maintain upright posture (Horak, 2006). The ANN topology might be improved by inputting position, velocity and acceleration information for multiple time delays information simultaneously (larger ANN input layer), or by having more processing nodes (larger ANN hidden layer), or by having output to multiple muscles with various different time delays (larger ANN output layer). The probes that we use to test the network sensitivity to position, velocity, and acceleration were also very simple, but more complex, nonlinear combinations of inputs might be important for posture control, as might be expected if the time-to-contact hypothesis (Slobounov, Cao, Jaiswal, & Newell, 2009) is correct. A combination of velocity and acceleration may also be useful for infant sitting postural control, as muscle activity in adult standing postural control has been shown to correlate with perturbation acceleration and velocity (Welch & Ting, 2009). Additional work is needed to address these issues.

Dynamic system theory, as used in the field of developmental psychology, accepts that an important aspect of motor development is the development of perception-action coupling, as a result of exploring a wide variety of coordination patterns, and eventually selecting those best suited to a particular motor task. Thelen (2000) has emphasized the close relationship between cognition and action-perception during development. An important aspect of perception is the cognitive task of sensory

integration that must occur in order to utilize the information content of the sensory input. Visual, vestibular, proprioceptive, and cutaneous sensory data must be integrated in order to estimate position, velocity, and acceleration information to be used for posture control. Although there is no theoretical guidance on whether position, velocity, or acceleration information would be most useful for postural control, work with adult standing anterior-posterior postural control indicates that velocity information is most useful (Jeka, Kiemel, Creath, Horak, & Peterka, 2004), and we have noted in this work that infants with typical development utilize velocity information more heavily in posture control in the anterior-posterior direction. Thus the infants with typical development appear to develop towards using sensory information in a manner similar to adult posture, with the underlying assumption that the infant is developing on a trajectory that will eventually led to the adult pattern of use of sensory information. However, this analysis may be overly simplistic. There is no reason to assume a linear trajectory in infant development (Adolf, Young, Robinson, & Gill-Alvarez, 2008). Development of proprioceptive sensory integration is not mature even in adolescents (Viel, Vaugoyeau, & Assaiante, 2009), so attainment of a fully adult response in infants, even in later sitting, is not likely. Instead, the use of velocity information for control in the anterior-posterior direction may emerge independently in both infant sitting and adult standing, as an efficient means of control for those particular postures, given the anatomical and physiological constraints of each of those systems. In discussing the anterior-posterior and medial-lateral differences in sensory information utilization in adult standing, O'Conner and Kuo (2009) stated that the task direction with the greatest instability requires more feedback, and applying this logic to our results suggests that control in the medial-lateral axis is less stable than the

anterior-posterior axis, as more types of sensory information are used for control in that axis, for infants with typical development.

In summary, we find that late sitting for infants with typical development is characterized by a high reliance on velocity information in control in the anterior-posterior axis, as is adult standing posture control (Jeka, Kiemel, Creath, Horak, & Peterka, 2004), with relatively more complicated control in the medial-lateral axis utilizing a wider range of information types. Infants with delayed development who are younger than 18 months do not develop the same reliance on velocity information. Infants with delayed development have less reliance on short latency control mechanisms compared to infants with typical development, perhaps due to altered stretch reflexes or generally slower sensorimotor dynamics, necessitating an adaptive switch to other longer latency control mechanisms.

References

Adolph, K.E., Robinson, S.R., Young, J.W., & Gill-Alvarez, F., (2008). What is the shape of developmental change? Psychological Review, 115(3), 527-43.

Ali, A.S., Rowen, K.A., & Iles, J.F., (2003). Vestibular actions on back and lower limb muscles during postural tasks in man. The Journal of Physiology, 546(Pt 2), 615-24.

Bumin, G., & Kavak, S.T., (2008). An investigation of the factors affecting handwriting performance in children with hemiplegic cerebral palsy. Disability and Rehabilitation, 30(18), 1374-85.

Bumin, G., & Kayihan, H., (2001). Effectiveness of two different sensory-integration programmes for children with spastic diplegic cerebral palsy. Disability and Rehabilitation, 23(9), 394-9.

Chen, J., & Woollacott, M.H., (2007). Lower extremity kinetics for balance control in children with cerebral palsy. Journal of Motor Behavior, 39(4), 306-16.

Downing, A.L., Ganley, K.J., Fay, D.R., & Abbas, J.J., (2009). Temporal characteristics of lower extremity moment generation in children with cerebral palsy. Muscle & Nerve, 39(6), 800-9.

Duda, R.O., Hart, P.E., Stork, D.G. (2001). Pattern Classification, 2nd Ed. New York: John Wiley & Sons.

Fedrizzi, E., Facchin, P., Marzaroli, M., Pagliano, E., Botteon, G., Percivalle, L., & Fazzi, E. (2000). Predictors of independent walking in children with spastic diplegia. Journal of Child Neurology, 15(4), 228-34.

Folio M.R., & Fewell, R.R. (2000). Peabody Developmental Motor Scales (2nd ed.). Austin, TX : Pro-ed, Inc.

Goble, D.J., Hurvitz, E.A., & Brown, S.H., (2009). Deficits in the ability to use proprioceptive feedback in children with hemiplegic cerebral palsy. International Journal of Rehabilitation Research, 32(3), 267-9.

Granata, K.P., Slota, G.P., & Bennett, B.C., (2004). Paraspinal muscle reflex dynamics. Journal of Biomechanics, 37(2), 241-7.

Hadders-Algra, M., van der Fits, I.B., Stremmelaar, E.F., & Touwen, B.C., (1999). Development of postural adjustments during reaching in infants with CP. Developmental Medicine and Child Neurology, 41(11), 766-76.

Harbourne, R.T., Giuliani, C., & Neela, J.M., (1993). A kinematic and electromyographic analysis of the development of sitting posture in infants. Developmental Psychobiology, 26(1), 51-64.

Hedberg, A., Carlberg, E.B., Forssberg, H., & Hadders-Algra, M., (2005). Development of postural adjustments in sitting position during the first half year of life. Developmental Medicine and Child Neurology, 47(5), 312-20.

Hedberg, A., Forssberg, H., & Hadders-Algra, M., (2004). Postural adjustments due to external perturbations during sitting in 1-month-old infants: evidence for the innate origin of direction specificity. Experimental Brain Research, 157(1), 10-7.

Hirschfeld, H., & Forssberg, H., (1994). Epigenetic development of postural responses for sitting during infancy. Experimental Brain Research, 97(3), 528-40.

Hoon AH, J.r., Stashinko, E.E., Nagae, L.M., Lin, D.D., Keller, J., Bastian, A., Campbell, M.L., Levey, E., Mori, S., & Johnston, M.V., (2009). Sensory and motor deficits in children with cerebral palsy born preterm correlate with diffusion tensor imaging abnormalities in thalamocortical pathways. Developmental Medicine and Child

Neurology, 51(9), 697-704.

Horak, F.B. (2006).Postural orientation and equilibrium: what do we need to know about neural control of balance to prevent falls? Age and Ageing, 35 (S2) ; ii2 – ii11.

Jahanshahi, M., Rowe, J., & Fuller, R., (2001). Impairment of movement initiation and execution but not preparation in idiopathic dystonia. Experimental Brain Research, 140(4), 460-8.

Jeka, J., Kiemel, T., Creath, R., Horak, F., & Peterka, R. (2004). Controlling human upright posture: velocity information is more accurate than position or acceleration. Journal of Neurophysiology, 92(4), 2368-79.

Kandel, E.R., Jessell, T.M., & Schwartz, J.H. (2000). Principles of Neural Science, 4th ed. McGraw-Hill, New York.

Kiemel, T., Oie, K.S., & Jeka, J.J., (2006). Slow dynamics of postural sway are in the feedback loop. Journal of Neurophysiology, 95(3), 1410-8.

Kyvelidou, A., Stuberg, W.A., Harbourne, R.T., Deffeyes, J.E., Blanke, D., Stergiou, N. (2009). Development of upper body coordination during sitting in typically developing infants. Pediatric Research, 65(5), 553-538.

Lesny, I., Stehlik, A., Tomasek, J., Tomankova, A., & Havlicek, I., (1993). Sensory disorders in cerebral palsy: two-point discrimination. Developmental Medicine and Child Neurology, 35(5), 402-5.

Milton, J., Cabrera, J.L., Ohira, T., Tajima, S., Tonosaki, Y., Eurich, C.W., & Campbell, S.A., (2009). The time-delayed inverted pendulum: implications for human balance control. Chaos, 19(2), 026110.

O'Connor, S.M., & Kuo, A.D., (2009). Direction-dependent control of balance during walking and standing. Journal of Neurophysiology, 102(3), 1411-9.

Peterka, R.J., (2002). Sensorimotor integration in human postural control. Journal of Neurophysiology, 88(3), 1097-118.

Sanger, T.D., & Kukke, S.N., (2007). Abnormalities of tactile sensory function in children with dystonic and diplegic cerebral palsy. Journal of Child Neurology, 22(3), 289-93.

Schouten, A.C., de Vlugt, E., van Hilten, J.J., & van der Helm, F.C., (2008). Quantifying proprioceptive reflexes during position control of the human arm. IEEE Transactions on Biomedical Engineering, 55(1), 311-21.

Slobounov, S., Cao, C., Jaiswal, N., & Newell, K.M., (2009). Neural basis of postural instability identified by VTC and EEG. Experimental Brain Research, 199(1), 1-16.

Thelen, E. (2000). Grounded in the World: Developmental Origins of the Embodied Mind. Infancy, 1(1), 3-28.

Thiel, A., Greschner, M., Eurich, C.W., Ammermuller, J., & Kretzberg, J., (2007). Contribution of individual retinal ganglion cell responses to velocity and acceleration encoding. Journal of Neurophysiology, 98(4), 2285-96.

van den Heuvel, M.R., Balasubramaniam, R., Daffertshofer, A., Longtin, A., & Beek, P.J., (2009). Delayed visual feedback reveals distinct time scales in balance control. Neuroscience Letters, 452(1), 37-41.

Viel, S., Vaugoyeau, M., & Assaiante, C., (2009). Adolescence: a transient period of proprioceptive neglect in sensory integration of postural control. Motor Control, 13(1),

25-42.

Welch, T.D.J. & Ting, L.H. (2009). A feedback model explains the differential scaling of human postural responses to perturbation acceleration and velocity. Journal of Neurophysiology, 101, 3294-3309.

Wilke, M., & Staudt, M., (2009). Does damage to somatosensory circuits underlie motor impairment in cerebral palsy? Developmental Medicine and Child Neurology, 51(9), 686-7.

Table 6.1.

Results of One Sample t-Tests With the Output of the ANN Less than the Neutral Value of 0.5.

ANN input	Axis	Time	Window (msec)	Mean	Standard deviation	p
Typical development (n=33)						
position	medial-lateral	late sitting	33.3	0.448	0.116	0.0076
position	medial-lateral	early sitting	83.3	0.412	0.155	0.0014*
velocity	medial-lateral	early sitting	83.3	0.407	0.173	0.0021*
acceleration	medial-lateral	early sitting	83.3	0.410	0.164	0.0018*
velocity	anterior-posterior	late sitting	83.3	0.431	0.129	0.0023
position	anterior-posterior	early sitting	133.3	0.431	0.157	0.0084
position	medial-lateral	early sitting	133.3	0.411	0.189	0.0053
velocity	medial-lateral	early sitting	133.3	0.411	0.198	0.0074
acceleration	medial-lateral	early sitting	133.3	0.406	0.191	0.0041
position	medial-lateral	late sitting	133.3	0.430	0.150	0.0056
velocity	medial-lateral	late sitting	133.3	0.425	0.166	0.0070
acceleration	medial-lateral	late sitting	133.3	0.425	0.154	0.0042
position	medial-lateral	early sitting	187.5	0.410	0.161	0.0016*
velocity	medial-lateral	early sitting	187.5	0.423	0.160	0.0046
acceleration	medial-lateral	early sitting	187.5	0.418	0.174	0.0053
position	medial-lateral	late sitting	250.0	0.438	0.131	0.0053

acceleration	medial-lateral	late sitting	250.0	0.433	0.152	0.0080
position	anterior-posterior	early sitting	500.0	0.414	0.153	0.0015*
velocity	anterior-posterior	early sitting	500.0	0.398	0.172	0.0009*
acceleration	anterior-posterior	early sitting	500.0	0.391	0.176	0.0006*
position	medial-lateral	early sitting	500.0	0.412	0.186	0.0054
velocity	medial-lateral	early sitting	500.0	0.405	0.178	0.0021
velocity	anterior-posterior	late sitting	500.0	0.423	0.174	0.0082
position	medial-lateral	late sitting	750.0	0.418	0.154	0.0022
velocity	medial-lateral	late sitting	750.0	0.418	0.166	0.0040
Delayed development (n=30)						
position	medial-lateral	early sitting	133.3	0.420	0.125	0.0008*
velocity	anterior-posterior	early sitting	187.5	0.406	0.169	0.0025
acceleration	anterior-posterior	early sitting	187.5	0.419	0.172	0.0075
acceleration	anterior-posterior	early sitting	250.0	0.428	0.152	0.0070
velocity	anterior-posterior	late sitting	250.0	0.416	0.167	0.0050
acceleration	anterior-posterior	late sitting	250.0	0.420	0.158	0.0046
position	medial-lateral	late sitting	250.0	0.413	0.178	0.0060
velocity	medial-lateral	late sitting	250.0	0.413	0.179	0.0063
velocity	anterior-posterior	early sitting	333.3	0.409	0.194	0.0081
acceleration	anterior-posterior	early sitting	333.3	0.409	0.177	0.0043
position	medial-lateral	early sitting	375.0	0.410	0.161	0.0023
acceleration	medial-lateral	early sitting	375.0	0.410	0.163	0.0025
acceleration	anterior-posterior	late sitting	375.0	0.415	0.153	0.0025

position	anterior-posterior	early sitting	500.0	0.424	0.124	0.0011*
acceleration	anterior-posterior	late sitting	500.0	0.432	0.142	0.0068
velocity	anterior-posterior	early sitting	750.0	0.405	0.171	0.0024
position	medial-lateral	late sitting	750.0	0.407	0.189	0.0058
velocity	medial-lateral	late sitting	750.0	0.403	0.160	0.0012*
acceleration	medial-lateral	late sitting	750.0	0.396	0.174	0.0014*

Note: Only conditions with $p<.01$ are included in the table, and * indicates conditions with $p<.0021$. The p values are for a one-sided t-test with null hypothesis mean=0.5 for each condition/ANN input combination. Comparisons with $p>.01$ are not shown.

Table 6.2. Information Type and Window Times (msec) for Significant Output of Infant Sitting ANN

Delayed development		Typical development	
Medial-lateral	Anterior-posterior	Medial-lateral	Anterior-posterior
		Early Sitting	
P 133*	P 500*	P 83*	P 133
P 375	V 187	P 133	P 500*
A 375	V 333	P 187*	V 500*
	V 750	P 500	A 500*
	A 187	V 83*	
	A 250	V 133	
	A 333	V 187	
		V 500	
		A 83*	
		A 133	
		A 187	
		Late Sitting	
P 250	V 250	P 33	V 83
P 750	A 250	P 133	V 500
V 250	A 375	P 250	
V 750*	A 500	P 750	
A 750*		V 133	
		V 750	
		A 133	
		A 250	

Note. P=position sensitivity of ANN, V=velocity sensitivity of ANN, A=acceleration sensitivity of ANN. Numerical value is window size in msec. * indicates ANN output was significantly different from 0.5 with $p<.0021$, and values without * were significantly different from 0.5 with $p< .01$, as indicated in Table 1.

Figure 6.1. Postural sway COP data is collected as an infant sits on a force plate. COP data was used to train the neural network.

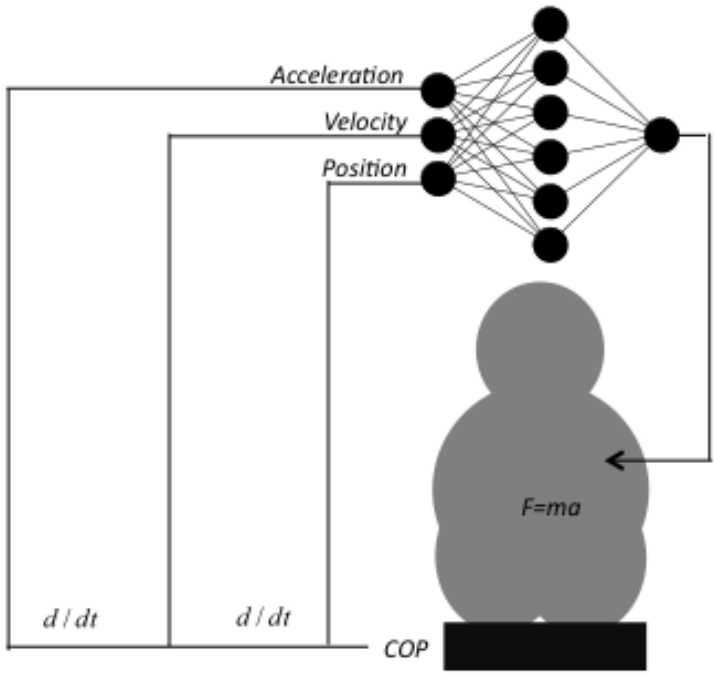

Figure 6.2. Model of infant as a sitting on a force plate, with a neural network controller. Force plate is indicated as a black box that outputs COP data, which is differentiated to get velocity and acceleration sensory information, the input to the neural network. The output of the network is a control signal that drives muscles in order to maintain upright sitting posture of the infant. We measure COP with the force plate to derive the position, velocity, and acceleration sensory data for the model, whereas the infant relies on visual, vestibular, proprioceptive, and cutaneous sensory input for this information.

CHAPTER 7

DISSERTATION CONCLUSION

Chapter 2 used linear and nonlinear measures to compare postural sway of infant early sitting, and finds significant differences with the largest Lyapunov exponent (LyE), but not any of the other measures, including approximate entropy. The sitting postural sway of infants with typical development had higher LyE that the sitting postural sway of infants with delayed development. The LyE calculated from experimental data is a measure of exponential divergence of nearby trajectories of a time series embedded in phase space. However, these trajectories must eventually fold back on longer time scales because the attractor is bounded (Figure 7.1), as unchecked exponential divergence would result in an unbounded system (Wolf, Swift, Swinney, & Vastano, 1985).

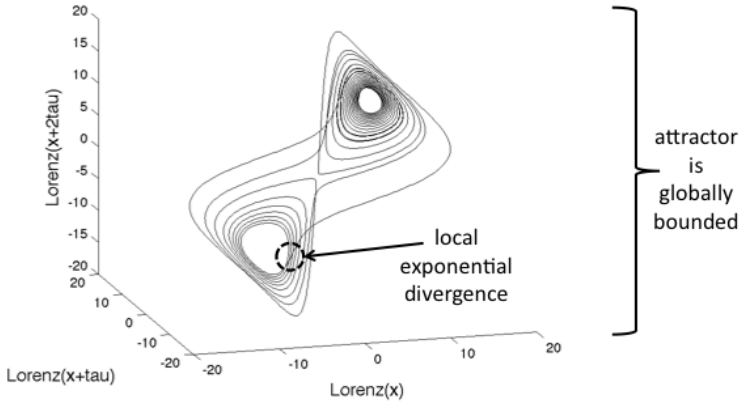

Figure 7.1. The attractor is globally bounded, even though local trajectories exhibit exponential divergence.

As discussed by Wolf, Swift, Swinney, and Vastano (1985), the exponential divergence that is measured in calculation of the LyE is on a much shorter time scale than the period of the attractor, in order to avoid underestimating the divergence as the attractor folds back on itself. Therefore, short time scale events (i.e. high frequency in the power spectrum) contribute more to the calculated LyE than long time scale events. While Wolf, Swift, Swinney, and Vastano (1985) discuss this in relation to the sensitivity of the analysis to experimental noise, the high frequency components in the postural sway data of infants with typical development not seen in the postural sway of infants with delayed development (see Figures 4.11 and 4.12 in Chapter 4) may be what is giving rise to the differences in LyE between these two groups.

In a mathematical system, where the system's governing equations are known explicitly, the largest Lyapunov exponent can be calculated analytically from the governing equations. When calculated from the governing equations, positive LyE is consistent with the system being chaotic, whereas negative LyE indicates the system is not chaotic. However, for the infant postural control system, the governing equations are not known explicitly, and the LyE can only be estimated from experimental time series data. In this work, the LyE was estimated from center of pressure data in this work using commercially available software, the Chaos Data Analyzer was used (professional version, Physics Academic Software; Sprott & Rowlands, 1998), which implements what is known as the Wolf algorithm for calculation of the LyE (Wolf, Swift, Swinney, & Vastano, 1985). Wolf, Swift, Swinney, and Vastano (1985) emphasize that the data used for the analysis must be sufficient in quantity (length of the time series), and quality (not

have excessive noise) for the algorithm to give meaningful results. The length requirement for the time series is based on the need to contain several orbital periods, and thus the length requirement for the time series depends on the dynamics of the system under study, and Wolf, Swift, Swinney, and Vastano (1985) find that 10^D to 30^D data points are required, where D is the dimension of the attractor. Again, we cannot directly calculate the dimension of the attractor for infant sitting postural control because the governing equations are not known. We can only estimate a dimensionality of the system from the data. One estimate of attractor dimension is the correlation dimension, and as reported in Chapter 2, we found a correlation dimension of about 4.2. The required time series length, based on this estimate of the attractor dimension, is at least 10^D, or 15,849 data points are required. Here we should note that this estimate of the required number of data points is based on the available data. Thus, it is unknown if the actual dimension is 4.2. It is possible that it will be higher or lower. However, Grassberger and Procaccia (1983) find that the correlation dimension is a good estimate of the attractor dimension if the time series is long enough, but may underestimate the attractor dimension if the time series is too short. Thus the requirement of 15, 849 data points is likely a conservative estimate of the length of the time series needed.

The infants are not able to sit for extended periods of time, and our data collections resulted in time series that were 2000 time steps (N=2001), or 8.3 seconds of data collected at 240 Hz. Of course, collecting data at 2400 Hz for 8.3 seconds of sitting would have resulted in 20,000 time steps, apparently meeting the requirement of 15,849 data points. Furthermore, increasing the sampling rate tenfold does not provide an increase in length of time the system dynamics the time series, and thus could not be an

appropriate solution to the time series length requirement. As a simple example, consider studying the dynamics of a sine function with a period of 2 seconds, i.e. a frequency of 0.5 Hz. The Nyquist criterion requires sampling at least 4 data points in those 2 seconds (i.e. sampling at 1 Hz is the minimum for a 0.5 Hz signal). For spectral analysis sampling rates higher than the Nyquist criterion present no problem, other that the extra data storage requirements for the longer time series. While the Nyquist criterion is widely accepted as determining the minimum necessary sampling rate for spectral analysis (sometimes called the Nyquist-Shannon criteria), the mathematical proof of the Nyquist sampling criterion requires data to cover a complete period (Shannon, 1949). Simply sampling at a very high sampling rate, and obtaining a time series with a certain number of data points does not allow characterization of the system dynamics if the time series does not sample for at least one period of the sine function. For the example of the 0.5 Hz sine function with a period of 2 seconds, mentioned above, sampling at a very high sampling rate for 0.2 seconds will not provide a description of the system dynamics, regardless of how many data points are collected in that 0.2 seconds. The requirement for the LyE using Wolf's algorithm is even more severe, in that multiple cycles are needed, because divergence values from multiple cycles are averaged in order to minimize the effect of noise on the estimate. The requirement of 15,849 data points for the length of the time series cannot be met simply by increasing the sampling rate, but that leaves open the question of what sampling rate should be used.

The sampling rate for nonlinear analysis has additional considerations as compared to spectral analysis, because it needs to be low enough that the system evolves sufficiently from one measurement to the next. Wolf, Swift, Swinney, and Vastano

(1985) suggest looking at delay plots (Figure 7.2) and visually determining if a given delay time has sufficiently opened up the attractor, as the attractor will appear as a line on x=y (or a line on x=y=z in three dimensions) if the delay is too low.

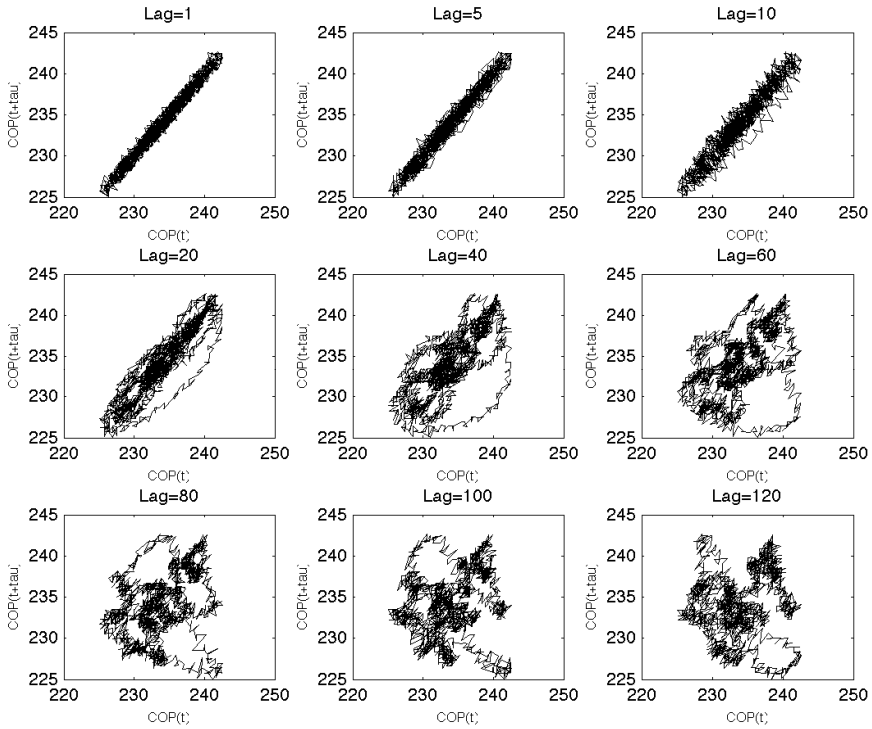

Figure 7.2. Delay plots for infant sitting time series at various lag values.

While the delay plots indicate that a lag less than about 40 is not unfolding the attractor enough, it is not clear which time lag is best. Additionally, if the data has a dimension greater than 3, this method could lead to erroneous conclusions, since higher dimensions cannot be visualized. Based on the correlation dimension data reported in Chapter 2, the dimension of this data might be 4 or higher, so we might suspect that a two

dimensional plot is not appropriate for judging the unfolding of the attractor for this data set. Another method that can be used to is to set the delay time based on the lag value at which the autocorrelation function reaches 1-1/e of its maximum value (Rosenstein, Collins & DeLuca, 1992). This method gives a median value of about 40, although for some time series the values are much higher (Figure 7.3).

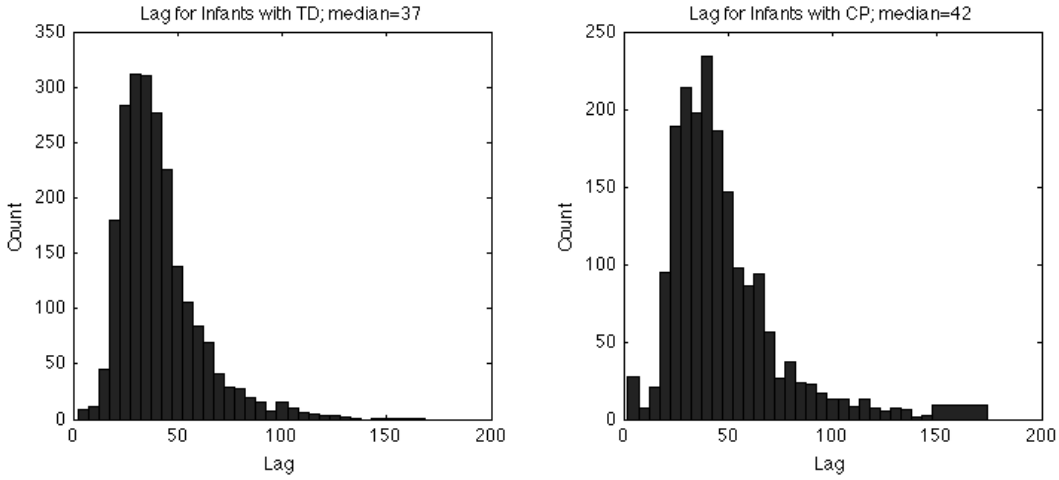

Figure 7.3. Histograms of lag values (τ) at which autocorrelation function falls below 1-1/e, for sitting COP data for infants with typical development (left) and infants with delayed development (right).

If a lag value of 40 is to be used for the infant sitting data with the Wolf algorithm, as implemented in the software Chaos Data Analyzer (professional version, Physics Academic Software; Sprott & Rowlands, 1998), then the data must be down sampled from a time series of 2000 time steps to a time series of just 50 time steps, where now each time step is lag 40/ 240 Hz= 166 msec. The net result is that the 8.3 seconds of infant sitting data that was acquired for each infant sitting trial provides just 50 data points, compared to the conservative estimate that 15,849 data points are needed. Based

on this approach, to acquire 15,849 data points at a lag of 166 msec, the infants would have to sit for 2631 seconds, or over 40 minutes, which is beyond the capability of most, if not all, of the infants in our study. Even if the infants could sit for this long, the dynamics of the postural control would likely change during these 40 minutes due to fatigue, so nonstationarity of the signal would compromise the outcome. Based on this analysis, further calculations with the LyE were not pursued.

Despite these limitations, the result from the LyE analysis presented in Chapter 2 is intriguing, because this algorithm did detect differences between the postural sway of infants with delayed development and infants with typical development. However, interpretation of the LyE in the same manner as analytically determined LyE, as an indicator of mathematical chaos, is troublesome, given that the data is so far away from meeting the criteria that the algorithm was designed to handle (Wolf, Swift, Swinney, and Vastano, 1985). With this limitation in mind, we should point out that this does not undermine the results of Chapter 2 but we suggest that they should be interpreted with caution if conclusions of chaos are to be made. We feel that conclusions on amount of divergence of the trajectories are safer and they have a more functional importance.

Entropy measures are thought to be more robust than other nonlinear measures to shorter time series (Pincus, 1991), so Chapters 3 and 4 pursued the use of entropy measures. In Chapter 3 symbolic entropy (Aziz & Arif, 2006) and approximate entropy (Pincus, 1991) were used to compare sitting postural sway of infants with typical development to sitting postural sway of infants with delayed development. Chapter 2 included approximate entropy analysis of early infant sitting postural sway, and found no significant difference between the two groups, but the parameters used by the algorithm

for the analysis in Chapter 2 were standard parameters that are widely used in other fields, as discussed in Chapters 2, 3, and 4. These parameters are comparison vector length m=2, and distance parameter r=.2 times the standard deviation of the time series. In Chapter 2, the lag parameter was adjusted to 4 because of contamination of the data with 60 Hz noise, and sampling at 240 Hz, resulted in a repeating cyclical pattern every 4^{th} data point. Thus Chapter 2 uses what would be referred to as ApEn(m=2, r=.2*std(Data), t @ 240 Hz, lag=1) using the nomenclature in Chapter 4. In Chapter 3 approximate entropy parameters are varied a bit, but it mostly focuses on the symbolic entropy analysis, and for both types of entropy analysis optimizes parameters to maximize the separation of the two groups of infants. Chapter 4 focuses exclusively on a systematically varying the parameters in the approximate entropy analysis.

Chapter 2 presents the conclusion that ApEn(m=2, r=.2*std(Data), t @ 240 Hz, lag=4) found no significant difference between these two groups of infants. Chapter 3 presents the conclusion that ApEn(m=2, r=3.0*std(Data), t @ 240 Hz, lag=4) found significant differences in infants with delayed versus typical development in developed sitting in the medial-lateral axis. Chapter 4 presents the conclusion that ApEn(m=1, r=1.0*std(Data), t @ 240 Hz, lag=8) found significant differences in infants with delayed versus typical development in early sitting in the anterior-posterior axis. A contributing factor to these various results is that different numbers of subjects were analyzed in each because the analyses were completed at different times, and each analysis used the subjects' data that was available when the analysis was performed. However, the choice of parameters for the analyses in Chapters 3 and 4 were made based on searching a large parameter space to find parameters that perform better at separating the developed sitting

in Chapter 3 and early sitting in Chapter 4. Thus using the standard parameters finds no difference, optimizing the parameters for developed sitting finds differences in the medial-lateral axis, and optimizing the parameters for early sitting finds differences in the anterior-posterior axis. That no difference was found using the standard parameters is due to experimental noise being the main determinate of approximate entropy using the standard parameters, a seen in Figure 3.3 in Chapter 4. Use of larger r values in the approximate entropy algorithm helped to correct for the high noise levels in the data, as this parameter specifies how closely two patterns in the data have to match before being counted as similar.

The net result is that early sitting differs in the anterior-posterior axis, and developed sitting differs in the medial-lateral axis, where typically developing infants have higher entropy in each case. The lag values found that show these differences are relatively short in the time scales usually associated with motor control, lag 4 (16.7 msec) and lag 8 (33.3 msec). Spectral analysis presented in Chapter 4 confirms the existence of higher frequency structure in the sitting postural sway of infants with typical development, and these higher frequency features are not seen in the postural sway of infants with delayed development. The origin of the high frequency features in the sitting COP data from infants with typical development is not clear, but may be due to the utilization of more functional stretch reflexes by infants with typical development, as discussed in more detail in Chapter 4, or due to an ability to perform sensory integration on a faster time scale, as discussed in more detail in Chapter 6.

Chapter 5 probes the fractal nature of early infant postural sway using detrended fluctuation analysis (DFA). Time series with fractal patterns have repeated patterns, but

the patterns are repeated on different time scales. Detrended fluctuation analysis, which involves least squares fitting of the data on different window lengths of the time series data, was used to probe the fractal properties of the time series. The reliance on least squares fitting means that DFA is quite robust to experimental noise and to nonstationarity in the data (Peng, Havlin, Stanley & Goldberger, 1995), important benefits for the infant sitting data set. Differences between early sitting postural sway for infants with typical development and infants with delayed development were seen in the anterior-posterior axis only, consistent with the approximate entropy with larger, more noise resistant, r value finding differences between groups in anterior posterior postural sway in early sitting. The early sitting postural sway of infants with delayed development had higher alpha values than sitting postural sway in the anterior-posterior axis of infants with typical development. The alpha value is related to the slope of a log-log plot of spectral density versus frequency of the time series (Heneghan & McDarby, 2000; note that this paper switches the usual convention of alpha as the DFA parameter and beta as the negative slope of the power spectral density). For example, white noise has equal contributions to the power spectra from all frequencies, so the slope of the log-log plot of the power spectrum is zero (beta = 0), and the alpha value from DFA is 0.5. For pink noise, also known as 1/f noise, the slope of the log-log plot of the power spectra is -1 (beta=1), and the alpha value from DFA is 1.0. For brown noise, so called because it is characteristic of Brownian motion, the slope of the log-log plot of the power spectra is -2 (beta=2), and an alpha value of 1.5. As the high frequency components in a time series decrease, the slope of the log-log plot of the power spectrum decreases, and the alpha value from DFA decreases. The result found from infant sitting DFA presented in

Chapter 5 is that infants with typical development have lower DFA alpha values in early sitting in the anterior-posterior axis. This result is consistent with the increased intensity in the high frequency range that was discussed previously in sitting postural sway for typically developing infants (see Figures 4.11 and 4.12, Chapter 4), and is more pronounced in early sitting in the anterior-posterior axis. The increase in intensity at high frequency reduces the slope of the power spectral density, and the DFA alpha value is reduced.

Chapter 6 used the infant sitting postural sway data to train an artificial neural network (ANN), and then the properties of the network were compared for networks trained with data from infants with typical development and infants with delayed development. The analysis was repeated with different time windows, where position, velocity, and acceleration were calculated for each window, and the ANN was trained to predict acceleration at a future window. In the infant, visual information, vestibular information, proprioceptive information, and cutaneous information are integrated to obtain position, velocity, and acceleration, whereas in the model these kinematic values are calculated from the time series data. Based on the kinematic information, the central nervous system calculates the appropriate response, resulting in muscle contractions. Muscle contractions produce force, and forces produce accelerations via Newton's second law, commonly written as F=ma. Thus the model is a simple feedback control model, where the kinematic values at time t are inputs to the ANN, and acceleration at time $t+\tau$ is the output. Once again, the result was that infants with typical development have a fast component to their postural control that infants with delayed development do not have, perhaps related to sensory integration.

Thus in all of the studies that found statistically significant differences between the two groups, the high frequency component in the postural sway of infants with typical development, and not seen in the postural sway of infants with delayed development, is important in determining the outcome of the analysis. An important question then is what is the physiological mechanism that is giving rise to these higher frequency components in the sitting postural sway of infants with typical development, and/or why is this component missing in the sitting postural sway of infants with delayed development. Most of the infants in the group that has been referred to as having delayed development have delayed development because of cerebral palsy, and the neurological impairments associated with cerebral palsy are likely responsible for the lack of ability to control postural sway with the same short time delays that infants with typical development use.

Children with cerebral palsy have been found to have an increased time to produce a given amount of force in lower extremity movements (Downing, Ganley, Fay, & Abbas, 2009), and patients with dystonia have slower reaction times in a visual stimulus and button-pushing task (Jahanshahi, Rowe, & Fuller, 2001). However, in infant sitting, infants with cerebral palsy do not have a slower latency to perturbation than infants with typical development, rather the control issue is one of inappropriate co-contraction and inappropriate muscle firing coordination (Brogren, Forssberg, Hadders-Algra, 2001). Using diffusion tensor imaging, infants and children with cerebral palsy were found to have more extensive damage to posterior thalamic radiation pathways (sensory processing) than to the descending corticospinal tracts (motor function), and damage to posterior thalamic radiation pathways was better correlated with motor function deficit than damage to descending corticospinal tracts (Hoon, et al, 2009). Thus

poor sensory processing may be important in altered sitting postural control in infants with cerebral palsy.

As discussed in Chapter 6, one commonly used tactic to study postural control involves studying the response to some type of external perturbation. Another type of study uses manipulation of sensory input, such as comparing postural control with open eyes to eyes closed, to study the effect of vision. These strategies may provide misleading information about the control of normal, unperturbed postural control. For example, in perturbation studies a seated subject is exposed to some type of external perturbation, such as a sudden acceleration, and stretch reflex latencies are measured (Granata, Slota, & Bennett, 2004). While this provides insight into postural response to an external perturbation, which may be important in injury in automobile accidents, for example, it does not answer the question as to whether stretch reflexes are important in unperturbed sitting. When visual sensory information is altered, sensory re-weighting occurs within 5-10 seconds (Jeka, Oie, Kiemel, 2008). Thus the postural control system studied is not merely postural control minus the altered sense, but a completely reweighted sensory control system, and the relationship of the reweighted sensory control system to the normal sensory control system is not clear. An advantage of the methods used in this dissertation work is that normal, unperturbed sitting can be studied. A disadvantage of this method is that the sensory system involved in estimations of the position, velocity, and acceleration cannot be identified. Thus the methods of perturbed postural control are complimentary to the unperturbed, unaltered sensory study performed here, with neither providing a complete understanding of the postural control system, and each adding insight that the other fails to give.

The discussion of postural control above, with the emphasis on sensory processing, and in Chapter 4, with the emphasis on stretch reflex, is tacitly assuming that the postural control is a feedback control system. Indeed, there must be a feedback component to postural control. However, feed forward contributions to postural control also occur, and it is possible that the differences between postural control of infants with typical development and infants with delayed development are due to feed forward differences rather than feedback differences. For example, if the infant decides to look over at a toy while sitting, anticipatory postural control can be used to adjust for the change in mass distribution that occurs as the head is moved. Children with cerebral palsy have been shown to have decreased anticipatory postural adjustment skills (Liu, Zaino, McCoy, 2007). More work is needed to understand the underlying mechanisms for the differences we have found in sitting postural control between infants with typical development and infants with delayed development.

A controversy in developmental psychology is whether development is a smooth progression (Kagan, 2008), or whether there are distinct stages and development is a progression from one stage to the next (Spencer & Perone, 2008). The traditional view is that there are distinct stages in human development, such as those described by Piaget (1928/2009). Others argue for a more continuous "developmental cascade" based on evolutionary and developmental biology analogies, and question whether stage theory is a useful description of development (Kagan, 2008). In motor control development there appear to be relatively well defined stages, and achievement of so-called "motor milestones" such as acquiring the ability to sit, then to crawl, then to stand, then to walk, etc. define entry into the next stage (World Health Organization, 2006). Dynamical

systems theory views the developmental process from the stage theory perspective, where stages are attractors. Maturation and developmental changes in response to environmental stimuli move the child to a new basin of attraction, and a new skill emerges as the child then evolves towards the attractor (Smith & Thelen, 2003; Spencer & Perone, 2008). From this perspective, the development of sitting behavior is a phase transition, where lying and rolling behaviors are displayed in the first phase, and sitting behavior is additionally displayed in the second phase, and the infants in this study are going through the phase change.

In developmental psychology then the time scale for the application of dynamical systems theory is on the order of months, as new motor milestones are achieved on this time frame (World Health Organization, 2006). In motor control, dynamical systems theory is also applied, but typically on a shorter time scale. For example, if I wiggle my index fingers on each of my hands, I can maintain an anti-phase relationship only up to a certain frequency, and attempting to wiggle them faster will result in a spontaneous transition to a in-phase (symmetric) relationship, despite my best attempts to maintain the anti-phase relationship (Kelso, 1995). The in-phase attractor basin includes high frequency finger wiggling, where as the anti-phase attractor basin does not include high frequencies. The frequency of the movement is a control parameter, and it helps to define which attractor basin(s) are available. Similarly, the transition from walking to running as the speed increases can be described as a phase transition, with speed being the control parameter (Diedrich & Warren, 1995), although whether increased variability is associated with the walk-run phase transition is controversial (Kao, Ringenbach, & Martin, 2003; Seay, Haddad, van Emmerik, & Hamill, 2006). Phase transitions may have

more variability associated with them, but experimental techniques must be sensitive enough to detect the increased variability.

While the word “sitting” sounds like a single attractor, there were two types of sitting displayed by infants. Typically in early sitting the infants in the study would sit in a “prop sit” position, with the arms on the ground close to hip or mid-thigh and the arms supporting some of the weight, where as in developed sitting typically a more upright posture was used, and the hands rarely touched the ground. In intermediate sitting, the infant might alternate between the two types of sitting, choosing one posture for a while, then the other, and back to the first, etc. This phase transition behavior is reminiscent of phase transitions in materials systems. For example, freezing or melting of water is a phase transition involving transition between frozen and liquid phases, where temperature and pressure are the control parameters. The interface between the two phases is very dynamic on the molecular level during a phase transition. For an individual water molecule near the ice-water interface, the molecule could at any instant be incorporated into the ice crystal (solid phase), and at a later instant be moving in the water (liquid phase), and even later be incorporated back into the ice crystal (solid phase again). One way to describe these dynamics is that the behavior of an individual near where the basins of two attractors meet in phase space is highly variable, and this variability is observed in the infant sitting dynamics as well as the molecular dynamics of the water. We did not do any sort of analysis of the prop sitting versus upright sitting in our study, and the observations discussed above were casual observations made during data collections. However, this transition might be of interest in future studies, as some infants in the developmental delay group never progressed from the prop sitting posture to the

upright sitting posture. For these infants, does the upright sitting attractor never emerge on a developmental time scale, and/or is there a difficulty in making the phase transition to upright sitting on shorter motor control time scales? Despite the apparent simplicity of maintaining sitting posture, it is a complex process, and more work is needed to understand this behavior.

Another interesting aspect of infant sitting postural control is the difference between control in the anterior-posterior axis versus control in the medial-lateral axis. Chapter 3 presents the conclusion that ApEn(m=2, r=3.0*std(Data), t @ 240 Hz, lag=4) found significant differences in infants with delayed versus typical development in developed sitting in the medial-lateral axis. Chapter 4 presents the conclusion that ApEn(m=1, r=1.0*std(Data), t @ 240 Hz, lag=8) found significant differences in infants with delayed versus typical development in early sitting in the anterior-posterior axis. Chapter 5 presents the conclusion that detrended fluctuation analysis found significant differences in infants with delayed versus typical development in early sitting in the anterior-posterior axis, and Chapter 6 presents the conclusion that typical infants rely more on velocity information in control in the anterior posterior axis, whereas control in the medial-lateral axis uses a wider range of types of information, and infants with delayed development do not develop the same reliance on velocity information. Statistical comparisons of measures of postural sway were not performed between medial-lateral and anterior-posterior sway in Chapters 2-5, where entropy measures and fractal measures were addressed. While most of the analyses presented in this dissertation were not really designed to address the differences between control in the medial lateral axis and the anterior-posterior axis, it appears that there are some interesting differences.

Because the postural control that emerges in the medial-lateral axis appears to be different than the control that emerges in anterior-posterior axis, it is of interest to discuss why this might occur. Anatomical differences may be important, for example stretch reflex associated with the hamstring muscle or spinal muscles may be contributing differently to control in the anterior-posterior axis, compared to stretch reflex in the external oblique and other muscles that provide postural control in the medial-lateral axis. Sensory differences may be important. Cutaneous feedback useful to postural control in the medial-lateral axis would include left-right pressure differences, whereas cutaneous feedback useful to postural control in the anterior-posterior axis would include pressure differences from the proximal to distal portions of the posterior surface of the leg. If neural processing of one type of pressure information is more rapid than another, then that may affect control in the corresponding axis. Alternatively, the dynamics of processing of visual information may differ between the two axes, resulting in differences in the postural control that emerges. Visual flow with movement in the anterior-posterior axis more strongly influences postural sway than in the medial-lateral direction in postural sway (Campbell, Vander Linden, & Palisano, 2006, p. 86-87). Given the different anatomical and sensory differences between the anterior-posterior and medial-lateral axes, it is perhaps not surprising that differences in postural control emerge with development. Based on the results presented in Chapter 6, that infants with typical development have larger differences between sensory information usage in the two axes than infants with delayed development, perhaps a useful measure of development and developmental pathology then is not the value of a particular measure, such as approximate entropy, but rather the ratio of that measure in the anterior-posterior axis to

the measure for the medial-lateral axis. While much of the work in the postural control literature examines the control in the medial-lateral axis independently from that in the anterior-posterior axis, as did this work, the sitting infant must accomplish both tasks simultaneously. In this sense, sitting postural control is a dual task, and as in many dual task experiments, an interaction between the tasks might be expected. Infants with typical development might be expected to perform better on a dual task experiment, compared to infants with cerebral palsy. Thus a measure that includes an interaction between the control along the two different axes, such as the entropy ratio described above, could be useful in elucidating differences between these two groups. The work in this dissertation has not satisfied the fundamental need for a useful clinical measure to quantify differences between infants with typical development and infants with delayed development, and to assess progress an infant has made as a result of therapeutic interventions, but perhaps it will provide insight for future researchers who work towards that goal.

CONCLUSION: The nonlinear algorithms discussed in this work require selection of parameters, unlike more straightforward measures such as mean or standard deviation. A significant aspect of this work for nonlinear analysis is that the standard parameters that are often used for the nonlinear analyses are not necessarily optimal for a particular data set. For example, in this work the approximate entropy did not find a significant difference between the postural sway of infants with typical development and infants with delayed development (Chapter 2). However, by searching the parameter space, parameters were found for approximate entropy that did find significant differences between the two populations (Chapters 3 and 4). As another example, the detrended

fluctuation analysis did not find a difference between infants with delayed development and brown noise using the standard linear detrending, but higher order detrending showed that the postural sway of infants with developmental delay is significantly different than brown noise (Chapter 5). The parameters make the analysis sensitive to different aspects of the data, and interpretation of the data needs to be done by relating the parameters to biomechanical and physiological aspects of the data. For example, the large r values used in approximate entropy that are sensitive to differences between the postural sway of infants with delayed versus typical development can be interpreted as differences in large excursions from the mean values, perhaps events where the infant nearly falls over. The short lag parameter can be interpreted as a short latency response, perhaps a stretch reflex. Making a better connection between the mathematical analysis and the biology of the system under study is a challenge for future work.

Postural control was found to be different comparing infants with developmental delay and infants with typical development. Velocity information was found to be more heavily weighted that position or acceleration in postural control in the anterior-posterior axis for infants with typical development, but not for infants with delayed development. For infants with typical development, control in the medial-lateral axis was more complex in that more different types of information were used. Thus differences between anterior-posterior control and medial-lateral control, as an indicator of developmental delay, might be an interesting concept to explore in future work. An important contribution to understanding developmental delay is the finding that postural control occurs on a faster time scale for infants with typical development than it does for infants with developmental delay. This result is a common thread through multiple types of

analyses. Short time lags in approximate entropy (Chapters 3 and 4), high frequency features in spectral analysis (Chapter 4), lower alpha values in detrended fluctuation analysis (Chapter 5), and more explicitly by the time lags used in the artificial neural network analysis (Chapter 6), all are consistent with a faster time scale for postural control in infants with typical development.

Dynamical systems theory has been used to describe infant development, but as described by Kelso (1995), not with much success. Kelso (1995, p. 181) states "Although 'dynamic systems' concepts are part of the intellectual heritage of developmental theory, they have in my view promised much and delivered little. … A more frank assessment is that as scientific theories go, these efforts are pretty barren." Kelso's (1995) complaint about much of the work that has purported to use dynamic systems theory is that proper application of the theory requires the identification of a control parameter. For example, in the phase change from walking to running that occurs as velocity increases, velocity is the control parameter. Kelso (1995, p. 182) cites the work of Ester Thelen as a rare example of making a good effort to apply dynamic systems theory to developmental changes, because she identifies mass (weight gain) as a control parameter that changes resulting in a change in stepping behavior (e.g. Thelen, Ulrich, & Wolf 1991). An important question is what is the control parameter that changes the infant's behavior to upright sitting?

As discussed in Chapter 6, one model of postural control is the inverted pendulum model, where a mass remains positioned above the ground on a vertical rod due to actuators controlled by a feedback controller. If the delay time of the feedback

controller exceeds a critical time delay, then the upright position cannot be maintained. The critical time is given by:

$$t_{critical} = \sqrt{\frac{2L}{3g}} \qquad \text{(equation 7.1)}$$

where L is the distance from ground to the center of mass of the pendulum, and g is the acceleration of gravity, which works out to 260 msec for adult standing (Milton, Cabrera, Ohira, Tajima, Tonosaki, Eurich, & Campell, 2009) . From this formula, the critical delay time for control of an inverted pendulum depends on the size of the pendulum, with taller pendulums able to be controlled using slower response times. For an infant, with a center of mass about 20 cm above the ground, the critical control time is 117 msec.

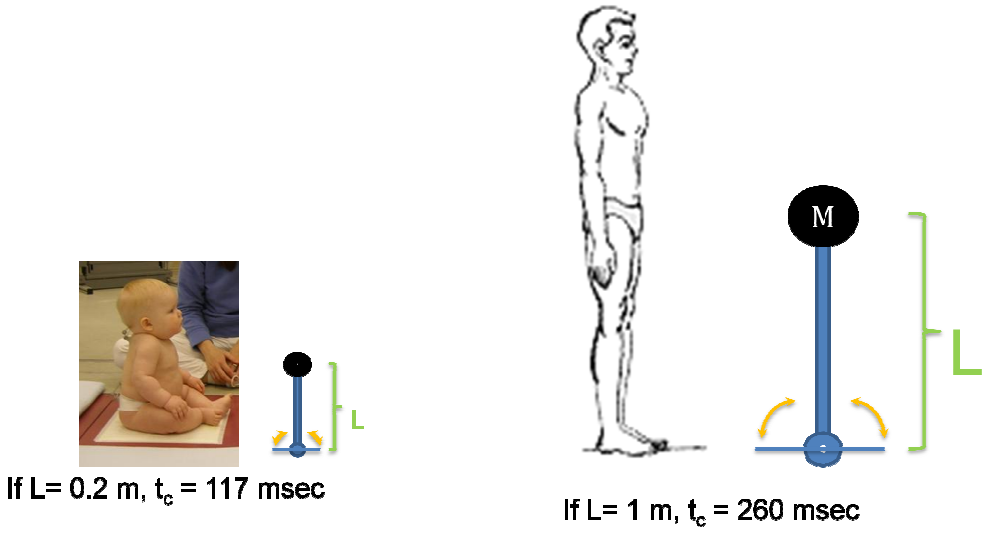

Figure 7.4. The critical control time for the sitting infant is much faster than the critical control time for the standing adult, based on an inverted pendulum model.

Note that none of the significant control time delays for infants with delayed development meet this criterion (Table 6.2). While the inverted pendulum is a very crude model of infant sitting postural control (Kyvelidou, Stuberg, Harbourne, Deffeyes, Blanke, Stergiou, 2009), and ignores what are likely important contributions from the viscoelastic properties of the infant's body as well as the pelvis and spine joints, the inverted pendulum model suggests that an infant who is not able to use fast latency control mechanisms may have a more difficult control problem to solve than infants with typical development.

A hypothesis can be made based on this model that the control parameter is length, and that length must exceed a certain value that can be calculated from the sensorimotor delay time using equation 7.1. The slower sensorimotor time delay, perhaps as a result of neurological damage associated with cerebral palsy, results in a requirement for a longer length to be achieved before upright posture can be controlled. This requirement for a longer length may be a contributing factor to the delay in meeting the upright sitting milestone, for the infants with developmental delay, especially since often they are small for their age. It should be re-emphasized that this is only a hypothesis, but future work on infant sitting with a dynamic systems theory perspective might make an important contribution to understanding the interaction of biomechanics of infant sitting and motor control development.

References

Aziz, W. & Arif, M. (2006). Complexity Analysis of Stride Interval Time Series by Threshold Dependent Symbolic Entropy. European Journal of Applied Physiology, 98, 30-40.

Brogren, E., Forssberg, H., Hadders-Algra, M. (2001). Influence of two different sitting positions on postural adjustments in children with spastic diplegia. Developmental Medicine and Child Neurology, 43, 534-546.

Campbell, S.K., Vander Linden, D.W. & Palisano, R.J. (2006). Physical Therapy for Children, 3rd Ed. Saint Louis, MO: Elsevier.

Diedrich, F.J., Warren, W.H. (1995). Why change gaits? Dynamics of the walk-run transition. Journal of Experimental Psychology: Human Perception and Performance, 21(1), 183-202.

Downing, A.L., Ganley, K.J., Fay, D.R., & Abbas, J.J., (2009). Temporal characteristics of lower extremity moment generation in children with cerebral palsy. Muscle & Nerve, 39(6), 800-9.

Heneghan, C. & McDarby, G. (2000). Establishing the relation between detrended fluctuation analysis and power spectral density analysis for stochastic processes. Physical Review E, 62(5), 6103-6110.

Granata, K.P., Slota, G.P., & Bennett, B.C., (2004). Paraspinal muscle reflex dynamics. Journal of Biomechanics, 37(2), 241-7.

Grassberger, P. & Procaccia, I. (1983). Measuring the strangeness of strange attractors. Physica D, 9, 189 - 208.

Jahanshahi, M., Rowe, J., & Fuller, R., (2001). Impairment of movement initiation and execution but not preparation in idiopathic dystonia. Experimental Brain Research, 140(4), 460-8.

Jeka, J.J., Oie, K.S., & Kiemel, T. (2008). Asymmetric adaptation with functional advantage in human sensorimotor control. Experimental Brain Research, 191(4), 453-463.

Kagan J. (2008). In defense of qualitative changes in development. Child Development, 79(6), 1606-1624.

Kao, J.C., Ringenbach, S.D., & Martin, P.E. (2003). Gait transitions are not dependent on changes in intralimb coordination variability. Journal of Motor Behavior, 35(3), 211-214.

Kelso, J.A.S. (1995). *Dynamic Patterns: The Self-Organization of Brain and Behavior.* Cambridge, MA: The MIT Press.

Liu, W.Y., Zaino, C.A., McCoy, S.W. (2007). Anticipatory postural adjustments in children with cerebral palsy and children with typical development. Pediatric Physical Therapy, 19(3), 188-95.

Milton, J., Cabrera, J.L., Ohira, T., Tajima, S., Tonosaki, Y., Eurich, C.W., & Campbell, S.A., (2009). The time-delayed inverted pendulum: implications for human balance control. Chaos, 19(2), 026110.

Peng, C.-K., Havlin, S., Stanley, H.E./, & Goldberger, S. (1995). Quantification of scaling exponents and crossover phenomena in nonstationary heartbeat time series. Chaos, 5(1), 82-87.

Piaget, J., (2009). La causalite chez l'enfant (Children's understanding of causality). In The British Journal of Psychology, 100, pt1a, 207-224 (original work published in 1928).

Hoon, A.H., Stashinko, E.E., Nagae, L.M., Lin, D.D., Keller, J., Bastian, A., Campbell, M.L., Levey, E., Mori, S., Johnston, M.V. (2009). Sensory and motor deficits in children with cerebral palsy born preterm correlate with diffusion tensor imaging abnormalities in thalamocortical pathways. Developmental Medicine and Child Neurology, 51(9), 697-704.

Kelso, J.A.S. (1995). Dynamic patterns: The self organization of brain and behavior. Cambrige, MA: MIT Press.

Pincus, S.M. (1991). Approximate Entropy as a Measure of System Complexity. Procedings of the National Academy of Sciences, 88, 2297-2301.

Rosenstein, M.T., Collins, J.J. & De Luca, C.J. (1993). A practical method for calculating largest Lyapunov exponents from small data sets. Physica D, 65, 117-134.

Seay, J.F., Haddad, J.M., van Emmerik, R.E., & Hamill, J. (2006). Coordination variability around the walk to run transition during human locomotion. Motor Control,10(2), 178-196.

Shannon, C.E. (1949). Communication in the presence of noise. Proceedings of the Institute of Radio Engineers, 37(1), 10–21, Reprinted in: Proceedings of the IEEE, 86 (2), 447-457, 1998.

Smith L.B. & Thelen E. (2003). Development as a dynamic system. Trends in Cognitive Science, 7(8), 343-348.

Spencer, J.P. & Perone ,S. (2008). Defending qualitative change: the view from

dynamical systems theory. Child Development, 79(6), 1639-1647.

Sprott, J.C., Rowlands, G., 1998. Chaos data analyzer: the professional version. Raleigh, NC: Physics Academic Software.

Thelen, E., Ulrich, B.D., & Wolf, P.H. (1991). Hidden Skills: A Dynamic Systems Analysis of Treadmill Stepping during the First Year. Monographs of the Society for Research in Child Development, 56(1), 1-98.

World Health Organization (2006). WHO Motor Development Study: Windows of achievement for six gross motor development milestones. Acta Paediatrica, Suppl 450, 86-95.

Wolf, A., Swift, J.B., Swinney, H.L., & Vastano, J.A. (1985). Determining Lyapunov exponents from a time series, Physica D, 16, 285-317.

APPENDIX A

MATLAB CODE FOR ANALYSIS OF INFANT SITTING POSTURAL SWAY

A.1. LINEAR ANALYSIS

This file is the main analysis function used for the NIDRR project that does all the linear analysis, calls approximate entropy, and also saves .dat files that CDA can read for LyE, etc, analysis

```
function [ProblemFlag]=AnalysisFunction(Filename, Pathname, StartVector, EndVector,...
        HeadVector, ArmsVector, LegsVector, TrunkVector, Print)


% AnalysisFunction performs analyses for NIDRR baby COP data.
%   AnalysisFunction(Filename, Pathname, StartVector, EndVector)
%   Call the function with the above syntax. StartVector and
%   EndVector are the start and end points (in 60 Hz Frames)
%   for each of the segments of interest in the file FileName.
%   Results are appended to BabyResults.dat that Excel can read.
%
%   The linear analysis is performed per Prieto, et al (1996)
%   IEEE Transactions on Biomedical Engineering, 43(9) 956-966,
%   except the window used in frequency analysis is a Hanning
%   window rather than the multi-taper method Prieto used.
%   The approximate entropy is from code the Max Kurz gave me,
%   which he apparently got off the internet. See comments in
%   that file for details. Also .dat files are saved so CDA
%   can read them (CDA is used to get Lyapunov exponent,
%   Correlation Dimension, and Hurst eponent in NIDRR study).
%
%   The files OpenCSVFIleFromMMI.m and apentropy.m need to be
%   in MatLab's path for AnalysisFunction to run.
%
%   The COP data is assumed to have been taken at 240 Hz, and the
%   video frames were at 60 Hz.
%
%   2005 Joan Deffeyes

ProblemFlag=0;
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%% Open file
FileData=importdata([Pathname,'\',Filename],'x');

%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%% Find COP data in
file
```

```
InputDataStart=1000000;
for i=(floor(length(FileData)/2)-10):(length(FileData)) %
   if length(FileData{i})==12
      if min(FileData{i}=='FORCE PLATES')==1
         InputDataStart=i+10; % to skip past text lines
      end
   end

   if i>InputDataStart  %% read in COPx and COPy

      %% Start by searching for COPx and COPy in each line of data
      CommaFinder=FileData{i}==',';
      Digit='0';
      for j= 1:5
         if CommaFinder(j)==0
            Digit(j)=FileData{i}(j);
         end
      end

      StartCOPx=0;
      StartCOPy=0;
      EndCOPx=0;
      EndCOPy=0;
      for j=15:45
         if CommaFinder(j-2)==1 & CommaFinder(j-1)==1 & CommaFinder(j)==0
            StartCOPx=j;
         elseif CommaFinder(j-2)==0 & CommaFinder(j-1)==1 & ...
               CommaFinder(j)==0  & StartCOPy==0
            StartCOPy=j;
            EndCOPx=j-2;
         elseif CommaFinder(j-2)==0 & CommaFinder(j-1)==1 & ...
               CommaFinder(j)==0 & StartCOPy~=0
            EndCOPy=j-2;
         end
      end

      %% Now read out the COPx and COPy for the line i
      %% If it crashes here, use Notepad to check the last couple of
      %% lines of the problem file. If there is no data in them, delete
      %% the lines and re-save the file.
      DataPointNumber(i-InputDataStart)= str2num(Digit);
      COPx(i-InputDataStart)=str2num(FileData{i}(StartCOPx:EndCOPx)); %Crash- see above  note
      COPy(i-InputDataStart)=str2num(FileData{i}(StartCOPy:EndCOPy));
   end
end
%% Note i is line number on the spread sheet
%%  DataPointNumber is the number in the first column
%%  time should correspond to DataPointNumber/240
%%    since data collection is at 240 hz
%%  StartPoint and EndPoint are DataPointNumbers
%%    for user selected range
%%  StartPointIndex and EndPointIndex are
%%    the indices into the array which holds COPx andCOPy
%%    for the user selected range

TrialNumber=str2num(Filename(length(Filename)-5:length(Filename)-4));
```

```
Names=[ 'a' 'b' 'c' 'd' 'e' 'f' 'g' 'h' 'i' 'j' 'k' 'l' 'm' 'n'];

for NumberOfSegs=1:length(StartVector);

   %%%%%%%%%%%%%% Select data range
   Screen = get(0,'ScreenSize');
   figure
   set(gcf,'Position',[Screen(3)/2+20 40 Screen(3)/2-20 Screen(4)-120]);

   subplot(2,1,1)
   plot(DataPointNumber/4,COPx,'b'); hold on
   plot(DataPointNumber/4,COPy,'g');
   xlabel('Frame Number')
   ylabel('COP Value (mm)')
   title(['Filename:',Filename,'  Blue=COPx; Green=COPy'])



   %%% DataPointNumber

   StartPoint=4*StartVector(NumberOfSegs);
   EndPoint=4*EndVector(NumberOfSegs);

   %% At this point, StartPointIndex is the same as StartPoint.
   %% Historically in this code they were different, and it
   %% doesn't seem worthwile to go change them now.
   StartPointIndex=find(DataPointNumber==StartPoint);
   EndPointIndex=find(DataPointNumber==EndPoint);

   if isempty(EndPointIndex) % problems with file loading!!!
      disp('Problems with file')
      LastDataPoint=max(DataPointNumber)
      EndPoint
      ProblemFlag=124;
   end

   subplot(2,1,1)
   plot(.25*(StartPoint:EndPoint), COPx(StartPointIndex:EndPointIndex),'r','LineWidth',3);
   plot(.25*(StartPoint:EndPoint), COPy(StartPointIndex:EndPointIndex),'r','LineWidth',3); hold off


   %%  The COPd is a distance term
   COPxNew=COPx(StartPointIndex:EndPointIndex)-mean(COPx(StartPointIndex:EndPointIndex));
   COPyNew=COPy(StartPointIndex:EndPointIndex)-mean(COPy(StartPointIndex:EndPointIndex));
   COPdNew=sqrt(COPxNew.^2+COPyNew.^2) ;%per Prieto(1996)

   subplot(2,1,2)
   plot(.25*(StartPoint:EndPoint),COPdNew,'r');
   xlabel('Frame Number')
   ylabel('COPd Value (mm)')
   title(['Range: ',num2str(StartPoint/4),' to ',num2str(EndPoint/4),...
         '  from: ',Filename,'...',Names(NumberOfSegs)])

   if Print==1
      print
      close
```

```
elseif Print==2
   saveas(gcf,[Pathname,'\',Filename(1:length(Filename)-4),...
         Names(NumberOfSegs),'TimeSeries.jpg'], 'jpg')

   close
end



%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%Save data range selected
%% Three data types are saved - COPx, COPy, and COPd.


if Pathname(1)=='E'
   [NewFilename, Pathname] = uiputfile('.dat', 'Select Location for SAVE');
   if NewFilename~='.dat'
      Filename=NewFilename;
   end
end

for DataType=1:3
   if DataType==1
      Suffix='COPx.dat';
      NewData=COPx(StartPointIndex:EndPointIndex);
   elseif DataType==2
      Suffix='COPy.dat';
      NewData=COPy(StartPointIndex:EndPointIndex);
   elseif DataType==3
      Suffix='COPd.dat';
      NewData=COPdNew;
   end
   SaveDATfile = [Filename(1:length(Filename)-4),...
         Names(NumberOfSegs),Suffix];
   fid = fopen([Pathname,'\', SaveDATfile],'w');

   for k=1:length(NewData)
      fprintf(fid,'%f\r\n',NewData(k));
   end
   fclose(fid);
end



%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%%%%%%%%%%%%%   LINEAR ANALYSES
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%

%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%

%%%%% Root Mean Square (x,y,d) - i.e. Standard deviation
%% Prieto equations 6 and 7, p 958.
RMSxMM=sqrt((1/length(COPxNew))*sum(COPxNew.^2)); %Prieto divides by n, not (n-1)
RMSyMM=sqrt((1/length(COPyNew))*sum(COPyNew.^2)); %Prieto divides by n, not (n-1)
RMSdMM=sqrt((1/length(COPdNew))*sum(COPdNew.^2))  %Prieto divides by n, not (n-1)
```

```
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%%%%%%%%%%
   %%%%% Range Anterior-Posterior
   RangeAPinMM=max(COPxNew)- min(COPxNew)


%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%%%%%%%%%%
   %%%%% Range Medial-Lateral
   RangeMLinMM=max(COPyNew)- min(COPyNew);


%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%%%%%%%%%%
   %%%%% Sway Path
   SwayPathMM=sum(abs(diff(COPdNew)))


%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%%%%%%%%%%
   %%%%% Area of 95% Confidence Circle
   % Note COPd data are the radii
   % Find 95% of radii below 95%Radius, i.e. one sided test
   % Distribution of radii is not a normal distribution, but
   % for now use 1.645 from the normal pdf. Chi-square pdf needed?
   % Prieto assumes normal distribution
   NintyFivePercentRadius=mean(COPdNew)+1.645*std(COPdNew);
   CircleAreaMM2=pi*NintyFivePercentRadius^2

%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%%%%%%%%%%
   %%%%% Area of 95% Confidence Ellipse per Prieto (1996)
   %%%%%%% from Sokal and Rohlf (1995) Biometry p589, cited by Prieto.

   sAP= sqrt((1/length(COPxNew))*sum(COPxNew.^2)); %Prieto
   sML= sqrt((1/length(COPyNew))*sum(COPyNew.^2)); %Prieto
   sAPML= (1/length(COPxNew))*sum(COPxNew.*COPyNew); %Prieto

   PrietoF=3;

   % Note Prieto has missed squaring the sum of the first two terms
   %  in his equation(16) page 959.
   % This equation is actually from Sokal and Rohlf (1995).
   PrietoD= sqrt((sAP^2+sML^2)^2-4*(sAP^2*sML^2-sAPML^2));

   PrietoEllipseRadiusA= sqrt(PrietoF*(sAP^2+sML^2+PrietoD)); %Prieto eq 14
   PrietoEllipseRadiusB= sqrt(PrietoF*(sAP^2+sML^2-PrietoD)); %Prieto eq 15
   EllipseAreaMM2= 2*pi*PrietoF*sqrt(sAP^2*sML^2-sAPML^2) %Prieto eq 18

   %Calculate these for plot
   PrietoLambda1=(sAP^2+sML^2+PrietoD)/2; % from Sokal and Rohlf
   PrietoSlope=sAPML/(PrietoLambda1-sML^2); % from Sokal and Rohlf
   PrietoAngle=atan(PrietoSlope);
```

```
%%%%%%%%%%%%%% Area of Ellipse
%Plot data in green
figure
set(gcf,'Position',[20 Screen(4)/2 Screen(3)/2-20 Screen(4)/2-120]);

plot(COPxNew,COPyNew,'.g'); hold on

Theta=(pi/180)*linspace(0,360);

%%%Now add circle to plot
x1=NintyFivePercentRadius.*cos(Theta);
y1=NintyFivePercentRadius.*sin(Theta);

plot(x1,y1,'b');


%%%Now add ellipse to plot
x1=PrietoEllipseRadiusA.*cos(Theta);
y1=PrietoEllipseRadiusB.*sin(Theta);

OrientRad=PrietoAngle;

x2=x1*cos(OrientRad)-y1*sin(OrientRad);
y2=x1*sin(OrientRad)+y1*cos(OrientRad);

plot(x2,y2,'r'); hold off

% make plot pretty
title(strcat('Green=data, Blue=95% circle, Red=95% Ellipse',...
   Filename,'...',Names(NumberOfSegs)));
xlabel('COPx')
ylabel('COPy')
axis image

if Print==1
   print
   close
elseif Print==2
   saveas(gcf,[Pathname,'\',Filename(1:length(Filename)-4),...
          Names(NumberOfSegs),'CircleEllipse.jpg'], 'jpg')
   close
end


%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
   %%%%%%%%%%%%%%  Frequency Domain Analyses %%%%%%%%%%%%%%%%%%

%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
   % Prieto, et al (1996) use a sinusiodal multitaper method with
   %  eight tapers for their spectral analyses. They cite Riedel and
   %  Sidorenko(1995), Minimum Bias Multiple Taper Spectral Emission.
   %  IEEE Transactions on Signal Processing 43(1) 188-195.
```

```
%  My implementation follows the equation
%  in paragraph 4, page 188 of Riedel and Sidorenko.

N=length(COPdNew);
n=1:N;
TaperWindow=0.5*(1-cos(2*pi*((n-1)/(N-1))));
WindowedData=(COPdNew.*TaperWindow);


TransformFFT=fft(WindowedData);

if length(TransformFFT)/2 ~= floor(length(TransformFFT)/2) % test for n even
   TransformFFT=TransformFFT(1:length(TransformFFT)-1); % if odd, toss one data point.
end

Spectrum=TransformFFT(1:length(TransformFFT)/2).*...
   conj(TransformFFT(1:length(TransformFFT)/2));

% This is why the index starts at 3 (so points 1 and 2 are removed)
% The big difference is here a Hanning window is used,
%  whereas Prieto used a multitaper method.
f=(.5/length(Spectrum))*240*(1:length(Spectrum));

figure
set(gcf,'Position',[20 40 Screen(3)/2-20 Screen(4)/2-120]);

subplot(3,1,1); plot(f,Spectrum);
title(strcat('Power Spectrum:',Filename,'...',Names(NumberOfSegs)));
% xlabel('Frequency (Hz)');
ylabel('Arbitrary Units');


subplot(3,1,2); plot(f,Spectrum);
title(strcat('Power Spectrum (60 Hz signal):',Filename,'...',Names(NumberOfSegs)));
% xlabel('Frequency (Hz)');
ylabel('Arbitrary Units');
SpectrumIndices=find(f>40 & f<80);
PlotMax=max(Spectrum(SpectrumIndices));
axis([50 70 0 PlotMax]);

subplot(3,1,3); plot(f,Spectrum);
title(strcat('Power Spectrum (to 5 Hz):',Filename,'...',Names(NumberOfSegs)));
xlabel('Frequency (Hz)');
ylabel('Arbitrary Units');
axis([0 5 0 max(Spectrum)]);

if Print==1
   print
   close
elseif Print==2
   saveas(gcf,[Pathname,'\',Filename(1:length(Filename)-4),...
         Names(NumberOfSegs),'Spectrum.jpg'], 'jpg')
   close
end
```

```
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%%%%%%%%%%
  %%%%% Median Frequency
  % Note Prieto discards the first two points in the spectra
  % and only uses data to 5 Hz. We have frequencies up at 7, so
  % cutoff here is at 10 Hz - to avoid 60 Hz noise
  % when doing power spectral densities. See left-top of p 960
  FreqIndex=1;
  while f(FreqIndex)<10
    FreqIndex=FreqIndex+1;
  end
  AnalysisSpectrum=Spectrum(3:FreqIndex);
  AnalysisFrequency=f(3:FreqIndex);

  CumSumPower=cumsum(AnalysisSpectrum);
  FindMedian=find(CumSumPower>.5*sum(AnalysisSpectrum));
  MedianIndex=min(FindMedian);

  MedianFrequencyHz=(.5/length(Spectrum))*240*MedianIndex


%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%%%%%%%%%%
  %%%%% Frequency Dispersion


  Mu0=(1/length(AnalysisSpectrum))*sum(AnalysisSpectrum);
  Mu1=(1/length(AnalysisSpectrum))*sum(AnalysisSpectrum.*AnalysisFrequency);
  Mu2=(1/length(AnalysisSpectrum))*sum(AnalysisSpectrum.*AnalysisFrequency.^2);


  FrequencyDispersion=sqrt(1-Mu1^2/(Mu0*Mu2))


%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%%%%%%%%%%
  %%%%% Approximate Entropy

  ApproxEntropyD=apentropy(COPdNew)
  ApproxEntropyX=apentropy(COPxNew)
  ApproxEntropyY=apentropy(COPyNew)


%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%%%%%%%%%%
  %%%%%%%%%%%%%    Save Results to File   %%%%%%%%%%%%%%%%%%%%%%

%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%%%%%%%%%%

  FilenameProblem=0;
  if Filename(1)=='T' % Typically Developing
    SubjectType(1)=0;
  elseif Filename(1)=='C' % Cerebral Palsy
```

```
   SubjectType(1)=1;
elseif Filename(1)=='H' % Hypotonic
   SubjectType(1)=2;
else
   disp('Error in filename - SubjectType, data not saved')
   FilenameProblem=1;
end


RestOfFilename=Filename(2:length(Filename)-4);


SubjectNumber=str2num(RestOfFilename(1:2));
if isempty(SubjectNumber)
   disp('Error in filename - SubjectNumber, data not saved')
   FilenameProblem=1;
   ProblemFlag=414
end

DataMonth=str2num(RestOfFilename(4:5));
if isempty(DataMonth)
   disp('Error in filename - DataMonth, data not saved')
   FilenameProblem=1;
   ProblemFlag=421
end

DataDay=str2num(RestOfFilename(7:8));
if isempty(DataDay)
   disp('Error in filename - DataDay, data not saved')
   FilenameProblem=1;
   ProblemFlag=428
end

DataYear=str2num(RestOfFilename(10:11));
if isempty(DataYear)
   disp('Error in filename - DataYear, data not saved')
   FilenameProblem=1;
   ProblemFlag=435
end
NS=N-1; % number of time steps= number of points minus 1.
DataToSave=[SubjectType, SubjectNumber, DataMonth, DataDay, DataYear, ...
      TrialNumber, NumberOfSegs, DateNum(Date)-693960,... %excel date format
      RMSxMM, RMSyMM, RMSdMM, RangeAPinMM, RangeMLinMM, ...
      SwayPathMM, CircleAreaMM2, EllipseAreaMM2, ...
      MedianFrequencyHz, FrequencyDispersion, ApproxEntropyD,...
      ApproxEntropyX,ApproxEntropyY, NS,...
      StartVector(NumberOfSegs),EndVector(NumberOfSegs),...
      HeadVector(NumberOfSegs), ArmsVector(NumberOfSegs),...
      LegsVector(NumberOfSegs), TrunkVector(NumberOfSegs)];

% stop execution if there is a problem
if ProblemFlag~=0 | length(DataToSave)~=28
   disp('Problem saving the data - analysis function line 449')
   return
end
```

```
    % Look for file named "BabyResults.dat"
    Directory=dir(Pathname);
    NumberOfItems=length(Directory);
    FileFound=0;
    for i=3:NumberOfItems
       if length(Directory(i).name)==length('BabyResults.dat')
          if Directory(i).name=='BabyResults.dat'
             FileFound=1;
          end
       end
    end

    if FileFound==1;  % open existing file
       CurrentFile= importdata([Pathname,'\','BabyResults.dat']);
       SaveFile=[CurrentFile;DataToSave];
    else
       SaveFile=DataToSave;
    end

    csvwrite([Pathname,'\','BabyResults.dat'], SaveFile);


end
```

A.2. SYMBOLIC ENTROPY ANALYSIS

The approximate entropy was calculated with Kaplan code that was available on his web site. This is the symbolic entropy code.

```
function [NCSE] = SymEntropy(Data,Thres,WordLen)

% Symbolic Entropy
% Based on: Aziz & Arif, Eur J Appl Physiol (2006) 98: 30-40.
% SymEntropy(Data,Thres,WordLen)
%   Data is the time series data
%   Thres is the threshold value
%   WordLen is the length of the word

% Check that data is a column vector
if size(Data,1)>1
   Data=Data';
end

Scale=2.^[WordLen-1:-1:0]; % for binary conversion

SymSeq=Data>=Thres; % Step 1 from Aziz & Arif

for i=1:(length(SymSeq)-WordLen+1)
   Word=SymSeq(i:i+WordLen-1); % Step 2

   WordCode(i)=sum(Word.*Scale); % Step 3
end

%% Calculate probabilities
for i=1:8
   p(i)=length(find(WordCode==(i-1)));
end

p=p/length(WordCode);% Probabilities sum to 1

% calculate Shannon Entropy
NonZeros=find(p); % don't include p=0 values
SE= -sum(p(NonZeros).*log2(p(NonZeros))); % Equation 4

% Calcualte corrected Shannon Entropy

Cr=length(unique(WordCode)); %number of occuring words
M= 2^WordLen; %Total number of words possible

CSE=SE + (Cr-1)/2*M*log(2); % Equation 5

CSEmax=-log2(1/M)+(M-1)/2*M*log(2); % Equation 6

% Normalized Corrected Shannon Entropy

NCSE=CSE/CSEmax; % Equation 7
```

DETRENDED FLUCTUATION ANALYSIS

The DFA was performed two ways – with a linear fit to the F vs window size, and with a third order fit and an analytical derivative evaluated in the middle of the plot. Below is the third order fit method (NonlinearDFA3), and below it is the liner fit method (NonlinearDFA).

```
function [alpha, Resids]= NonlinearDFA3(DataInput,Order,varargin)
% Do DFA using polynomial of selected order
% alpha= NonlinearDFA(Data,Order)
% alpha= NonlinearDFA(Data,Order,Plot,PlotTitle)
%       Plot = 0 no plot made (defalt)
%       Plot = 1 to get plot and see fit
%       PlotTitle is a string
% Variables: LengthWin: size of current window
%           NumWin: number of windows of this size
%            i : index into level
%            j : index across time -position of the current window


if isempty(varargin)
   MakePlot=0; % defalt is for no plot
else
   MakePlot=varargin{1};
   PlotTitle=varargin{2};
end

% Integrate data first
Data=cumsum(DataInput);
% Check for row vector
if size(Data,1)>size(Data,2)
   Data=Data';
end

LengthWin=length(Data); %will get divided by 2 in loop
i=1;
%while LengthWin >= 2*2^Order % higher order needs longer data sets?
while LengthWin >= 8
   NumWindows=floor(length(Data)/LengthWin);
   for j=1:NumWindows
      LowerIdx=(j-1)*LengthWin+1;
      UpperIdx=j*LengthWin;
      Fwin(j)=CalcResids(Data(LowerIdx:UpperIdx),Order);
   end

   n(i)=LengthWin; % n collects the window length used
   F(i)=mean(Fwin); % F collects the F function results
   i=i+1; % Update index into level
   LengthWin=floor(LengthWin/2);% reset for next level
end

pCoeffs=polyfit(log(n),log(F),3); % third order fit
% for slope take derivative and evaluate at middle of plot
Middle=floor(length(n)/2);
MidVal=mean([n(Middle),n(Middle+1)]);
alpha=3*pCoeffs(1)* log(MidVal)^2+ 2*pCoeffs(2)*log(MidVal)+pCoeffs(3);
```

```
if MakePlot==1
   %figure
   nVals=linspace(min(n),max(n),500);
   FitData=exp(polyval(pCoeffs,log(nVals)));
   loglog(n,F,'ok','MarkerFaceColor','k'); hold on

   %%%%%%%%% Plot pt where slope is evaluated, and slope line
   % plot([MidVal,MidVal],[F(1),F(end)],'g:');
   yVal=polyval(pCoeffs,log(MidVal));
   SlopeLineData=exp(polyval([alpha,yVal-alpha*log(MidVal)],log(n)));

   % loglog(n(Middle-1:Middle+2), SlopeLineData(Middle-1:Middle+2),'g');
   loglog(n(Middle:Middle+2), 2*SlopeLineData(Middle:Middle+2),...
      'Color',[.7 .7 .7],'LineWidth',5); %Plot line with slope alpha in middle
   loglog(nVals, FitData,'k:'); %fit data
   loglog(n,F,'ok','MarkerFaceColor','k');

   % plot pt where slope is calculated
   %loglog(MidVal,exp(yVal),'kd','MarkerSize',5);

   xlabel('n','FontSize',16)
   ylabel('F','FontSize',16)
   if isempty(PlotTitle)
   else
      title([PlotTitle,'  Order for DFA=',num2str(Order),...
         '  alpha=',num2str(alpha)])
   end
   disp('Hit return to continue')
   %pause
   %close
end

yVal=polyval(pCoeffs,log(MidVal));
SlopeLineData=exp(polyval([alpha,yVal-alpha*log(MidVal)],log(n)));
Resids=sum((log(F)-log(SlopeLineData)).^2);
% figure
% loglog(n,F,'o'); hold on
% loglog(n,SlopeLineData,'og')
% legend('Data','Fit To Data')
% title(['SumSquareError=',num2str(Resids)]);
```

```
function [alpha, Resids]= NonlinearDFA(DataInput,Order,varargin)
% Do DFA using polynomial of selected order
% alpha= NonlinearDFA(Data,Order)
% alpha= NonlinearDFA(Data,Order,Plot)
%       Plot = 0 no plot made (defalt)
%       Plot = 1 to get plot and see fit

% Variables: LengthWin: size of current window
%           NumWin: number of windows of this size
%            i : index into level
%            j : index across time -position of the current window


if isempty(varargin)
   MakePlot=0; % defalt is for no plot
elseif length(varargin)==2
   MakePlot=varargin{1};
   PlotTitle=varargin{2};
end

% Integrate data first
Data=cumsum(DataInput);
% Check for row vector
if size(Data,1)>size(Data,2)
   Data=Data';
end

LengthWin=length(Data); %will get divided by 2 in loop
i=1;
%while LengthWin >= 2*2^Order % higher order needs longer data sets?
while LengthWin >= 8
   NumWindows=floor(length(Data)/LengthWin);
   for j=1:NumWindows
      LowerIdx=(j-1)*LengthWin+1;
      UpperIdx=j*LengthWin;
      Fwin(j)=CalcResids(Data(LowerIdx:UpperIdx),Order);
   end

   n(i)=LengthWin; % n collects the window length used
   F(i)=mean(Fwin); % F collects the F function results
   i=i+1; % Update index into level
   LengthWin=floor(LengthWin/2);% reset for next level
end

pCoeffs=polyfit(log(n),log(F),1);
alpha=pCoeffs(1);

if MakePlot==1
   FitData=exp(polyval(pCoeffs,log(n)));
   loglog(n,F,'ok','MarkerFaceColor','k'); hold on
   loglog(n, FitData,'k:');

   loglog(n(3:end-2), 2*FitData(3:end-2), 'Color',[.7 .7 .7],'LineWidth',5);

   xlabel('n','FontSize',16)
   ylabel('F','FontSize',16)
```

```
%     title([PlotTitle,'  Order for DFA=',num2str(Order),...
%         '  alpha=',num2str(alpha)])
end

FitData=exp(polyval(pCoeffs,log(n)));
Resids=sum((log(F)-log(FitData)).^2);
% figure
% loglog(n,F,'o'); hold on
% loglog(n,FitData,'og')
% legend('Data','Fit To Data')
% title(['SumSquareError=',num2str(Resids)]);
```

A.4. ARTIFICIAL NEURAL NETWORK

The code for the artificial neural network includes a script that takes the COP data, chops it into windows, calculates the position, velocity, and acceleration for that window, and then saves the results. The main script then reads the file created, and calls BabyANNFunctCh5.m that does the ANN calculation. All three files are listed below.

```
%% Opens all files in a directory, calculates an average position,
%%  velocity, and acceleration for each group of 24 data points.
%%  This data will be used to train the neural network.
clear all

load cpData
load tdData


idxCpAP=find(cpFilenames(:,21)=='x');
idxCpML=find(cpFilenames(:,21)=='y');

idxTdAP=find(tdFilenames(:,21)=='x');
idxTdML=find(tdFilenames(:,21)=='y');

cpSubjs=unique(cpFilenames(:,1:3),'rows');
tdSubjs=unique(tdFilenames(:,1:3),'rows');

for s=1:length(cpSubjs)
   idxSubj=strmatch(cpSubjs(s,:),cpFilenames(:,1:3));
   Year=str2num(cpFilenames(idxSubj,11:14));
   Month=str2num(cpFilenames(idxSubj,5:6));
   Day=str2num(cpFilenames(idxSubj,8:9));
   Date=365*(Year-2005)+31*Month+Day;
   DayF=find(Date==min(Date)); %First day
   DayL=find(Date==max(Date)); % last day

   idxCPFirstDay{s,1}= intersect(idxSubj(DayF),idxCpAP);
   idxCPLastDay{s,1}= intersect(idxSubj(DayL),idxCpAP);
   idxCPFirstDay{s,2}= intersect(idxSubj(DayF),idxCpML);
   idxCPLastDay{s,2}= intersect(idxSubj(DayL),idxCpML);



end

for s=1:length(tdSubjs)
   idxSubj=strmatch(tdSubjs(s,:),tdFilenames(:,1:3));
   Year=str2num(tdFilenames(idxSubj,11:14));
   Month=str2num(tdFilenames(idxSubj,5:6));
   Day=str2num(tdFilenames(idxSubj,8:9));
   Date=365*(Year-2005)+31*Month+Day;
   DayF=find(Date==min(Date)); %First day
   DayL=find(Date==max(Date)); % last day

   idxTDFirstDay{s,1}= intersect(idxSubj(DayF),idxTdAP);
   idxTDLastDay{s,1}= intersect(idxSubj(DayL),idxTdAP);
```

```
    idxTDFirstDay{s,2}= intersect(idxSubj(DayF),idxTdML);
    idxTDLastDay{s,2}= intersect(idxSubj(DayL),idxTdML);


end


save idxFirstLastDays  idxCPFirstDay idxCPLastDay idxTDFirstDay idxTDLastDay


%% %%%%%%%%% now load files and calculate
clear all
load cpData
load tdData
load idxFirstLastDays
Lag=20;
idxAll=0;
for DataType=1:4
    for Side=1:2 % 1=AP,2=ML
        if DataType==1
            Idxs=idxCPFirstDay;
        elseif DataType==2
            Idxs=idxCPLastDay;
        elseif DataType==3
            Idxs=idxTDFirstDay;
        elseif DataType==4
            Idxs=idxTDLastDay;
        end


        for Subj=1:length(Idxs)

            if DataType==1 | DataType==2
                Datas=cpData(:,Idxs{Subj,Side});
                SN=cpFilenames(Idxs{Subj,Side},1:3);

            elseif DataType==3 | DataType==4
                Datas=tdData(:,Idxs{Subj,Side});
                SN=tdFilenames(Idxs{Subj,Side},1:3);
            end

            for Trial=1:size(Datas,2)
                idxAll=idxAll+1;
                SubjNames(idxAll,:)=SN(1,:); % collect subject names
                DataTypes(idxAll)=DataType; % collect type of data
                AxisAPML(idxAll)=Side;

                % select data to be choppped up
                Data=Datas(:,Trial)-mean(Datas(:,Trial));


                DataChops=floor(length(Data)/Lag);
                for k=1:DataChops
                    ThisData=Data(Lag*k-(Lag-1):Lag*k);
```

```
            Vel=diff(ThisData);
            Accel=diff(Vel);

            Position(k,idxAll)=mean(ThisData);
            Velocity(k,idxAll)=mean(Vel);
            Acceler(k,idxAll)=mean(Accel);

        end


      end
    end
  end
end

%Save chopped data and info on each trial
 save DataForBabyANNChapter5Lag20 Position Velocity Acceler SubjNames DataTypes AxisAPML
```

```
% %% Main program calls BabyANNFunctCh5 to do ANN analysis for each file
clear all


% N= number of neurons in hidden layer
N=6;

%%%%%%%%%%%%%%%%%% Load training data
% this data was calculated from the center-of-pressure data
% see BabyPosVelAccer4ANNChapt5.m code for details
Lag=[8, 12, 20, 32, 45, 60, 64, 70, 80, 90, 120, 180];
for L=1:length(Lag)
   if L==1
      load DataForBabyANNChapter5Lag8
   elseif L==2
      load DataForBabyANNChapter5Lag12
   elseif L==3
      load DataForBabyANNChapter5Lag20
   elseif L==4
      load DataForBabyANNChapter5Lag32
   elseif L==5
      load DataForBabyANNChapter5Lag45
   elseif L==6
      load DataForBabyANNChapter5Lag60
   elseif L==7
      load DataForBabyANNChapter5Lag64
   elseif L==8
      load DataForBabyANNChapter5Lag70
   elseif L==9
      load DataForBabyANNChapter5Lag80
   elseif L==10
      load DataForBabyANNChapter5Lag90
   elseif L==11
      load DataForBabyANNChapter5Lag120
   elseif L==12
      load DataForBabyANNChapter5Lag180
   end
   % % Rescale
% rescale for Norm ; Rescaling in BabyANNFunctChapt5 turned off
   Acceler=(Acceler-mean(Acceler(:)))/std(Acceler(:));
   Velocity=(Velocity-mean(Velocity(:)))/std(Velocity(:));
   Position=(Position-mean(Position(:)))/std(Position(:));

   % do ANN analysis
   PlotIt=0; %=1 make plot, =0 no plot
   for Trial=1:size(Position,2);
      TrainIn=[Position(:,Trial),Velocity(:,Trial),Acceler(:,Trial)];
      [Weights1(:,:,Trial),Weights2(:,Trial),...
         TimesThruLoop(Trial),Redo(Trial)]=BabyANNFunctCh5(TrainIn,N,PlotIt);
      ResultPVA(Trial,1:3)=(Weights1(:,:,Trial)*Weights2(:,Trial))';
      disp(['Trial ',num2str(Trial),' done.  Lag=', num2str(Lag(L))])
   end

   if L==1
      save ANNResultsCh5NormLag8  Weights1 Weights2 TimesThruLoop ResultPVA Redo
   elseif L==2
```

```
      save ANNResultsCh5NormLag12 Weights1 Weights2 TimesThruLoop ResultPVA Redo
    elseif L==3
      save ANNResultsCh5NormLag20 Weights1 Weights2 TimesThruLoop ResultPVA Redo
    elseif L==4
      save ANNResultsCh5NormLag32 Weights1 Weights2 TimesThruLoop ResultPVA Redo
   elseif L==5
      save ANNResultsCh5NormLag45 Weights1 Weights2 TimesThruLoop ResultPVA Redo
   elseif L==6
      save ANNResultsCh5NormLag60 Weights1 Weights2 TimesThruLoop ResultPVA Redo
   elseif L==7
      save ANNResultsCh5NormLag64 Weights1 Weights2 TimesThruLoop ResultPVA Redo
   elseif L==8
      save ANNResultsCh5NormLag70 Weights1 Weights2 TimesThruLoop ResultPVA Redo
   elseif L==9
      save ANNResultsCh5NormLag80 Weights1 Weights2 TimesThruLoop ResultPVA Redo
   elseif L==10
      save ANNResultsCh5NormLag90 Weights1 Weights2 TimesThruLoop ResultPVA Redo
   elseif L==11
      save ANNResultsCh5NormLag120 Weights1 Weights2 TimesThruLoop ResultPVA Redo
   elseif L==12
      save ANNResultsCh5NormLag180 Weights1 Weights2 TimesThruLoop ResultPVA Redo
   end


   clear Weights1 Weights2 TimesThruLoop ResultPVA Redo
end


%% analyze weights
clear all
Lag=[8, 12, 20, 32, 45, 60, 64, 70, 80, 90, 120, 180];
AllLabels='';
CpPVA=[];
TdPVA=[];
for L=1:length(Lag)
   if L==1
      load ANNResultsCh5NormLag8  Weights1 Weights2 %TimesThruLoop ResultPVA Redo
   elseif L==2
      load ANNResultsCh5NormLag12 Weights1 Weights2 %TimesThruLoop ResultPVA Redo
    elseif L==3
      load ANNResultsCh5NormLag20 Weights1 Weights2 %TimesThruLoop ResultPVA Redo
    elseif L==4
      load ANNResultsCh5NormLag32 Weights1 Weights2 %TimesThruLoop ResultPVA Redo
   elseif L==5
      load ANNResultsCh5NormLag45 Weights1 Weights2 %TimesThruLoop ResultPVA Redo
   elseif L==6
      load ANNResultsCh5NormLag60 Weights1 Weights2 %TimesThruLoop ResultPVA Redo
   elseif L==7
      load ANNResultsCh5NormLag64 Weights1 Weights2 %TimesThruLoop ResultPVA Redo
   elseif L==8
      load ANNResultsCh5NormLag70 Weights1 Weights2 %TimesThruLoop ResultPVA Redo
   elseif L==9
      load ANNResultsCh5NormLag80 Weights1 Weights2 %TimesThruLoop ResultPVA Redo
   elseif L==10
      load ANNResultsCh5NormLag90 Weights1 Weights2 %TimesThruLoop ResultPVA Redo
   elseif L==11
```

```
   load ANNResultsCh5NormLag120 Weights1 Weights2 %TimesThruLoop ResultPVA Redo
elseif L==12
   load ANNResultsCh5NormLag180 Weights1 Weights2 %TimesThruLoop ResultPVA Redo
end

%%%%%%%%%% Propagate [100],[010],[001]
for Trial=1:720
   for i=1:3
      Input=-1*[1 1 1];
      Input(i)=0; % value that gets propagated
      Result1=Input*Weights1(:,:,Trial);
      Result1=1./(1+exp(-Result1));% output of hidden layer
      Result2=Result1*Weights2(:,Trial);
      Result2=1./(1+exp(-Result2));% Output of output layer

      %
      ResultPVA(Trial,i)=Result2;
   end
end
%%%%%%%%%%%%%%%%%


% Just to get datatypes load this
load DataForBabyANNChapter5Lag8
idxCPFirstDay=find(DataTypes==1);
idxCPLastDay=find(DataTypes==2);
idxTDFirstDay=find(DataTypes==3);
idxTDLastDay=find(DataTypes==4);

idxAP=find(AxisAPML==1);
idxML=find(AxisAPML==2);

Subjs=unique(SubjNames,'rows');

CPidx=0;
TDidx=0;
for s=1:size(Subjs,1)
   if Subjs(s,1)=='C'
      CPidx=CPidx+1;
      %first day
      idxDayF=intersect(idxCPFirstDay,strmatch(Subjs(s,:),SubjNames));
      idxDayFAP=intersect(idxDayF,idxAP);
      idxDayFML=intersect(idxDayF,idxML);
      %last day
      idxDayL=intersect(idxCPLastDay,strmatch(Subjs(s,:),SubjNames));
      idxDayLAP=intersect(idxDayL,idxAP);
      idxDayLML=intersect(idxDayL,idxML);

      if length(idxDayFML)>1
         CPSubjPVA(CPidx,1:6)=[mean(ResultPVA(idxDayFAP,:)),...
            mean(ResultPVA(idxDayFML,:)),...
            ];
      else
         CPSubjPVA(CPidx,1:6)=[ResultPVA(idxDayFAP,:),...
            ResultPVA(idxDayFML,:),...
            ];
```

```
        end

        if length(idxDayLML)>1
           CPSubjPVA(CPidx,7:12)=[...
              mean(ResultPVA(idxDayLAP,:)),...
              mean(ResultPVA(idxDayLML,:)),...
              ];
        else
           CPSubjPVA(CPidx,7:12)=[...
              ResultPVA(idxDayLAP,:),...
              ResultPVA(idxDayLML,:),...
              ];
        end


     elseif Subjs(s,1)=='T'
        TDidx=TDidx+1;
        %first day
        idxDayF=intersect(idxTDFirstDay,strmatch(Subjs(s,:),SubjNames));
        idxDayFAP=intersect(idxDayF,idxAP);
        idxDayFML=intersect(idxDayF,idxML);
        %last day
        idxDayL=intersect(idxTDLastDay,strmatch(Subjs(s,:),SubjNames));
        idxDayLAP=intersect(idxDayL,idxAP);
        idxDayLML=intersect(idxDayL,idxML);
        if length(idxDayFML)>1 % average over multiple trials
           TDSubjPVA(TDidx,1:6)=[mean(ResultPVA(idxDayFAP,:)),...
              mean(ResultPVA(idxDayFML,:)),...
              ];
        else
           TDSubjPVA(TDidx,1:6)=[ResultPVA(idxDayFAP,:),...
              ResultPVA(idxDayFML,:),...
              ];
        end

        if length(idxDayLML)>1 % average over multiple trials
           TDSubjPVA(TDidx,7:12)=[...
              mean(ResultPVA(idxDayLAP,:)),...
              mean(ResultPVA(idxDayLML,:)),...
              ];
        else
           TDSubjPVA(TDidx,7:12)=[...
              ResultPVA(idxDayLAP,:),...
              ResultPVA(idxDayLML,:),...
              ];
        end

     end% ends if (Cp and TD)
  end % ends s

  %%

  Labels=char(...
     ['AP_PositionWeight_FirstDay_Lag',num2str(Lag(L))],...
     ['AP_VelocityWeight_FirstDay_Lag',num2str(Lag(L))],...
     ['AP_AccelerationWeight_FirstDay_Lag',num2str(Lag(L))],...
```

```
        ['ML_PositionWeight_FirstDay_Lag',num2str(Lag(L))],...
        ['ML_VelocityWeight_FirstDay_Lag',num2str(Lag(L))],...
        ['ML_AccelerationWeight_FirstDay_Lag',num2str(Lag(L))],...
        ['AP_PositionWeight_LastDay_Lag',num2str(Lag(L))],...
        ['AP_VelocityWeight_LastDay_Lag',num2str(Lag(L))],...
        ['AP_AccelerationWeight_LastDay_Lag',num2str(Lag(L))],...
        ['ML_PositionWeight_LastDay_Lag',num2str(Lag(L))],...
        ['ML_VelocityWeight_LastDay_Lag',num2str(Lag(L))],...
        ['ML_AccelerationWeight_LastDay_Lag',num2str(Lag(L))]);

    %collect results for this lag
    AllLabels=char(AllLabels,Labels);
    CpPVA=[CpPVA, CPSubjPVA];
    TdPVA=[TdPVA, TDSubjPVA];
    clear CPSubjPVA TDSubjPVA

end % ends L
AllLabels=AllLabels(2:end,:);

% create speadsheet for SPSS to do repeated measure ANOVAs
%column with Group (1=CP, 0=TD)
% csvwrite('ANN4SPSSNormLag832.xls',[ones(size(CPSubjPVA,1),1);...
%     zeros(size(TDSubjPVA,1),1)],1,0)
% for i=1:24
%     L{1,i+1}=deblank(Labels(i,:));
% end
% M=mat2cell([CPSubjPVA;TDSubjPVA],ones(1,63),ones(1,24));
%
% xlswrite('ANN4SPSSNormLag832.xls',M)
%
% csvwrite('ANN4SPSSNormLag7080.xls',[ones(size(CPSubjPVA,1),1);...
%     zeros(size(TDSubjPVA,1),1)],1,0)
% for i=1:24
%     L{1,i+1}=deblank(Labels(i,:));
% end
% M=mat2cell([CPSubjPVA;TDSubjPVA],ones(1,63),ones(1,24));

M=[zeros(size(TdPVA,1),1),TdPVA;ones(size(CpPVA,1),1),CpPVA];
xlswrite('ANN4SPSSNormalizedFinalFinalProp1Neg.xls',M)
clc
AllLabels
```

```
function [BestWeights1, BestWeights2,TimesThruLoop,Redo] = BabyANNFunctCh5(TrainIn,N,PlotIt)

% This network has 3 input neurons (posiiton, velocity, & acceleration)
% and one output neuron for acceleration. There are N neurons in the
% hidden layer (in order to test different numbers of neurons)

ErrorImproved=0;
minError=10^10;
Redo=0;
while ErrorImproved==0 %redo if error not improved by learning

   % Rescale to range -1 to +1
   %TrainIn= 2*(TrainIn- mean([max(TrainIn(:)),min(TrainIn(:))]))/(max(TrainIn(:))-min(TrainIn(:)));

   Input=TrainIn(1,:);


   % Calculate target accelerations that we want to calculate
   % i.e. this is the desired output of the ANN
   TrainOut=(TrainIn(2:end,3));
   % since sigmoid output is 0 to 1, need to scale acceleration to that
   % range, so error calculation is meaningful.
   TrainOut= (TrainOut+abs(min(TrainOut)))/range(TrainOut);  %added for dissertation

   % Initial weights are random
   Weights1=randn(3,N); % three input neurons
   Weights2=randn(N,1); %only one output neuron

   % Find initial cumulative error
   for i=1:size(TrainIn,1)-1
      Result1=TrainIn(i,:)*Weights1;
      Result1=1./(1+exp(-Result1));% output of hidden layer
      Result2=Result1*Weights2;

      % sigmiodal function for use with backpropagation
      Result2=1./(1+exp(-Result2));% Output of output layer


      % desired result-calculated result, beta in notes
      Error3(i)=TrainOut(i)-Result2;
   end

   % sum error over all 249 time steps
   MeanError=mean(Error3);
   PrevError=10^10; % set previous error arbitarily high so real
   % error will be lower, and loop will be executed.

   % %% Continue training as long as error is being reduced
   TimesThruLoop=0;
   %while abs(PrevError)>abs(MeanError)
   while abs(PrevError-MeanError)>.00001 % i.e. while error is changing
      TimesThruLoop=TimesThruLoop+1;
      %BackPropagate Error
      Error2=(Result2.*(1-Result2).*MeanError*Weights2)'; % layer 3=>2
      for i=1:3 % number of neurons in input layer is three
         Error1(i)=mean(TrainIn(:,i)).*(1-mean(TrainIn(:,i))).*sum(Error2.*Weights1(i,:)); % layer 2=>1
```

```
    end

    %Calculate weights
    LearnRate=10; %slow learning
    Weights1=Weights1 + LearnRate*(TrainIn(i,:).*Error1)'*(Result1.*(1-Result1));
    Weights2=Weights2 + LearnRate*(Result1.*Error2)'*(Result2.*(1-Result2));

    % Calculate result using new weights
    for i=1:size(TrainIn,1)-1
      Result1=TrainIn(i,:)*Weights1;
      % sigmiodal function for use with backpropagation %Changed!!!
      Result1=1./(1+exp(Result1));
      Result2=Result1*Weights2;
      Result2=1./(1+exp(Result2));

      Error3(i)=TrainOut(i)-Result2;
    end

    PrevError=MeanError;
    if MeanError<minError
      minError=MeanError;
      BestWeights1=Weights1;
      BestWeights2=Weights2;
    end
    MeanError=mean(Error3);
    SaveError(TimesThruLoop)=MeanError;
  end


  if PlotIt==1

    plot(1:TimesThruLoop,SaveError.^2)
    xlabel('Iteration')
    ylabel('Error squared')
    pause
    close

  end

  if abs(SaveError(end))<abs(SaveError(1))
    ErrorImproved=1;
  else
    disp('Redo')
    Redo=Redo+1;
    clear  Error3 SaveError
  end
end
```