CHANGES IN GAIT VARIABILITY ACROSS THE LIFESPAN IN PERSONS WITH DOWN SYNDROME

by

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ABSTRACT

Variability is always present during repetitive movements. Scholars have studied human movement patterns for years, but have only recently begun to focus on variability as something other than noise or error. I followed the theoretical perspective that optimal amount and form of variability in a biological system supports being stable yet adaptable.

I used tools from nonlinear dynamics, Lyapunov Exponent (LyE) and Approximate Entropy (ApEn), to measure form of variability and a traditional linear measure, Coefficient of Variation (*CV*), to measure quantity of variability. I tested walking patterns in toddlers, preadolescents and older adults with Down syndrome (DS) and typical development (TD). Participants walked on a treadmill at preferred, faster and slower speeds while we collected 3-D movement data. I also assessed changes in overground gait parameters and variability in older adults with DS under common environmental perturbation conditions.

Overall, two themes emerge from the work presented here. The first theme is that preadolescents with DS and TD are more adaptive and flexible in their movement patterns as compared to their older and younger peers. Although the quantity of variability in walking patterns generally decreases from toddlers to preadolescents to

adults, preadolescents demonstrate higher ApEn and LyE values than their peers indicating they have learned to use variability to be optimally adaptive.

The exception to this general pattern, however, is step width variability, representing the second major theme of this work. As opposed to a decreasing trend in the amount of variability across the lifespan, preadolescents in both groups produce larger amounts of step width variability than their older and younger peers, possibly reflecting efficient use of the passive pendular dynamics of walking. In addition, participants with DS consistently produced smaller amounts of step width variability than their peers with TD. This robust group difference may reflect that step width is more actively controlled in persons with DS; they are less willing or able to adjust it. Linear and nonlinear measures reflected less stability in the gait patterns of older adults with DS, and nonlinear measures showed they are less capable than preadolescents with DS at utilizing variability adaptively.

CHAPTER I
INTRODUCTION

Scholars have been studying human movement patterns for years, but have only recently begun to focus on variability as something other than noise or error. Variability is present in all human movement; we move through a slightly different trajectory with each repetition within a series of repeated movements, and we sway around a central point when attempting to stand without moving. The quantity of variability is important, too much or too little leads to instability. The form and pattern (quality) of variability is also important; very regular patterns are rigid and unstable while very random patterns are unpredictable and unstable. Somewhere in the middle of this continuum is a state that provides variability for a balance between flexibility and stability of behavior (Stergiou, Harbourne, & Cavanaugh, 2006).

Until recently, tools to measure the quality of variability did not exist. Researchers were limited to studying quantity of variability, through the use of linear measures such as the standard deviation and coefficient of variation. We now have tools from nonlinear dynamics, such as Approximate Entropy (ApEn) and Lyapunov Exponent (LyE), which measure quality of variability. Our goal was to apply linear and nonlinear measures to better understand quantity and quality of variability in walking patterns

across the lifespan in persons with Down syndrome (DS). By using both types of tools, we believe we will come to a more complete understanding of control strategies for walking in the population with DS, a population that faces inherent challenges to walking stability and efficiency.

Persons with DS differ from persons with typical development (TD) in some neurophysiologic characteristics, including hypotonia, high ligamentous laxity and reduced capacity to produce muscle force. We believe these conditions increase their stability challenge and lead to the emergence of their observed unique gait patterns and higher amounts of variability as compared to their peers with TD, across the lifespan (Ulrich, Haehl, Buzzi, Kubo, & Holt, 2004; Looper, Wu, Angulo-Barroso, Ulrich, & Ulrich, 2006; Kubo & Ulrich, 2006; Smith, Kubo, Black, Holt, & Ulrich, 2007; Smith and Ulrich, 2008). Adults with DS face an even greater challenge to walking stability than their younger peers with DS. They experience the effects of aging layered onto the inherent effects of DS, creating more stress on the system than either effect in isolation. In response, adults with DS show precocious stability-enhancing changes in gait. Adults with DS, ages 35-62 years, walk slower and take shorter strides with a wider base of support than their peers with TD (Smith & Ulrich, 2008).

To address issues of gait stability and control across the lifespan in persons with DS, we assessed the amount and form of variability in walking patterns across the lifespan. We used tools from nonlinear dynamics, LyE and ApEn, and a traditional linear measure, Coefficient of Variation, to measure variability of walking patterns in toddlers, preadolescents and older adults with DS and TD. We also focused specifically on issues of gait stability and control in older adults with DS. We assessed changes in gait

parameters and variability during common environmental perturbation conditions. The results help us understand the progression of gait changes and control strategies across the lifespan in persons with DS, with application to clinical interventions to measure and achieve optimal amounts and form of variability to promote stability in walking patterns.

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CHAPTER II
VARIABILITY OF WALKING PATTERNS ACROSS THE LIFESPAN IN PERSONS WITH AND WITHOUT DOWN SYNDROME: NONLINEAR AND TRADITIONAL APPROACHES

ABSTRACT

We used tools from nonlinear dynamics, Lyapunov Exponent (LyE) and Approximate Entropy (ApEn), and a traditional linear measure, Coefficient of Variation (*CV*), to measure variability of walking patterns across the lifespan in persons with Down syndrome (DS) and their peers with typical development (TD). Nonlinear measures provide information about quality of movement variability, while linear measures describe quantity of variability. Participants were toddlers, preadolescents and older adults, who walked on a treadmill while we collected 3-D motion analysis data. We used LyE to analyze the stability of the knee trajectory and *CV* of stride length to measure the amount of variability across successive strides. ApEn measured the regularity of pattern of step lengths while *CV* of step length quantified the amount of variability. Although the quantity of variability in walking patterns generally decreases from toddlers to preadolescents to adults, preadolescents demonstrate higher ApEn and LyE values than their peers indicating they have learned to use variability to be optimally adaptive.

INTRODUCTION

When we attempt to stand quietly, we sway around a central equilibrium point without intending to move. If we swing a hammer, we may hit the nail every time, but we produce the movement producing muscle and joint activity in combinations of timing and amount of activity that are not exactly the same during each swing. Scholars have been studying human movement patterns for years, but have only recently begun to focus on the variability as something other than noise or error.

Variability is always present during repetitive human movement, and can be examined for its spatial or temporal characteristics. Here we follow the theoretical perspective that there is an optimal amount and form of variability in a biological system that supports being stable yet adaptable. The system maintains a rich repertoire of movement strategies while avoiding both instability (one end of the continuum) and rigidity (the other end). For example, in their studies of stride width variability in older adults, Brach and colleagues found that both too much and too little were predictive of falls in older adults, while values of non-fallers were positioned mid-range (Brach, Berlin, VanSwearingen, Newman, & Studenski, 2005). When considering form, as opposed to amount, of variability, ideal patterns are somewhere between too patterned and rigid or too random and unstable. As described by Harbourne & Stergiou (2009), implications of this theoretical perspective apply to clinical interventions to measure and achieve optimal amounts and form of variability in movement patterns (Harbourne & Stergiou, 2009).

Traditional (linear) vs. nonlinear approaches

Variability is inherent to human movement, affecting both the quantity and quality of movement. While some researchers focus their assessments of fluctuations in movement on quantitative variables such as precise distance from a target, others evaluate quality of movement, as in the smoothness of the pointing trajectory. Movement scientists have a long history of using linear methods to analyze variability; linear tools focus on the quantity of variability. Newer nonlinear methods, however, focus on the quality of variability. Nonlinear methods offer ways to explore directly how one movement influences the next, that is, how and why variability emerges.

Traditional linear analysis examines the average behavior of a person or group, usually the endpoint or outcome of behavior. The overall quantity of variability is noted, assuming more variability represents greater deviation from the goal and more "noise" or error in the behavior. The standard deviation quantifies the magnitude of variability in a set of values, independently of their order in the distribution. Even if one looks at the amount of variability at each point in time, all data at that time point must be averaged to create the range, and information about how one time point influences the next is lost. This is precisely the drawback to linear approaches; we know that during motor sequences behavior at each moment influences the next (Harbourne & Stergiou, 2003; Hausdorff et al., 1996; Miller, Stergiou, & Kurz, 2006).

In newer methods derived from nonlinear analysis, the influence of time is retained and the structure of the pattern or quality of variability is the focus, as opposed to merely its quantity. Quality of variability during movement can differ between

persons, as can its quantity, and both variations provide different information about the behavior and control. Within any quantity of variability, different qualities may exist. This is important because the balance between stability and flexibility of behavior has often been linked to the role of the quality of variability in the health of biological systems. Both complete order in variability (periodicity) and lack of order in variability (randomness) have been linked to poor health in cardiac, respiratory, and neurologic disease (Goldberger et al., 2002; Peng, Havlin, Stanley, & Goldberger, 1995; Seely & Macklem, 2004). These states can be thought of as opposite ends of a continuum. In the middle of this continuum is chaos, a deterministic yet non-periodic state that provides variability for a balance between flexibility and stability of behavior (Stergiou, Harbourne, & Cavanaugh, 2006).

Nonlinear Tools

There are many nonlinear techniques available to analyze aspects of movement. Over the past decade, scientists studying human movement have illustrated and developed the utility of several nonlinear and/or dynamic measures in studies of locomotion. Appendix 2.1 contains a brief overview of these options, their unique attributes and some examples of their application. Following is a brief description of the nonlinear tools we chose to use.

Lyapunov Exponent (LyE) measures divergence within the trajectories of movement patterns by quantifying their exponential separation in state space. Essentially, the time series of multiple repetitions of a movement are overlaid, one repetition on top of

another, and the divergence at each time point from one repetition to the next is calculated. Larger values indicate more variability in the system, more divergence and possibly randomness. Shifts toward smaller values indicate less variability, less divergence and possibly rigidity (see Figure 2.1). While multiple LyE values are calculated for each data set of multiple strides, the largest LyE value is used to represent the entire set of points.

Approximate Entropy (ApEn) quantifies the regularity of an inherently patterned time series. It assesses the repeatability of portions of the behavior within the overall behavior by quantifying the probability that these specific sub-patterns will repeat themselves (see Figure 2.2). For example, although a behavior may be clearly observed to be cyclic, such as walking, this tool can quantify the regularity of each stride cycle in relation to the next. A long stride length alternating exclusively with a short stride length represents a more regular pattern than a random series of unique stride lengths, although both behaviors would be recognizable as cyclic strides of walking with similar overall range.

Motor Control Application of LyE and ApEn

Initially researchers in motor control used ApEn to investigate changes in center of pressure complexity while participants stood with eyes open and eyes closed (Sabatini, 2000). Cavanaugh and colleagues extended this idea and used ApEn to measure postural sway patterns in a population with neurophysiologic changes: athletes who had experienced a concussion. They found that, even in the absence of increased postural sway, athletes demonstrated a more regular and less random pattern of postural sway for

a period of time following the concussion. This analysis represents a useful tool to distinguish athletes that are still experiencing sequela of a concussion from those who have recovered, a difficult problem in sports medicine (Cavanaugh, Guskiewicz & Stergiou, 2005; Cavanaugh et al., 2005).

Researchers have used ApEn and LyE to explore dynamics of the ACL-deficient knee, which exhibits more regular (lower ApEn values) and less locally stable patterns (higher LyE values) than the participants' contralateral ACL-intact knee (Georgoulis, Moraiti, Ristanis, & Stergiou, 2006; Stergiou, Moraiti, Giakas, Ristanis, & Georgoulis, 2004) and higher LyE values than the knee of participants with bilaterally intact knees (Moraiti, Stergiou, Ristanis, & Georgoulis, 2007). These scientists suggest the increased regularity may decrease the adaptability of the ACL-deficient knee to perturbations.

LyE has also been used to explore the local stability of walking kinematics in healthy adults and adults with peripheral neuropathy. Dingwell and colleagues found small increases in local stability for treadmill as compared to overground walking and more local stability in the gait of healthy young adults and older adults with peripheral neuropathy, despite their slower walking speeds and increased quantity of variability (Dingwell & Marin, 2006; Dingwell & Cusumano, 2000; Dingwell, Cusumano, Cavanagh, & Sternad 2001; Dingwell, Cusumano, Sternad, & Cavanagh, 2000). One note of caution in the interpretation of these studies, however, is the use of only 4-10 strides for the calculation of LyE values, a much lower number of strides than is typically used for LyE analysis (England & Granata, 2007; Kang & Dingwell, 2006; Stergiou et al., 2004).

In a study of multiple joints, LyE values of ankle, knee and hip angles of healthy adult participants walking on a treadmill at various speeds showed a monotonic trend between walking speed and LyE (England & Granata, 2007). In studies using LyE of the vertical displacement of the head and ankle and other nonlinear methods, preferred walking speed is associated with the highest levels of stability and adaptability in adults with TD, as compared to slower or faster than preferred (Jordan, Challis, Cusumano, & Newell, 2009; Jordan, Challis, & Newell, 2007).

Variability across the lifespan- Nonlinear approaches

Nonlinear tools have allowed researchers to investigate changes in the quality of variability and behavior as children and adults change across the lifespan. These studies have led to novel insights on how behavior shifts as we grow and develop, especially at either end of the lifespan where the rate of change is accelerated.

Acquiring the motor milestone of independent sitting is a dynamic process during which an infant learns to control multiple available degrees of freedom to achieve control of seated posture. Harbourne and Stergiou used LyE and ApEn analysis of the center of pressure time series to show that the quality of variability changes as the infant learns to control their trunk within stability limits in the sitting position. Over time, stability and regularity increase, revealing a more stable and periodic strategy. Interestingly, the dimensionality of the state space for the movement is initially large, and then becomes much smaller as the infant freezes out many degrees of freedom. It then becomes larger again (but not as large as initial levels) as the infant learns to successfully integrate degrees of freedom (Harbourne & Stergiou, 2003).

Nonlinear tools have also been used to differentiate typical and atypical development. Ohgi and colleagues calculated LyE values for acceleration signals of the spontaneous arm movements of premature infants with and without brain injury. They found higher LyE values for infants with brain injury than without, indicating that movements of the premature infants with brain injuries demonstrated characteristics of increased disorganization compared to movements of infants without brain injury (Ohgi, Morita, Loo, & Mizuike, 2008).

Hausdorff and colleagues measured stride-to-stride variability in 50 healthy children ages 3 to 14 years. The fractal scaling index, α, after adjusting for height, was similar in the two youngest age groups and tended to decrease in the oldest children (Hausdorff, Zemany, Peng, & Goldberger, 1999). At the other end of the age spectrum, the authors investigated the stride dynamics of healthy elderly adults. They used fractal analysis and Detrended Fluctuation Analysis to show that older adults' sequential walking strides are more uncorrelated than their younger peers (Hausdorff et al., 1997; Hausdorff et al., 2001; Herman, Giladi, Gurevich, & Hausdorff, 2005). Both young children and older adults demonstrate different gait qualities than adults in the middle of the lifespan. In children, gait becomes less random as they gain walking experience, while in older adults stride-to-stride fluctuations become more random.

In another study investigating nonlinear aspects of walking in older adults, older adults with TD (age 71-79 yr) demonstrated significantly higher LyE values than did younger adults (20-39 yr) for knee angle and hip, knee and ankle vertical displacement while walking on a treadmill. Nonlinear analysis revealed that fluctuations in these

variables demonstrated more unstable trajectories in older participants (Buzzi, Stergiou, Kurz, Hageman, & Heidel, 2003).

Variability across the lifespan- Why use nonlinear approaches?

Scholars have documented that the quantity of movement pattern variability in persons with TD has an inverted U shape across the lifespan. We attribute this pattern to learning at the early end (higher variability), minimal variability after much practice, and high variability returning as the effects of aging emerge. We do not know if this pattern holds true for the population with DS. We do know they demonstrate an increased amount of variability compared to their age-matched peers with TD, however they could show an elevated level of inconsistency that is persistent, or even increasing, across their lifespan. If we can understand how the constraints on performance are unique at a population level, we can begin to understand what aspects of performance are amenable to intervention and how we can maximize performance.

In addition to the quantity of variability in measures such as step length and duration, stability of walking also changes across the lifespan reflected in the fact that falls are much more prevalent in older adults than younger adults. Researchers and clinicians alike propose that walking is not just more variable but also more unstable and prone to falls at either end of the lifespan. This outcome maps directly onto the inverted U shape amount of variability that has been quantified. Stability of gait, however, is hard to quantify and is often reported simply in terms of number of falls or quantity of variability. A change in the quantity of variability, though, does not necessarily represent a change in the quality of movement or the stability of the behavior. Using nonlinear

analysis we can directly measure changes in the quality of walking pattern variability across the lifespan.

In older adults with impaired gait without an obvious identifiable cause, often referred to as a 'higher level gait disturbance (HLGD)' or cautious gait, quantity of variability does not distinguish fallers from non-fallers (Nutt, Marsden & Thompson 1993). Variability of gait parameters is increased in all patients with a HLGD, while the fractal scaling index better reflects fall risk (Herman et al., 2005).

As Hausdorff summarizes in his 2007 review,

> "Measures of gait dynamics, how walking varies from stride-to-stride, characterize a dimension of locomotor function that is often distinct from more traditional measures. For example, stride-to-stride variability prospectively identifies elderly fallers, even when standard measures (e.g., average gait speed) may not. Similarly, a fractal measure of gait identifies subtle changes in 'successful' aging and distinguishes between older adults with a 'higher-level' gait disturbance who fall and those who do not, while other indices of mobility fail to discriminate between these groups. It is fair to suggest that measures of gait dynamics may serve as a sensitive and clinically relevant parameter in the evaluation of mobility and fall risk and the response to therapeutic interventions (Hausdorff, 2007)."

Developmental disability with increased variability: Down syndrome

Persons with Down syndrome (DS) demonstrate a higher quantity of variability in most aspects of their movements across the lifespan when compared to their peers with typical development (TD). Work in our lab has shown that toddlers with DS generate more sagittal plane variability at the onset of walking than toddlers with TD (Looper, Wu, Angulo-Barroso, Ulrich, & Ulrich, 2006), as well as large amounts of variability in stride length, step width and center of mass movement (Kubo & Ulrich, 2006). Preadolescents with DS demonstrate more variability in stiffness and impulse values than

their peers with TD, and preadolescents and adults with DS appear to show larger amounts of variability in stride length than their peers with TD (Smith, Kubo, Black, Holt, & Ulrich, 2007; Ulrich, Haehl, Buzzi, Kubo, & Holt, 2004; Smith & Ulrich, 2008).

Persons with DS differ from persons with TD in some neurophysiologic characteristics, including hypotonia, high ligamentous laxity and reduced capacity to produce muscle force. We believe these conditions increase their stability challenge and lead to the emergence of their observed unique gait patterns. Toddlers with DS, after one month of walking experience, demonstrate shorter normalized stride length, slower normalized velocity and a trend towards wider normalized step width than their peers with TD (Kubo & Ulrich, 2006). Following years of walking practice, however, some of these group differences disappear. Although normalized step width remains larger in preadolescents with DS than in those with TD, these groups do not differ on normalized velocity or stride length (Ulrich et al., 2004; Smith et al., 2007). Preadolescents with DS are likely at their performance stability peak; they have had 6-8 years of walking experience, are not yet in a rapid physical growth spurt, and are not old enough to begin experiencing age-related problems that impact gait quality, such as arthritis. With increasing age, decrements in performance as compared to healthy peers again become more apparent. Older adults with DS (ages 35-62 years) walk slower and take shorter strides with a wider base of support than their peers with TD (Smith & Ulrich, 2008).

The ability of nonlinear analysis to differentiate performance among the increased quantity of variability of persons with higher level gait disturbance suggests that the use of nonlinear tools may also help us explain the increased variability demonstrated by persons with DS. In one study published to date, LyE and ApEn analyses were used to

investigate the dynamic stability of the thigh, shank and foot segmental angles while preadolescent participants walked on a treadmill. Despite likely being at a performance peak, preadolescents with DS do show decreased dynamic stability in all segments as compared to peers with TD (Buzzi & Ulrich, 2004).

Based on multiple studies, we know that persons with DS adapt their walking patterns fairly well to the inherent characteristics of DS as well as neurophysiologic changes associated with aging, yet their motor behavior remains unique and more variable than that of their peers with TD across the lifespan. What we do not understand well is how persons with DS control this variability. Are persons with DS more inconsistent because they are unable to be less so? Is this level of variability merely a physiological function of their unique system? Or perhaps they can control it, but it would be energetically inefficient to do so. From an intervention standpoint we need to answer these questions. Whether or not, or to what degree, their variability is amenable to intervention is also an open question. Before we attempt to change patterns we need to understand how they occur and why. We must be careful not to assume the "normal performance" is the optimal goal for all individuals.

GOALS AND HYPOTHESES

In this study we compared changes in quality and quantity of walking variability across the lifespan in persons with and without DS. We used the nonlinear tools of LyE to assess quality of variability in the knee joint trajectory and ApEn to assess quality of variability of step lengths and widths. We used the linear tool Coefficient of Variation (*CV*) to provide information on the quantity of variability present in stride lengths and

step lengths and widths. By including both linear and nonlinear tools, we created a more complete picture of gait and how it is changing than by using either type of tool in isolation.

We hypothesized that, because preadolescents are at their performance peak in terms of skill and efficiency, new walkers and older adults with DS would show higher quantities of variability (larger *CV*) and more random, less stable trajectories of movement (larger ApEn and LyE values) than preadolescents with DS. Further, due to the inherent differences in subsystems between persons with DS and TD, we predicted that persons with DS would demonstrate higher quantities of variability (larger *CV*) and more random, less stable trajectories of movement (larger ApEn and LyE values) across the lifespan as compared to their age or experience-matched peers with TD.

METHODS

Participants with DS and TD, representing three developmental levels: toddlerhood, preadolescence and older adulthood, came to the Motor Development Laboratory at the University of Michigan (total n= 70; see Table 1 for specific ages and numbers per group). As detailed below, we asked participants to walk at their comfortable overground speed and walk on a treadmill. We used a 6-camera Peak Motus real-time system (Peak Performance Technologies, Centennial, CO) to collect 3-dimensional reflective marker position data at a sampling rate of 60 Hz. Three cameras were distributed evenly on each side, and a video camera provided visual records of performance.

The University of Michigan Institutional Review Board approved all procedures. Prior to participation, we explained the purposes of our study and all procedures to participants and parents, caregivers or legal guardians. Participants signed an assent or consent form as appropriate, with consent for assenting adults and children provided by a legal guardian. New walker participants wore a diaper covered by black tights. When preadolescent and adult participants arrived in the lab they changed into a bathing suit or close-fitting shorts and a tank top. We marked the skin surface of each site requiring a reflective marker with hypoallergenic eyebrow pencil and attached markers (2.5 cm diameter) bilaterally at the temperomandibular joint, shoulder at acromion process, elbow at lateral humeral epicondyle, wrist at styloid process, greater trochanter, femoral condyle, ankle at 10 cm above lateral malleolus, heel at bony prominence and third metatarsophalangeal joint. We also collected EMG data for the tibialis anterior, gastrocnemius, rectus femoris and biceps femoris muscles. Results for EMG, anthropometric and resultant center of mass data (which required multiple reflective markers) will not be discussed further here.

Participants walked barefoot and performed 4-6 repetitions of walking at their preferred speed over a 5.3-m GAITRite mat (CIR Systems, Inc., Havertown, PA). We used GAITRite software to calculate the average walking speed of each participant, which we used to adjust the belt speed for the treadmill phase of testing. For the treadmill portion of the data collection, participants walked on a motorized treadmill (Parker brand, LET Medical Systems Corp., Miami Lakes, FL) for 30-s trials without holding onto the handle of the treadmill. New walkers were guarded closely as they walked. Based on previous work in our lab (Smith et al., 2007; Ulrich et al., 2004), we operationalized

comfortable treadmill speed for all participants as 75% of their self-selected overground speed. Comfortable speeds on a treadmill are slower than overground (Alton, Baldey, Caplan, & Morrissey, 1998) and participants with DS are cognitively not able to select their most comfortable speed in this novel context. Participants performed 2-30 s trials each at 45%, 75% and 110% of their preferred overground walking speed, with trials progressing from slower to faster speeds.

We took anthropometric measurements using a Healthometer (Precision Weighing Balances, Bradford, MA) beam scale to obtain body weight and a GPM anthropometer (Siber Hegner and Co., Zurich, Switzerland) to record height and body segment lengths. To assess performance on related motor control tasks we used three different age-appropriate instruments. For toddlers we administered the motor component of the Bayley Scales of Infant Development (The Psychological Corporation, San Antonio, TX); we tested preadolescents via the 8-item balance subtest of the Bruininks-Oseretsky Test of Motor Proficiency (American Guidance Service, Circle Pines, MN). Adults completed the Berg Balance Scale (Berg, Wood-Dauphnee, Williams, & Gayton, 1989; Berg, Wood-Dauphnee, Williams, & Maki, 1992).

DATA REDUCTION AND ANALYSIS

Embedding Dimension and Time Delay

We used the Tools for Dynamics software (Applied Nonlinear Sciences, LLC and Randle, Inc, Del Mar, CA) to identify the embedding dimension of our data using the Global False Nearest Neighbor algorithm (Abarbanel, 1996). The embedding dimension represents the number of dimensions needed to unfold the structure of a given dynamical

system in space (Mitra, Riley, & Turvey, 1997). Our calculations indicated that 8 embedding dimensions were necessary to form a valid state space from the toddlers' knee time series, while 5 dimensions were sufficient for preadolescent and adult gait data. This finding of different embedding dimensions for different age groups reflects the increased noise present in toddler data. In addition, we calculated a time delay of 3 using the first minimum of the Average Mutual Information function. This function evaluates the amount of information (in bits) shared between two data sets over a range of time delays, and the first minimum indicates the least shared information (Dingwell et al., 2001; Stergiou et al., 2004).

Surrogate Data

In general terms, surrogation is a technique used to determine if the observed data from alternating walking strides meets the mathematical definition of periodicity. If surrogation is successful, we can assume that our algorithms are able to identify periodicity in the observed data despite any noise present. Please see Smith, Stergiou and Ulrich (under review) for discussion of our choice of a surrogation algorithm (Smith, Stergiou & Ulrich, under review).

More specifically, the surrogation process removes any deterministic structure from the original data set and generates a random equivalent of it. We created surrogate datasets for all knee time series using CDA software (Sprott & Rowlands, 1992). The surrogation procedure shuffles the data set while preserving its probability distribution, mean, and variance, using the null hypothesis that the original time series is an independent and identically distributed noise (Theiler, Eubank, Longtin, Galdrikian, &

Doyne Farmer, 1992). Subsequently, we computed the largest LyE values for all surrogate time series and compared them to the values obtained from the original time series. A significant difference between the two values indicated that the original data were not randomly derived and supports the idea that they are deterministic. Further analysis was conducted only on significantly different original data sets.

Lyapunov Exponent (LyE)

We used Chaos Data Analyzer (CDA) software Professional Version (Physics Academic Software; Sprott & Rowlands, 1992) to calculate LyE values for the anterior-posterior and vertical direction time series of the left knee 3-D data. In combination, these data represent the majority of the flexion-extension motion of the knee during walking, as well as the pendular motion of the swinging leg. Appendix 2.2 details the pilot work conducted that resulted in the selection of the left knee marker to represent limb movement and method used to calculate LyE values.

Length of available time series varied from 276 points for the new walkers to 1800 points for preadolescents and adults, and the number of data points analyzed was consistent within age group. For new walkers, these points correspond to 7 or 8 strides, the maximum amount they are able to produce continuously at this point in developmental time. Depending on the relative speed, the point values represent approximately 18-30, 24-39, or 30-42 strides for preadolescents and adults.

Approximate Entropy

We calculated step length and step width for all trials. Step length was defined as the anterior-posterior direction distance from one heel contact to the following heel contact of the other foot while step width was defined as the distance between the heel of one foot and the line of progression of the other foot. Depending on the relative speed, this represents approximately 36-60, 48-78, or 60-84 steps for preadolescents and adults. Toddlers were only able to produce 14-16 continuous steps at this point in developmental time. Following the calculation of step lengths and widths, we used custom MATLab programs to calculate ApEn values to quantify regularity of pattern in step length and width from step to step. To calculate ApEn, 2 input parameters, m and r, must be selected before computation: m is the "length" of compared runs, and r is the tolerance filter (Pincus & Goldberger, 1994). We set m = 2 and r = 0.2 x the standard deviation of the data (Stergiou et al., 2004).

Linear Measures

Means, standard deviations and *CV* were calculated for stride lengths, step lengths and step widths of each trial. The *CV* reflects the quantity of variability of the parameters, as compared with quality of variability (ApEn and LyE).

RESULTS

In most cases, we used a 2 (group) by 3 (age) ANOVA full factorial model with Bonferroni corrections. The TD older adult group was excluded because it was a fourth level for the TD group without a matched chronological age level for the DS group. This

allowed use of a more powerful standard ANOVA addressing group differences and interactions. In the case of anterior-posterior LyE data, because the new walker data could not be included, we used a 2 (group) by 2 (age) ANOVA full factorial model with Bonferroni corrections. In follow-up analysis, we used linear and quadratic trend tests to assess the shape of change across the lifespan within each group, using one test to examine the trend across the 3 groups with DS and another to examine the 4 groups with TD. Results are grouped into two sections: lifespan changes in linear and nonlinear measures of stride to stride variability and divergence, followed by lifespan changes in linear and nonlinear measures of step to step variability and regularity.

Linear and Nonlinear Measures of Stride to Stride Variability and Divergence

Linear Measure: Quantity of Stride Variability

To test for differences in *CV* stride length values across the lifespan, we used a 2 (group) by 3 (age) ANOVA. The age effect was significant ($F[2, 50] = 18.15$, $p < 0.01$) while the group effect was not. The group by age interaction was significant ($F[2, 50] = 3.73$, $p = 0.03$). Follow-up inspection of the means revealed the DS group had smaller stride length *CV* values than the TD group as new walkers, a pattern that reversed by preadolescence and adulthood (see Figure 2.3).

In follow-up analysis, we tested for linear and quadratic trends within the DS and TD groups. For the DS group, we obtained a significant linear trend ($p < 0.01$) but not a quadratic trend. Follow-up pairwise comparisons revealed that the DS new walker group had significantly larger *CV* stride length values than the DS adult group. For the TD

group, we obtained a significant linear trend ($p < 0.01$) and quadratic trend ($p < 0.01$). The quadratic trend reflected larger *CV* stride length values in new walkers and older adults and smaller values in preadolescents and adults. Follow-up pairwise comparisons revealed that the TD new walker group had significantly larger *CV* stride length values than the preadolescent, adult and older adult groups ($p < 0.01$ for all).

Nonlinear Measure: Divergence of Limb Trajectories

To test for differences in divergence from stride to stride in knee trajectories in the vertical direction across the lifespan, we used a 2 (group) by 3 (age) ANOVA with vertical direction LyE values as the dependent variable. The age effect was significant ($F[2, 46] = 17.53$, $p < 0.01$), while the group effect and group by age interaction were not (see Figure 2.4).

For follow-up analysis, we tested for linear and quadratic trends within groups. For the DS group, the quadratic trend test was significant ($p < 0.01$). Follow-up pairwise comparisons revealed that preadolescents had higher vertical direction LyE values than new walkers or adults ($p < 0.01$ for all). For the TD group, the quadratic trend test was again significant ($p < 0.01$). Follow-up pairwise comparisons revealed that preadolescents had higher vertical direction LyE values than new walkers, adults or older adults ($p < 0.01$ for all).

We used a similar a 2 (group) by 2 (age) ANOVA for differences in LyE values in the anterior-posterior direction. This analysis did not include the new walker groups, whose anterior-posterior direction data failed surrogation analysis. The group effect was significant ($F[1, 34] = 14.44$, $p < 0.01$), as was the age effect ($F[1, 34] = 18.92$, $p < 0.01$).

The group by age interaction was not significant (see Figure 2.5). Inspection of the means for the group effect revealed higher LyE values in the anterior-posterior direction for the group with DS, while the age effect showed higher LyE values in preadolescents as compared to adults.

Follow-up trend analysis for the DS group showed a significant linear trend (p = 0.01), reflecting a decrease in anterior-posterior LyE values from preadolescence to adulthood. Follow-up in the TD group also revealed a significant linear trend (p = 0.04), again reflecting a decrease in anterior-posterior LyE values from preadolescence to adulthood and older adulthood.

Linear and Nonlinear Changes in Step to Step Variability and Regularity

Linear Measure: Quantity of Step Length and Width Variability

To test for differences in *CV* of step length values across the lifespan, we used a 2 (group) by 3 (age) ANOVA. The group effect (F[1, 49] = 6.32, p = 0.02) and age effect (F[2, 49] = 11.00, p < 0.01) were significant, while the group by age interaction was not (see Figure 2.6). Inspection of the means revealed larger values in the DS group for the group effect and larger values in new walkers for the age effect.

Follow-up analysis revealed there was not a linear or quadratic trend for the DS group, however the linear trend approached significance (p = 0.07). For the TD group, both linear and quadratic trends were significant (p < 0.01 for both). The quadratic trend revealed larger values in new walkers and smaller values in preadolescents and adults, followed by an increase in older adults.

To test for differences in *CV* of step width values across the lifespan, we used a 2 (group) by 3 (age) ANOVA. The group effect ($F[1, 49] = 11.88$, $p < 0.01$) and age effect ($F[2, 49] = 5.85$, $p < 0.01$) were significant, while the group by age interaction was not (see Figure 2.7). Inspection of the means revealed larger values in the TD group for the group effect and larger values in preadolescents for the age effect.

Follow-up analysis of the DS group revealed significant linear and quadratic trends ($p < 0.01$ for both). Significant follow-up pairwise comparisons showed that new walkers had significantly smaller values than both preadolescent and adult groups ($p < 0.01$ for both). The quadratic trend revealed larger values in preadolescents than younger and older groups. For the TD group, the linear and quadratic trend tests were not significant.

Nonlinear Measure: Pattern of Successive Step Lengths and Widths

To test for differences in step length ApEn values across the lifespan, we used a 2 (group) by 3 (age) ANOVA. The age effect was significant ($F[2, 49] = 9.37$, $p < 0.01$), while the group effect and group by age interaction were not (see Figure 2.8). Inspection of the means revealed an inverted "U" shape with highest values in preadolescents.

In follow-up analysis for the DS group, we obtained significant linear ($p = 0.03$) and quadratic ($p = 0.05$) trends. Follow-up pairwise comparisons revealed that the DS new walker group had significantly smaller ApEn step length values than the DS preadolescent ($p = 0.01$) or adult groups ($p = 0.01$) while the quadratic trend indicated higher values in the preadolescents than younger or older groups. For the TD group, the

quadratic trend was significant ($p = 0.02$) with higher values in preadolescents and lower values in older and younger groups.

To test for differences in ApEn of step width values across the lifespan, we used a 2 (group) by 3 (age) ANOVA. The age effect was significant ($F[2, 49] = 15.23$, $p < 0.01$), while the group effect and group by age interaction were not (see Figure 2.9). Inspection of the means revealed an inverted "U" shape with highest values in preadolescents.

For the DS group, in follow-up analysis, there were significant linear and quadratic trends ($p < 0.01$ for both) indicating higher ApEn values for preadolescents, lower values for adults and lowest values for new walkers. We obtained a significant quadratic trend ($p = 0.01$) for the TD group, with higher ApEn values for preadolescents and lower values for adults and new walkers.

DISCUSSION

Overall, our results suggest that the lifespan developmental/aging influence is stronger than most group differences and there are very strong developmental factors affecting both groups. New walkers show larger quantities of variability (*CV* stride length and *CV* step length) early on, while preadolescents, adults and older adults have learned to control walking more efficiently and produce less variability. Nonlinear measures show a different side of the story, however, preadolescents are more flexible and adaptable in their movement patterns (higher LyE and ApEn values) than new walkers, adults and older adults despite, often, a larger quantity of variability. Preadolescents have learned to use their variability to be optimally adaptive.

The exception to this general pattern, however, is step width variability. As opposed to a decreasing trend in the amount of variability across the lifespan, preadolescents in both groups produce larger amounts of variability in step width than their older and younger peers. The increase in step width variability from new walkers to preadolescents represents the emergence of the use of the pendular, passive dynamics of walking (Looper et al., 2006), while the decrease in step width variability from preadolescence to adulthood may represent a shift away from the use of a passive dynamic control strategy. Researchers have shown in passive dynamic robots and in-vivo studies that step width is actively controlled to provide medial-lateral stabilization during walking. This active control leads to larger amounts of variability, as compared to the more passive and less variable dynamics in the anterior-posterior direction, as measured by (e.g., step length) (Bauby & Kuo, 2000; Kuo, 1999). Thus higher quantities of variability in preadolescents reflect active control of step width and medial-lateral stability and effective use of passive anterior-posterior pendular dynamics. Consequently, effective exploitation of the dynamics of walking by preadolescents is also reflected in ApEn step width values. This age group demonstrated more flexibility and adaptability (higher ApEn values) than their older and younger peers in their pattern of step width variability from one step to the next.

Although the lifespan differences tend to overshadow any groups differences, we did observe some robust and informative group differences. One such difference was step width. Participants with DS produced smaller amounts of variability in step width than their peers with TD. Step width is thus more actively and tightly controlled in persons with DS; not only do they use a wider step width than their peers with TD across the

lifespan to stabilize their center of mass as they walk (Kubo & Ulrich, 2006; Ulrich et al., 2004; Smith et al., 2007; Smith & Ulrich, 2008), they are also less willing or able to adjust step width.

With the lifespan approach we took here, we can see that persons with DS, across their lifespan, increase mechanical stability by using a wider step width and controlling it to allow less variability as compared to their peers with TD. Quantity and quality measures for the other variables we tested supported the idea that persons with DS, especially preadolescents, are able to use higher amounts of variability in an adaptive way. This finding is in agreement with our recent results from Uncontrolled Manifold (UCM) analysis. In the UCM study, variance of the head position and body center of mass were analyzed at one time point in the gait cycle, heel contact. We found that preadolescents with DS partition more variance parallel to the manifold than their peers with TD during treadmill walking (Black, Smith, Wu, & Ulrich, 2007). This result implies that, although they demonstrate a higher quantity of variability, preadolescents with DS show functional adaptations to successfully achieve the task by partitioning more variability into “areas” that do not detract from task performance. They use this as a control strategy to allow themselves to be “ready” for their increased need to adapt to perturbations. Our results here for step width, however, suggest something different. Persons with DS demonstrate a smaller quantity of step width variability than their peers with TD, and, although not statistically significant, appear to also show more regularity and less adaptability in step width, as reflected by lower ApEn values. These results indicate step width is uniquely controlled across the lifespan in persons with DS. We need to recognize that increased step width and decreased step width variability reflect a

robust strategy for gait stability in persons with DS, and this is not a parameter we should expect, or attempt, to change directly with intervention. Decreases in step width and increases in step width variability may occur as a reflection of changes in behavior and increased stability, however the goal of intervention should be overall stability and not changing step width.

In addition to step width, we also observed group differences in the other *CV* variables. The DS group had *smaller CV* stride length values than the TD group as new walkers, a pattern that reversed by preadolescence and adulthood. Participants with DS produced *larger* quantities of variability in step length than participants with TD across the lifespan. We believe that this may occur because new walkers with DS have more variability than their peers with TD in the length of their swing phases, leading to more variability in step length (reflecting swing phase only), but new walkers with DS compensate successfully for a shorter stance with a longer swing, and vice versa, producing less variability overall in stride length (reflecting both swing and stance). In addition, *CV* step length values were larger, overall, than *CV* stride length values. This may result from the constraints imposed by the treadmill context, where the treadmill belt moves at a constant speed and imposes this speed on the performer. A shorter stance phase must be paired with a longer swing phase in order to continue walking in place on the treadmill. Thus the high variability observed in step length was fairly rectified by the time the movement was defined as a stride.

The nonlinear measures, for the most part, reflected lifespan differences and did not reflect overall differences between the groups in this study. We did not find group differences in ApEn values for step length or width or for LyE values in the vertical

direction. In the anterior-posterior direction, however, participants with DS demonstrated higher LyE values reflecting more adaptability in knee trajectories from one stride to the next, demonstrating a functional solution to their increased amounts of movement variability.

Some of the lack of group differences in ApEn and vertical direction LyE values appears to be related to statistical analysis characteristics. It was difficult to statistically demonstrate differences between groups when the much larger age effects were included in the same analysis. In a study with similar dependent variables and only one age group of interest (8 children with DS and 8 with TD, 8-10 years of age) there was enough statistical power to show group differences in LyE and ApEn of lower extremity segmental angles. Results indicated more adaptability in children with DS as compared to those with TD, as measured by higher LyE and ApEn values (Buzzi & Ulrich, 2004). Group differences that we were not able to show statistically but appear to be present here (vertical direction LyE and ApEn step length) would be consistent with the Buzzi and Ulrich study. ApEn step width group difference results, however, would show the opposite pattern, as discussed previously.

It is difficult to compare the actual LyE and ApEn values we obtained to those of other studies, as different variables of interest lead to different values of LyE and ApEn. Our calculations of LyE and ApEn, however, do appear to be in similar range as results from other studies of treadmill walking in various populations. Buzzi and Ulrich (2004) calculated LyE values ranging from approximately 0.12 to 0.2 and ApEn values of around 0.22 to 0.52 for lower extremity segmental angles of children with DS and TD (Buzzi & Ulrich, 2004). Jordan and colleagues (2009) calculated LyE values of around

0.1 at the ankle near the walk-run transition speed in healthy adult females (Jordan, Challis, Cusumano, & Newell, 2009). Stergiou and colleagues (2004 and 2006) obtained LyE values around 0.10-0.12 and ApEn near 0.20 to 0.26 from the knee flexion/extension angle from participants with and ACL-deficient and contralaterally-intact knee (Stergiou, Moraiti, Giakas, Ristanis, & Georgoulis, 2004; Georgoulis, Moraiti, Ristanis, & Stergiou, 2006).

One can, however, only interpret values in a relative way, on a continuum as compared to similar data collected an analyzed in the same manner. LyE values are on a continuum of 0 to 0.5. A periodic sine wave, with no divergence from one trajectory to the next, produces an LyE value of 0. A random signal, with maximal divergence, produces an LyE value of 0.5. Our results showed LyE values ranging from approximately 0.15 to 0.20, indicating that divergence in participants' knee trajectories was slightly closer to the periodic end of the continuum (0 end of the scale). Occasions where participants with DS had higher LyE values than their peers with TD reflected more divergence in their movement trajectories, indicating more adaptability. In our data, ideal values for LyE appeared to be around 0.20, indicating maximal flexibility and adaptability of performance. This is not an ideal value, however, that would necessarily apply in a different population or to any other variable of interest.

ApEn values exist on a continuum of 0 to 2. Complete regularity of pattern produces ApEn values of 0, while complete irregularity and lack of a pattern is represented by an ApEn value of 2. Our results showed ApEn values ranging from approximately 0.12 to 0.48, indicating that step widths and lengths were closer to the regular pattern end of the continuum. This is not unexpected, as consecutive walking

steps represent a more periodic and regular pattern as compared to variables such as center of pressure sway. For step length and width data, preadolescents demonstrated higher ApEn values than their older and younger peers, indicating less regularity of pattern across successive steps and more flexibility of behavior. In our data, ideal values for ApEn appeared to be around 0.48, indicating maximal flexibility and adaptability of performance. As with our LyE results, this is not an ideal value that would necessarily apply in a different population or to any other variable of interest.

Overall, results from this work support the idea that persons with DS tend to walk in a way that is most functional for them, based on the inherent constraints of their system. This does not mean, however, that every child or adult with DS will spontaneously discover the most efficient solution or that they will maximize their efficiency and performance. The use here of both nonlinear and linear measures enabled a better understanding of developmental trajectories and group differences in control strategies for walking in persons with DS and TD. Across the lifespan, persons with DS control step width in a unique way. Further, the use of nonlinear tools in these studies has allowed for interpretations and conclusions that would not be possible using only traditional linear tools. We have shown that preadolescents are at a performance peak of their lifespan, as compared to toddlers and older adults. Although quantities of variability may be larger or smaller, nonlinear measures reflect that preadolescents are more flexible and adaptable in their walking patterns than younger and older age groups.

Table 2.1

Age ranges and number of participants per group

Group	Age Range	N (total = 70)
New walkers	DS =17.5-46.5 mo.	9
(3 mo. experience)	TD = 13-22.5 mo.	9
Preadolescents	DS = 10-12 yrs.	8
	TD = 10-12 yrs.	8
Adults	TD = 35-54 yrs.	12
Older Adults	DS = 35-62 yrs.	12
	TD = 70-83 yrs.	12

DS = Down syndrome, TD = typical development.

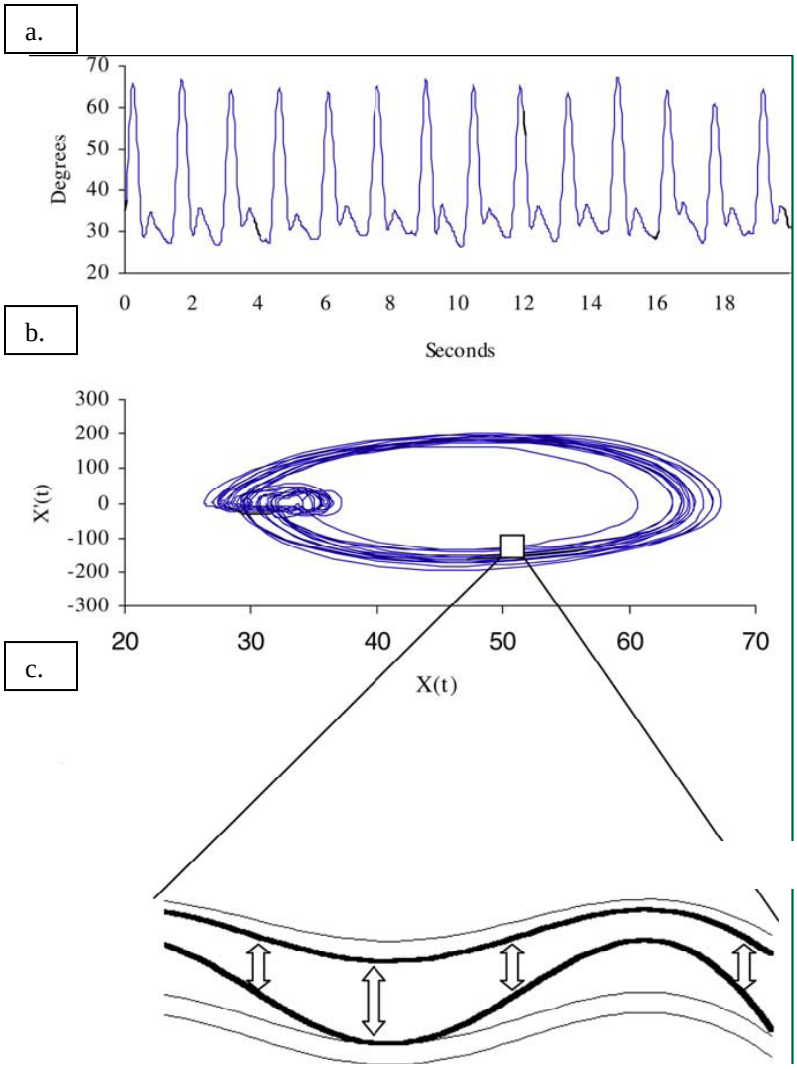

Figure 2.1. Largest Lyapunov Exponent (LyE) values for a representative time series. From Stergiou et al. (2004) using CDA software (Sprott & Rowlands, 1992) demonstrating the calculation of LyE. a) is the time series of the knee angle in degrees, b) is the state space of two dimensions (knee angle vs. angular velocity) and c) demonstrates the divergence between neighboring trajectories in the state space (LyE).

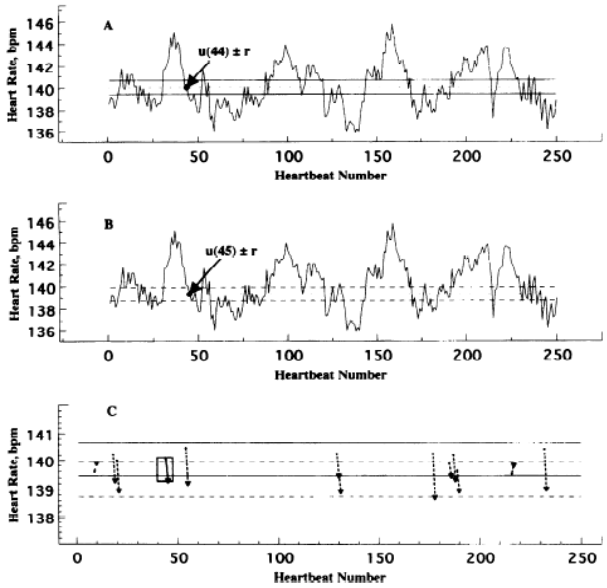

Figure 2.2. To calculate Approximate Entropy (ApEn), start with the first two data points of your time series. How often does this pattern of two points (within a specified range) repeat throughout the length of your data? Now take the next two data points and see how often they repeat. More repetition creates a lower ApEn value, indicating more order in the series. From Pincus & Goldberger (1994).

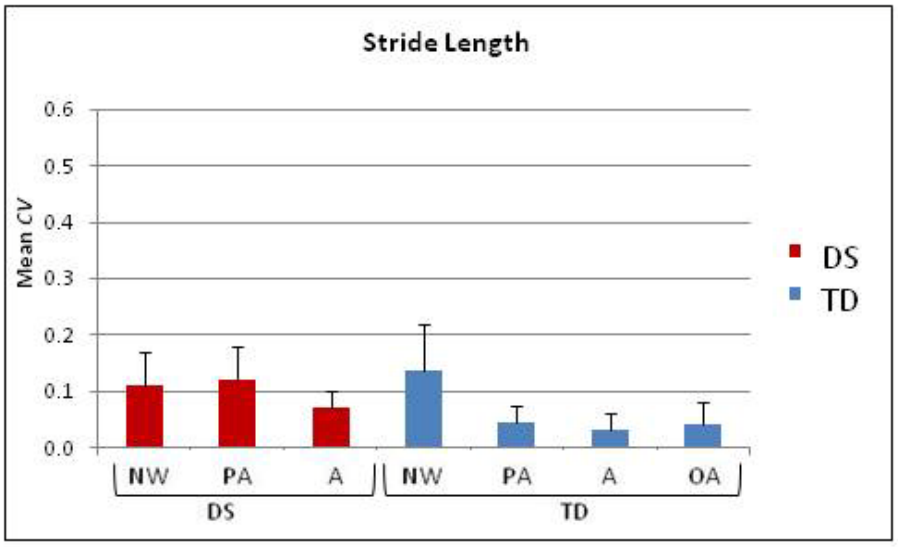

Figure 2.3. Coefficient of Variation (*CV*) of stride length for participants with Down syndrome (DS) and typical development (TD). Age groups are as follows: NW = new walkers, PA = preadolescents, A = adults, OA = older adults.

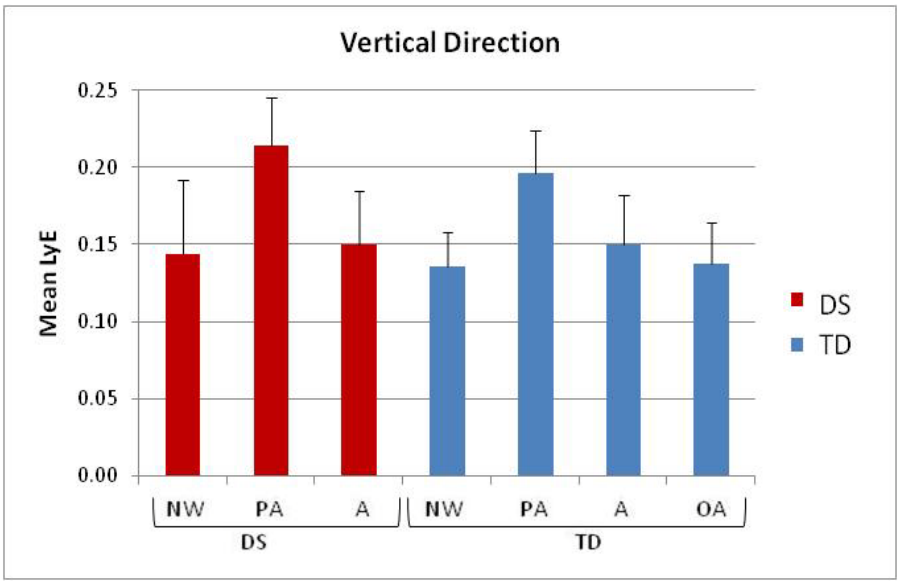

Figure 2.4. Vertical direction Lyapunov Exponent (LyE) values for participants with Down syndrome (DS) and typical development (TD). Age groups are as follows: NW = new walkers, PA = preadolescents, A = adults, OA = older adults.

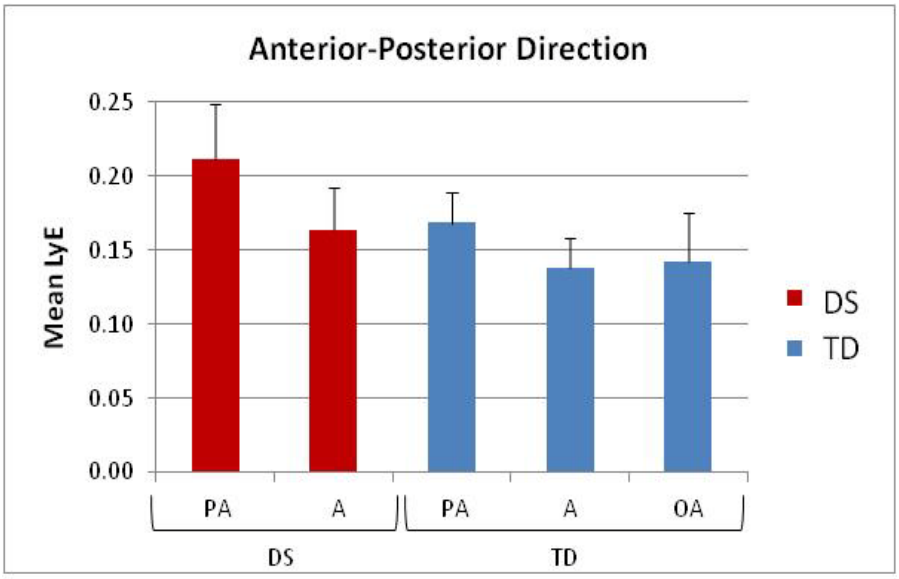

Figure 2.5. Anterior-posterior direction Lyapunov Exponent (LyE) values for participants with Down syndrome (DS) and typical development (TD). Age groups are as follows: NW = new walkers, PA = preadolescents, A = adults, OA = older adults.

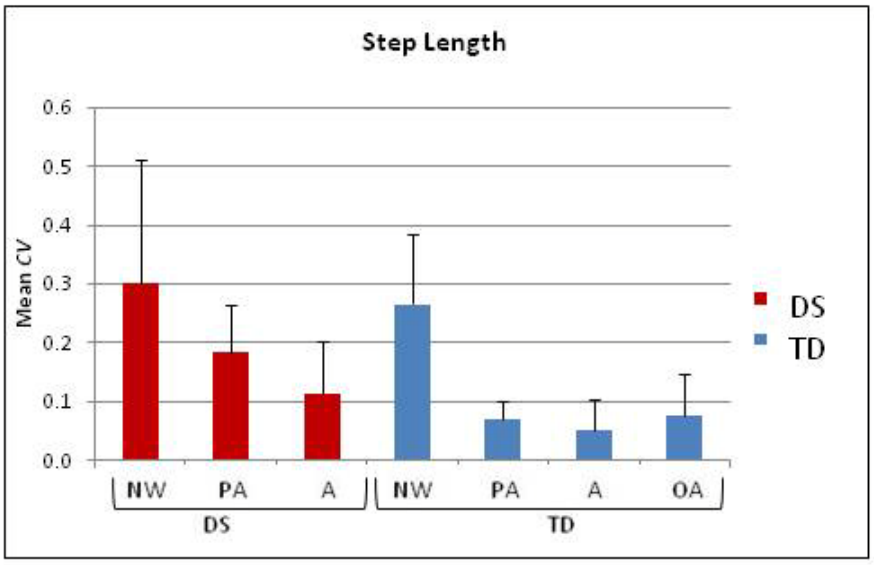

Figure 2.6. Coefficient of Variation (*CV*) of step length for participants with Down syndrome (DS) and typical development (TD). Age groups are as follows: NW = new walkers, PA = preadolescents, A = adults, OA = older adults.

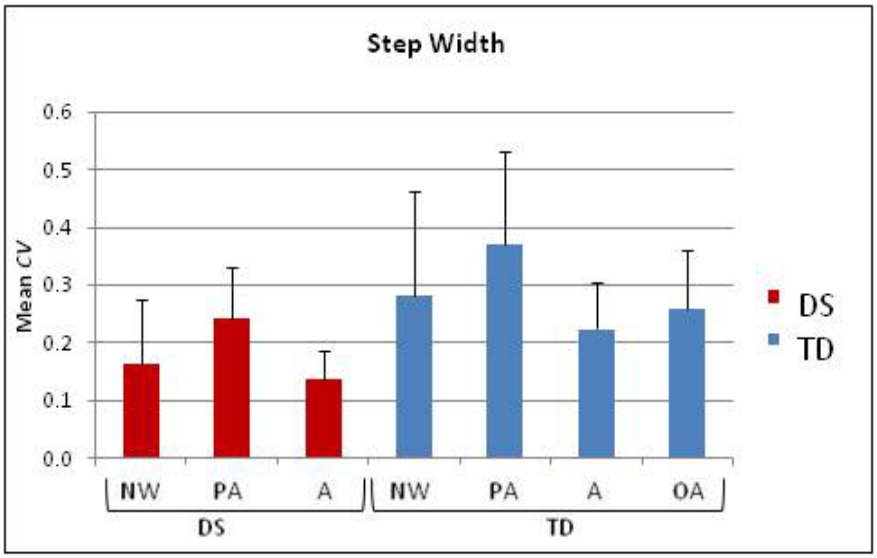

Figure 2.7. Coefficient of Variation (*CV*) of step width for participants with Down syndrome (DS) and typical development (TD). Age groups are as follows: NW = new walkers, PA = preadolescents, A = adults, OA = older adults.

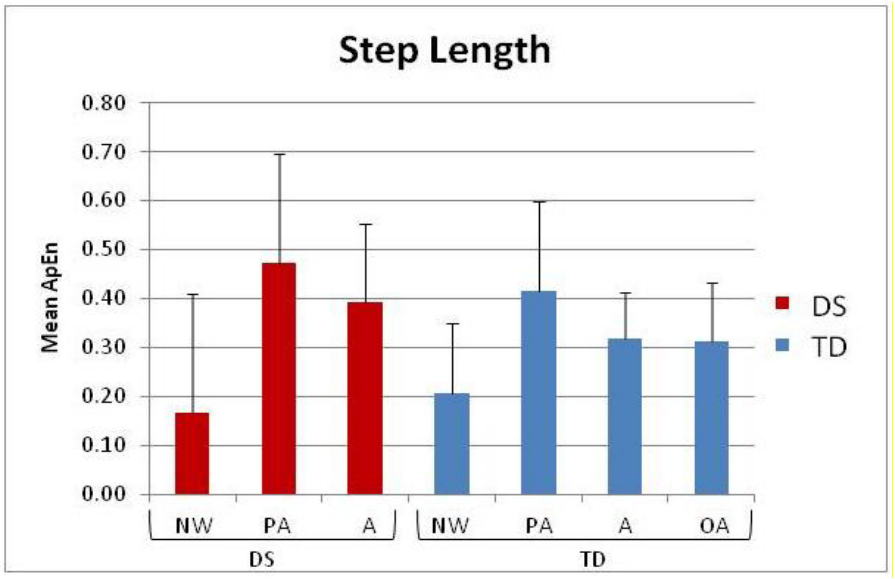

Figure 2.8. Approximate Entropy (ApEn) of step length for participants with Down syndrome (DS) and typical development (TD). Age groups are as follows: NW = new walkers, PA = preadolescents, A = adults, OA = older adults.

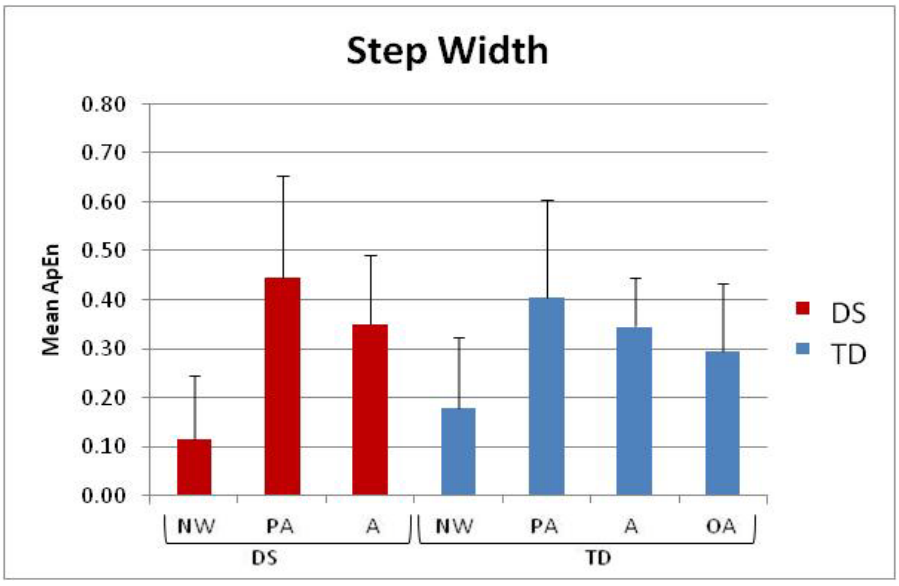

Figure 2.9. Approximate Entropy (ApEn) of step width for participants with Down syndrome (DS) and typical development (TD). Age groups are as follows: NW = new walkers, PA = preadolescents, A = adults, OA = older adults.

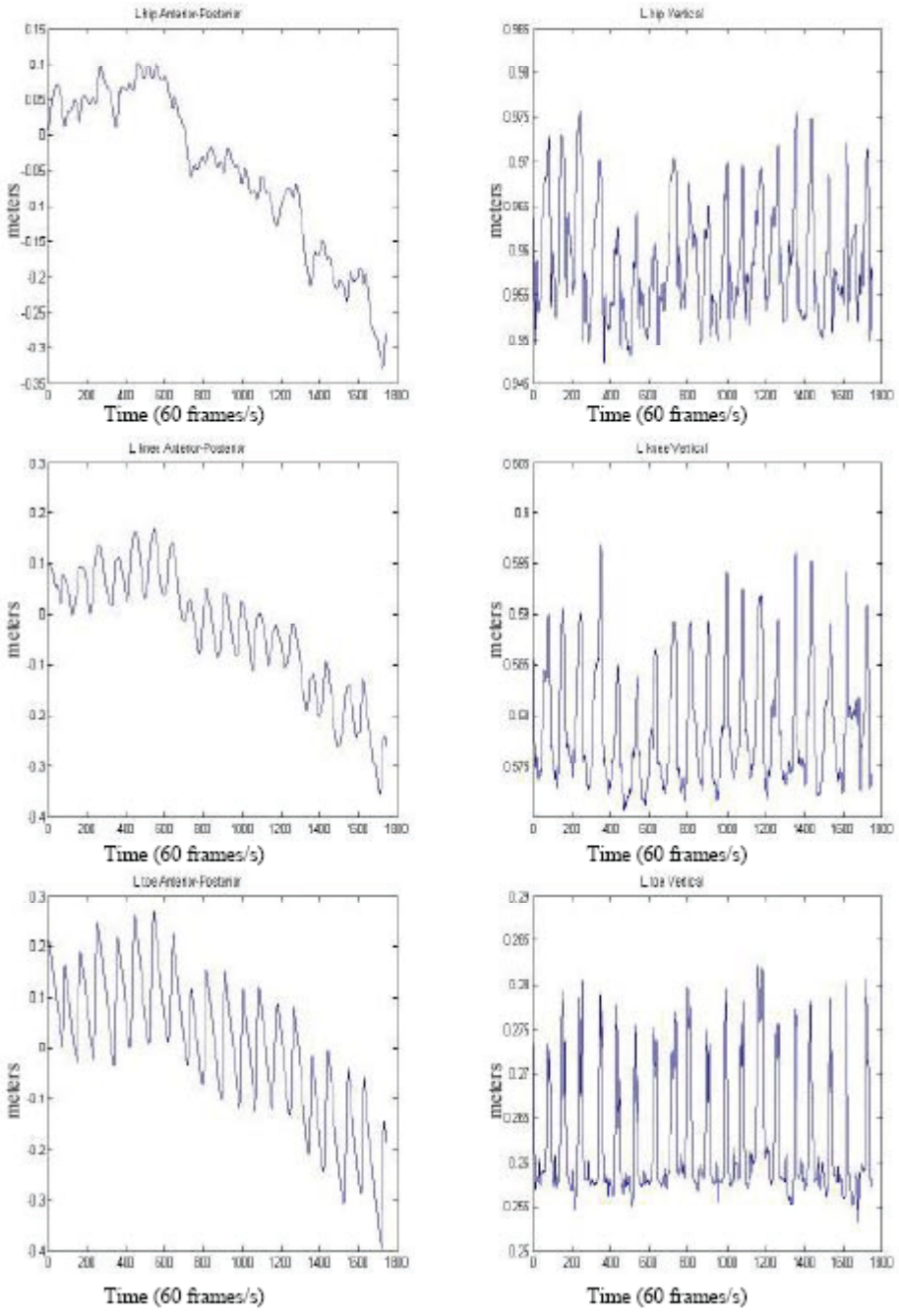

Figure 2.10. For an adult with DS walking on the treadmill: anterior-posterior direction time series are in the left column for hip (top), knee (middle) and toe (bottom). Vertical direction time series are in the right column for hip (top), knee (middle) and toe (bottom). For the hip, the cyclic motion of the leg is not clear in the anterior-posterior direction. The toe displays cyclic motion in both directions; but noise in the vertical direction data, particularly in the troughs, would decrease accuracy of results.

APPENDIX 2.1

The Uncontrolled Manifold (UCM) uniquely allows one to partition the overall variability into "bad" variations in movement that affect an important performance variable and cause error or "good" variations that keep the performance variable unchanged and allow flexibility and adaptability to maintain a successful outcome. In the analysis one defines a multi-dimensional space to represent the movement under investigation and then partitions multi-joint covariation into one of two categories, adversely affecting performance or not (Latash & Anson, 2006).

Recurrence Quantification Analysis (RQA) is a visualization technique using a square and its diagonal. As a signal grows in complexity, recurrence in the pattern of the signal occurs less often (Zbilut & Webber, 1992). An RQA plot with many single dots and very few diagonal lines represents a signal that is not very recurrent and is not predictable, while a deterministic process is recurrent and predictable and shows a plot with few single dots and many diagonal lines. One of the many quantifiable measures of this technique is a parameter named determinism, which represents the predictability of the signal by quantifying the percentage of recurrent points that form upward diagonal line segments.

Fractals and Power Law Analysis includes techniques such as Hurst Exponent and Detrended Fluctuation Analysis (DFA). Fractal analysis concerns the scale with which we choose to measure, and how patterns are repeated within an object shape or time

series regardless of which level you choose. Power laws describe the relationship of the variable on one level to itself on another level of measurement, thus quantifying the self-similarity of the pattern (Riley & Van Orden, 2005). The Hurst exponent represents the typical scaling component of the series, and its value indicates persistent correlations, antipersistent correlation, or no correlation (Delignieres et al., 2006). DFA was developed to distinguish between intrinsic fluctuations generated by complex systems and those caused by external stimuli acting on the system. Variations that arise because of extrinsic stimuli are presumed to cause a local effect, whereas variations due to the intrinsic dynamics of the system are presumed to exhibit long-range correlation (Peng et al., 1995).

Previous Application of Nonlinear Tools

Physiology

Nonlinear tools have been successfully applied in physiological research to refute the long held notion of homeostatic physiological systems maintaining a stable state and to promote the theory that optimal levels of variability and adaptability are the keys to survival. As Goldberger (1991) points out, the notion of a physiological steady state is refuted by recent observations that indicate a good deal of intrinsic variability in many aspects of healthy function. For example, the normal heartbeat is not predictably regular. The normal electroencephalogram shows erratic brain wave activity. Hormone levels, assayed in the serum of healthy individuals, fluctuate in a manner that also seems to

violate the constancy required of unperturbed homeostatic systems (for review see Goldberger, 1991).

Focusing on the cardiovascular system, decreased heart rate variability is currently recognized as a hallmark of cardiac disease. Blunted cardiovascular response to exercise and patterned arrhythmias are common clinical manifestations of this decreased variability (Paz & Panik, 2002). Decreased heart rate variability is significantly associated with subsequent cardiac events even when controlling for relevant clinical risk factors including frequent supraventricular premature beats (>120/h), smoking, diabetes, systolic blood pressure, left ventricular hypertrophy on ECG, diuretic use, ß-blocker use, other cardiac medication use, and mean heart rate (Tsuji et al., 1996).

Despite knowledge of this association, assessment of heart rate variability has been challenging with many measures unable to differentiate between patient groups or predict future cardiac events. Nonlinear analysis, however, has been promising. Makikallio et al. (1999) state, "The traditional methods of analyzing heart rate variability have failed to predict imminent ventricular fibrillation (VF). We sought to determine whether new methods of analyzing resting rate (RR) interval variability based on nonlinear dynamics and fractal analysis may help to detect subtle abnormalities in RR interval behavior before the onset of life-threatening arrhythmias". Using DFA, they observed abnormalities in RR interval dynamics before the spontaneous onset of VF that were not detectable by traditional time- and frequency-domain methods. For the DFA scaling exponent α, an average value of 0.67 was observed in patients who demonstrated VF. This is in contrast to an α of 1.0 (fractal-like correlation properties) observed in

uncomplicated post-infarction control patients and in healthy subjects or an α of 0.5 predicted for completely random behavior (Mäkikallio et al., 1999).

Another example of altered dynamics visible only through nonlinear techniques involves the cardiac output of critically ill intensive care unit (ICU) patients. Seiver, Daane, and Kim (1997) reported a serendipitous finding during development of an automated electronic flow chart system to gather data on ICU patients: the observation of low frequency oscillations in blood pressure that were not explained by the environment. They observed low-frequency periodic oscillations in the cardiac output of ten patients, with regular periodicities of 4 to 280 minutes (average = 34 minutes). The mortality rate in these patients was 40%, while the mortality was only 10.8% in 83 similarly monitored ICU patients who did not develop regular oscillations in cardiac output. In many cases, onset of the oscillations closely followed clinical situations where there was inadequate resuscitation (such as temporary loss of an infusion of epinephrine for cardiac support), or increased metabolic stress (such as a prolonged high fever) (Seiver, Daane, & Kim, 1997). This "serendipitous" finding is a wonderful example of complexity theory and the importance of optimal variability in a healthy system, although we are still attempting to understand how it all fits together.

We still do not fully understand how complexity and optimal variability emerge. In the case of heart rate variability, heart rate is directly modulated by autonomic inputs. Parasympathetic stimulation decreases the firing rate of pacemaker cells of the heart's atrioventricular node while sympathetic stimulation increases the rate. There is also indirect control of heart rate variability through release of epinephrine and norepinephrine (both increase heart rate) from the adrenal medulla. This secondary

response occurs within minutes of increased physical activity, or in response to fear (Paz & Panik, 2002). At rest it is the competition between the parasympathetic and sympathetic input results in the chaotic heart rate variability that is recorded in healthy subjects (Goldberger, 1991). What, then, is affecting the parasympathetic and sympathetic inputs? There are so many interrelationships, the system so complex, that we can never understand every interaction leading to a specific outcome. We can, however, identify key relationships and the effects of intervention on the emergent behavior.

Viewed from a complex systems mathematical assessment standpoint, systems are typically composed of interacting units that communicate information and are able to process and withstand a broad range of stresses. In physiology, free-running healthy systems typically generate complex output signals that have long-range correlations (α of 1.0) (Amaral, Díaz-Guilera, Moreira, Goldberger & Lipsitz, 2004). This means that the history of the system influences its current state with input on its behavior coming from many other systems, and that a healthy system is complex, robust and adaptable. Deviations from the α of 1.0 pattern have been associated with disease or aging in various contexts (Goldberger et al., 2002; Lipsitz & Goldberger, 1992). The loss of this pattern indicates that the system becomes less complex, less robust and less adaptable with aging or disease. The authors do not state whether the loss of complexity and adaptability is from too much variability (unstable) or too little variability (rigid).

Based on the studies mentioned above, the application of nonlinear tools to physiological systems gives us a new way to look at data to see behaviors we otherwise could not, as well as new measures with which to assess behavioral outcomes. Nonlinear

tools allow us to address issues of quality of variability and its relationship to the complexity and adaptability of systems' behavior.

Motor Control

Relatively few researchers have applied nonlinear analysis to study human movement. Goldberger and colleagues extended their work from physiology to walking to quantify the stride-to-stride fluctuations of healthy young men (20–30 years) as they walked continuously on level ground. Their DFA analysis indicated long-range, fractal correlations in the data (Goldberger et al., 2002; Hausdorff, Peng, Ladin, Wei, & Goldberger, 1995; Hausdorff et al., 1996).

Moving on to other nonlinear tools, RQA, specifically the parameter percent determinism, has been applied to detect an increase in the regularity of surface electromyographic muscle activity with time as motor unit synchronization occurs and force is produced (Filligoi & Felici, 1999). It has also been used to assess changes in fatigue resistance of paraspinal muscles in participants receiving physical therapy services for back pain. An increase in the RQA variable percent determinism correlated well with muscular fatigue. Following physical therapy, percent determinism indicated less motor unit recruitment, indicative of increased fatigue resistance in participants who, more importantly, reported less pain (Liu, Kankaanpaa, Zbilut, & Webber, 2004).

UCM has been used to identify what is controlled in order to stabilize the body during a sit-to-stand movement (Scholz & Schoner, 1999), as well as changes in force variance to increase efficiency during a finger-pressing task in adults with DS (Latash, Kang, & Patterson, 2002; Scholz, Kang, Patterson, & Latash, 2003). In addition, Black

and colleagues applied the UCM analysis to a cyclical task, walking, to determine if preadolescents with DS partition goal-equivalent variability (UCM(||)) and non-goal equivalent variability differently than peers with typical development (TD) and whether treadmill practice would result in utilizing greater amounts of functional, task-specific variability to accomplish the task goal. We found that children with DS partition more UCM(||) variance than children with TD across all speeds and both pre and post practice (Black, Smith, Wu, & Ulrich, 2007). This implies that, although they demonstrate a higher quantity of variability, preadolescents with DS show functional adaptations to successfully achieve the task.

The use of nonlinear tools in these studies has allowed for interpretations and conclusions that would not be possible using only traditional linear tools. In many cases, the amount of variability does not change, although the quality of the behavior does. Nonlinear tools offer the ability to interpret changes in the quality of movement, which allows researchers to consider new types of questions. Specifically, we have chosen to use LyE and ApEn based on the characteristics of our data and our desired variables and analysis.

ApEn and LyE can be used with relatively shorter time series, while power law techniques such as DFA and Hurst exponent require 5 minutes of continuous data for an estimate of and 24 hours of data for assessment of true long range correlations (Hausdorff et al., 1997; Nazeran et al., 2006; Neumeister, Cellucci, Rapp, Korn, & Faber, 2004). Some populations, including new walkers and older adults with DS, are unable to walk continuously for 5 minutes, limiting the applicability of these latter techniques. In addition, DFA focuses on separating external and internal perturbations. In the

comfortable speed treadmill-walking context we are using, we are interested in focusing on group differences in variability without separating, statistically, the internal and external components.

Other nonlinear methods we chose not to use include RQA and UCM. RQA is primarily a visualization tool. Although outcome values of RQA recurrence plots, specifically percent determinism and the maximal diagonal line length, quantify the predictability and divergence of a signal, they are calculations obtained from the image of a recurrence plot (Riley & Van Orden, 2005) and are therefore indirect measures of what LyE and ApEn calculate directly. UCM has potential to offer some excellent insights to understanding the "good" and "bad" variability during walking. However, techniques developed to date do not allow analysis of the full trajectory. Currently, one is limited to picking a critical discrete point in the behavior to represent the entire movement (Black, Smith, Wu, & Ulrich, 2007), or to repeating the process over multiple points. We are interested in how the joint trajectory throughout the stride relates to variability in gait parameters. Looking at discrete points in the gait cycle, even at every point, would not work well for our specific questions.

Each nonlinear tool has its own strengths. Of the better known options outlined above, ApEn and LyE will best address variability in joint trajectories and the effects of this variability on quantity and quality of subsequent gait parameters. LyE will reflect the quality of the joint trajectory, while the Coefficient of Variation is a linear tool to address quantity of variability. ApEn will summarize the step-to-step consistency, while the Coefficient of Variation will quantify variability of the outcomes – step lengths and widths.

APPENDIX 2.2

We chose to analyze unfiltered 3-D data from the knee of new walkers, preadolescents and older adults with and without DS walking on a motorized treadmill. Because the patterns of variability are the focus, most researchers agree on using unfiltered data for this type of analysis (Dingwell & Marin, 2006; Rapp, 1994; Stergiou et al., 2004). We conducted pilot work to examine the joint marker motion of the hip, knee, ankle, heel and toe markers and found the knee to be most representative of the pendular stance and swing phases of lower leg trajectory during walking. The ankle, heel and toe markers show much variability in addition to the cyclic motion, while the hip does not adequately show the cyclic motion (see Figure 2.10). We evaluated treadmill walking rather than overground data because it increased the number of continuous strides we had available for analysis. Due to space constraints of our 3D motion analysis calibrated volume we were often able to collect only 5 or 6 consecutive overground strides. Previous work has shown that 50 data points are the minimum for ApEn calculations (Pincus & Goldberger, 1994) and 35 gait cycles are recommended for LyE analysis (Stergiou et al., 2004).

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CHAPTER III
STABILITY AND VARIABILITY DURING PERTURBED WALKING IN ADULTS WITH DOWN SYNDROME

ABSTRACT

To extend our understanding of gait adaptation and stability in older adults with DS, we assessed changes in gait parameters and variability during common environmental perturbation conditions. We used 3-D motion analysis to capture the gait patterns of 14 adults with DS and 14 with TD, 35 to 65 years of age. Adults with DS and TD adapted with complex adjustments to parameters and variability; adults with DS adapted well to anticipated perturbations. Adults with DS demonstrated unique responses, however, to the divided attention, low light and obstacle conditions. They are influenced by visual distractions and rhythmical tasks, and take longer than their peers with TD to prepare for obstacles. These effects may be detrimental to gait stability in real-world, uncontrolled situations. They need to explore a rich repertoire of variability and movement strategies in order to obtain and maintain flexible yet stable solutions.

INTRODUCTION

Persons with Down syndrome (DS) are now living well into adulthood. The median age at death has increased to nearly 60 years, with some people with DS living

into their 70s (Day, Strauss, Shavelle, & Reynolds, 2005; Glasson et al., 2002). Premature aging has been noted in this population; the rate of physiological aging is nearly twice that of adults with typical development (TD) (Nakamura & Tanaka, 1998).

Adults with DS show precocious age-related changes in several respects, both in physiologic function and in resulting motor performance. They demonstrate decreased ability to perform activities of daily living by 40 years of age (Maaskant et al., 1996) while adults with only intellectual disability do not demonstrate a decline until 50 years of age (Janicki & Jacobson, 1986). They often also experience premature problems with osteoarthritis (Diamond, Lynne, & Sigman, 1981), hearing loss (Evenhuis, van Zanten, Brocaar, & Roerdinkholder 1992), increased body weight (Melville, Cooper, McGrother, Thorp, & Collacott, 2005) and Alzheimer's type dementia (Lott & Head, 2001; Schupf et al., 2003; Teipel et al., 2004).

Locomotor stability is a challenge for people with DS across their lifespan. Due to low tone and ligamentous laxity, achieving stable upright locomotion is a more difficult problem than for their peers with TD; average onset of independent walking in those with DS is 2 years of age (Kubo & Ulrich, 2006; Ulrich, Ulrich, Angulo-Kinzler, & Yun, 2001) as compared to 1 year in the population with TD. Their solution to this stability problem has unique attributes; after one month of walking experience, compared to their peers with TD, toddlers with DS show shorter stride length, slower velocity and a trend towards wider step width (Kubo & Ulrich, 2006). Following years of walking practice, however, most of these group gait parameter differences disappear; of the parameters just listed only step width remains larger in preadolescents with DS as compared to their

peers with TD (Smith, Kubo, Black, Holt, & Ulrich, 2007; Ulrich, Haehl, Buzzi, Kubo, & Holt, 2004).

In addition to the stability challenges inherent to DS, there are several factors known to negatively affect gait in adults with TD that may also be relevant for adults with DS. These factors include a sedentary lifestyle (Fujiura, Fitzsimons, Marks, & Chicoine, 1997), obesity (Melville et al., 2005) and neurophysiological changes associated with aging. The gait characteristics of sedentary but otherwise healthy older adults suggest that they adopt a more cautious walking style than active older adults, exhibiting shorter step lengths and slower step velocities (Rosengren, McAuley, & Mihalko, 1998). Obese persons walk more slowly (Spyropoulos, Pisciotta, Pavlou, Cairns, & Simon, 1991) and with a larger step width (Browning & Kram, 2005; Spyropoulos et al., 1991). Neurophysiological changes associated with aging, such as decreased tactile sensation, proprioception, vision and strength, as well as increased reaction time all contribute challenges to body control (Delbono, 2003; Lord, Clark, & Webster, 1991; Matsumura & Ambrose, 2006; Speers, Kuo, & Horak, 2002; Woollacott & Tang, 1997).

Researchers interpret age-related adjustments in gait as strategies adopted to increase walking stability (Cromwell & Newton, 2004; Maki, 1997; Menz, Lord, & Fitzpatrick, 2003; Menz, Lord, & Fitzpatrick, 2007; Winter, Patla, Frank, & Walt, 1990). These adaptations include reduced stride length, reduced velocity, increased step width and more time in double support and are observed starting around 64-70 years of age in healthy adults (Samson et al., 2001; Stolze, Friedrich, Steinauer, & Vieregge, 2000; Cromwell & Newton, 2004).

There are many reasons why walking requires stability-enhancing adaptations as adults with DS age. In pre-adolescents, merely increasing step width is an adequate adaptation to provide the greater than normal stability needed to control self-paced, unperturbed over-ground walking (Smith et al., 2007; Ulrich et al., 2004). As they age, constraints affecting their ability to maintain walking stability, such as obesity and arthritis, increase, and perhaps they simultaneously experience a decrease in their ability to adapt their gait patterns, stiffness and impulse. They also experience the typical physiologic changes associated with aging, which further affect their ability to sense and respond to perturbations. In response, they demonstrate an early onset of stability-enhancing adaptations in gait characteristics. They adapt in ways seen across the lifespan in those with DS (e.g. wider step width) and add strategies used by elderly adults with TD (e.g. shorter step lengths, more time in double support, more time in stance and slower velocity), although at a much younger chronological age (Smith & Ulrich, 2008).

Based on these studies, we know that adults with DS adapt self-selected comfortable gait as they experience gradual changes in subsystems, and these differences emerge at a younger age than their peers with TD. They also demonstrate a chronologically earlier shift in adaption of gait performance for more complex tasks, such as crossing an obstacle. Adults with DS (*M* age 43 years) stepped differently than their peers with TD (*M* age 45 years), making earlier and larger adjustments to cross a visually apparent 12 cm-high obstacle. Adults with DS started their crossing step further away from the object, causing the obstacle to be further forward in their crossing step. Consequently, they produced a lower, flatter trajectory of the lead foot, with less dorsiflexion at crossing. This pattern of stepping also led to decreased trailing toe

clearance (Smith and Ulrich, 2008). Similar obstacle clearance patterns have been observed in elderly adults with TD (*M* age 71 years) (Chen, Ashton-Miller, Alexander, & Schultz, 1991).

We do not, however, know the effects of other common environmental perturbations on the gait of adults with DS. Perturbations that occur during daily living such as divided attention, low lighting, or irregular surfaces are known to decrease gait stability and elicit subsequent adaptations in older adults with TD (see Appendix 3.1). For example, gait changes observed in dual task walking indicate that cognitively demanding tasks during walking have a destabilizing effect on gait in older adults with TD (Hollman, Kovash, Kubik, & Linbo, 2007). If adults with DS show stability-enhancing adaptations during unperturbed walking and when faced with minimal perturbations, are they able to adapt further, and successfully, when faced with larger perturbations or is there a relatively low limit to their stability adaptation capacity? Are they more likely to fall than their peers with TD? Are some contextual constraints more problematic than others for this population than the population with TD, given the unique neurophysiological characteristics of those with DS?

Our contention that stability-enhancing gait adaptations in adults with DS are necessitated by multiple causes is in agreement with Hale and colleagues (2007), who concluded that the increased risk of falling in adults with intellectual disabilities is multi-factorial (Hale, Bray, & Littmann, 2007). However, information allowing us to determine if there is a link between impact of common environmental perturbations and stability-enhancing adaptations of overground gait to increased fall risk does not exist for the DS population. Adults with DS face multiple inherent constraints to walking stability that

require adaptations earlier in life than their peers with TD. Consequently, they may be at increased risk of falling at an earlier age. In this study we will test the link between a specific set of common environmental perturbations and the overground gait adaptations of adults with DS.

To explore the multi-factorial aspects of sensori-motor perturbations of gait performance in adults with DS, we compared unperturbed comfortable walking with performance in five single sensori-motor perturbation conditions and two double perturbation conditions. We hypothesized that some of the conditions would create more challenge than others for maintenance of gait stability in adults with DS, and they would adapt by making larger adjustments in gait parameters and variability in more challenging conditions. In comparison to their peers with TD, we hypothesized that adults with DS would show greater variability in gait parameters when walking in both the unperturbed and perturbed conditions. Further, as the perturbation conditions were meant to be challenging for adults with DS but, with the exception of the irregular surface, not for their peers with TD, we anticipated adults with DS would show significant change in amount of variability from baseline to all perturbation condition, while adults with TD would only demonstrate significant change in amount of variability from baseline to the irregular surface perturbations. In addition, the double perturbation conditions should have created a greater need for adaptation than the single perturbation conditions, thus we believed adults with DS would show significantly greater change in amount of variability from baseline to double perturbation combination conditions than they did from baseline to single perturbation conditions.

METHOD

Participants

Fourteen adults with DS and 14 with TD between ages 35 and 65 years participated in the study. Individuals were matched *a priori* for height, weight and age. Exclusion criteria include a history of knee or hip arthroplasty, fractures or sensori-motor deficits of the lower extremity, or current medications that alter cardiac response to exercise. Adults with DS were recruited through Ann Arbor area community recreation groups and support groups, work programs and group homes for adults with disabilities in Michigan and northern Ohio. Adults with TD were recruited from the University of Michigan clinical research volunteer website Engage.

Procedures

Participants came to the University of Michigan Biomechanics Research Laboratory for 1.5 to 2 hours of testing on one occasion. As described below, the data collection consisted of obtaining informed assent and/or consent, questions about fall status and general health and activity status, walking comfortably overground, walking in perturbation conditions, balance assessment and anthropometric measurements.

The University of Michigan Institutional Review Board approved all procedures. Prior to participation, we explained the purposes of our study and all procedures to participants and any caregivers or legal guardians. Participants signed an assent or consent form as appropriate, with consent for assenting adults provided by a legal guardian.

Participants changed into their own socks, close-fitting shorts and t-shirt. In most cases, they wore standard New Balance brand lace-up walking shoes that we provided for them in a size they choose as comfortable (narrow and wide sizes from 5.5 to 10 for women and 9.5 to 16 for men were available). If we were unable to fit them comfortably or they typically wore orthoses, they wore their own standard lace-up sneakers (often New Balance brand due to the availability of wider widths in this brand). In addition, all participants wore a safety harness tailored to their height and weight. During walking trials, the harness was attached to an overhead track. Before starting data collection, we adjusted the suspension to assure that participants' knees could not come into contact with the floor should they lose their balance while walking during a test trial. All participants were allowed at least 5 minutes to stand and walk around the room and hallway to accommodate to the harness and shoes before we attached the harness to the overhead track and started testing.

After the equipment accommodation period, we palpated bony landmarks for placement of markers for motion analysis. We applied infrared emitting diodes bilaterally at the knee (proximal edge of the patella) and ankle (anterior to the lateral malleolus). We also placed markers bilaterally on the heel of the shoe above the bony prominence of the heel and on the toe of the shoe at the distal end of the third metatarsophalangeal joint. Finally, markers were placed bilaterally on the anterior trunk to provide information about overall walking speed (see Appendix 3.2) for further information on diode placement). Diode wires were secured to the participants' legs with tape and attached to power supply boxes secured to a strap on the back of the harness. We positioned wires to allow adequate limb range of motion without pulling or tangling. As

participants walked across the room in unperturbed and perturbed conditions, we used a 6-camera optoelectronic system (Optotrack; Northern Digital Corporation, Waterloo, Canada) to collect diode position data at a sampling rate of 100 Hz. Three cameras were placed at each end of the walkway, resulting in 3 cameras in front of participants and 3 behind.

First, participants performed 4 repetitions of the unperturbed condition and walked along the flat 10 m walkway at a comfortable self-selected speed. The 4 repetitions consist of walking from one side of the room to the other, and then back the opposite direction, twice. Next, they completed a 4-repetition block of each perturbation condition, with the conditions sequenced in a random order. We provided visual and verbal instruction to participants to describe each condition, allowing them to practice each task with verbal feedback until they indicated they were ready and able to perform it successfully. Participants with TD required practice infrequently. Participants with DS were more variable; some participants understood the task with only verbal description, some required verbal description and physical demonstration, and others required 1 or 2 practice repetitions with feedback. Perturbation conditions are described briefly as follows (for further information please see Appendix 3.2):

Divided Attention: We asked participants with DS to start counting out loud by 1, and then asked them to start walking. They continued counting and walking until they reached the end of the walkway. In some cases we had to cue them verbally to continue counting. Participants with TD were also asked to count out loud as they walked, however they counted by 4. Based on our previous work with adults with DS, counting

by 1 was chosen to provide a similar level of difficulty as counting by 4 for adults with TD.

Distracting sounds: Prior to the initiation of walking, we began playing sounds of a street corner in the background. The sounds, consisting of cars and a scooter driving by and undistinguishable voices, were played at moderate volume (average 64 dB). This selection was chosen for its inconsistent nature, as opposed to something rhythmical like music, to avoid entrainment of gait. We want to see if participants are able to block out the distraction or are perturbed by it.

Irregular surface: To create an irregular walkway surface, we modified a 1.5- by 10-m piece of industrial carpet by randomly arranging prism-shaped pieces of wood (height = 1.5 cm, width = 3.5 cm, length = 6–16 cm) beneath the middle 6.5-m section of the carpet at a density of 26 pieces per meter^2.

Obstacle: Participants walked, stepped over an 8 cm peak, and continued walking. The obstacle was made of blue construction paper (83 cm in width, 8 cm in height, 4 cm in length, placed with its length parallel to the walkway) and moved if touched or collapsed to flat if stepped on.

Low light condition: Room lights were dimmed to an even, low level (average 8.6 lux). This level of lighting allows a participant to see the other end of the walkway but not to make out object details. In all other conditions the lighting was, on average, 400 lux, the

level of brightly lit office space and likely brighter than the average home or public space.

Divided attention and low light combination: a combination of these two conditions.

Irregular surface and distracting music combination: a combination of these two conditions.

To assure persons with DS did not become overly fatigued, we monitored their level of exertion subjectively by asking them if they were tired and needed to rest, and objectively using a portable pulse oximeter to assess heart rate at rest and every three minutes, between trials. Participants were not taking any medications that alter cardiac response to exercise, allowing us to use the formula 220-age-32 bpm for persons with DS (Fernhall et al., 2001). Participants were allowed to rest at their request. In addition, we would have asked participants with DS to rest to rest if they exceed 70% of their maximal predicted heart rate, a common heart rate goal for sedentary persons beginning aerobic exercise and below the range of submaximal exercise treadmill tests (Noonan & Dean, 2000). This did not occur, as participants' heart rates did not ever reach our threshold.

Participants completed the Berg Balance Scale, a standardized balance assessment instrument (Berg et al., 1989; Berg et al., 1992) with demonstrated reliability for adults with DS (Sackley et al., 2005). The assessment consists of 14 different tasks including sitting, standing, reaching, leaning over, turning and stepping. In addition, participants with DS completed the Timed Up and Go, a timed assessment of standing, walking and

turning that is predictive of falls in community-dwelling older adults with TD (Shumway-Cook, Brauer, & Woollacott, 2000). For all participants, we recorded anthropometric measurements including height, weight, thigh length, shank length and foot length.

During an in-person interview, before data collection as the participants became familiar with the lab staff or during collection as the participant was resting, we asked about living arrangements, employment status, and exercise or recreational activities. With assistance from caregivers as needed, prior to data collection, participants completed a paper survey addressing general health and medication questions, fall status, and the Adaptive Behaviour Dementia Questionnaire, a screening questionnaire for dementia in Alzheimer's disease in adults with Down syndrome (Prasher, Farooq, & Holder, 2004). The questionnaire consists of 15 multiple-choice questions regarding changes in behavior and ability to perform activities of daily living over the last 6 months.

Data reduction

Real-time marker visibility allowed us to monitor the quality of data during the collection to ensure four trials per condition when all markers were visible. Data were collected at 100 Hz and transformed into 3-D coordinates using the Optotrak system and software, then further analyzed using custom MATLab programs. We analyzed data for the period of steady state walking, after acceleration and before deceleration, operationally defined as when the pelvis marker velocity was maintained above 85% of the mean walking speed of the trial (Demott et al., 2007).

Dependent variables we calculated include percent stance, step width and stride length, velocity and frequency. Percent stance phase represents the percent of the stride cycle of one leg from heel contact to toe off. Step width was defined as the distance between the heel of one foot and the line of progression of the other foot while stride length was defined as the distance from the heel to its successive placement. Stride frequency was determined based the time elapsed between successive heel contacts of the same foot. Stride velocity was calculated based on the mean velocity of the heel marker throughout the swing phase. In general, there were from 12 to 20 strides of steady state walking available for analysis per participant per condition. For further statistical analyses, we randomly selected 12 strides from the available strides and calculated a mean value per condition. In addition, we calculated overall walking speed by taking the derivative of the anterior-posterior position of the pelvis marker. Walking speed, step width and stride length, velocity and frequency values were converted to dimensionless values using the formulas in Appendix 3.3. We chose to use dimensionless values as participants were matched for height, but not leg length. At younger ages, persons with DS have shorter legs relative to their trunk (Kubo & Ulrich, 2006; Smith et al., 2007; Ulrich et al., 2004), a difference that appears to persist at least slightly into adulthood (Smith & Ulrich, 2008).

To represent amount of variability in these gait parameters, we calculated standard deviation (SD) of percent stance and the Coefficient of Variation (*CV*) of step width and stride length, velocity and frequency values. An SD or *CV* was calculated for each of the four trials per condition. For further statistical analyses, we calculated a mean SD or *CV* per condition.

RESULTS

Participants

Adults were matched for height, weight and age (see Table 3.1), as confirmed by one-way ANOVA to test for group differences in each variable. No significant group differences emerged. Six adults with DS reported a history of falls and 8 did not. Three adults with DS had a loss of balance during the data collection. One participant was able to regain stability with a very large lateral step, while the other two required assistance from the spotter to avoid a fall to the ground. No adults with TD reported a history of falls, and none lost their balance during the data collection. Adults with DS scored significantly lower than adults with TD on the Berg Balance Scale, indicating poorer performance [one-way ANOVA ($F[1, 26] = 13.58$, $p = 0.01$)], DS median score 52 with range 40-56, TD median score 54 with range 48-56].

Out of the 14 adults with DS, 7 lived with their parents and 7 lived in supervised apartments or group homes. Nine of them worked part-time, ranging from 8-25 hours per week across 2- 5 days per week. Three reported minimal regular physical activity (PA), performing sedentary jobs and infrequent PA. Eight reported moderate PA, described as non-sedentary jobs and regular PA 15-30 minutes, 3-5 days per week. Maximal PA, defined as longer than 30 minutes most days, was reported by 3 adults. PA usually consisted of walking, aerobics, cycling on a stationary bicycle, and/or recreational sports such as bowling or swimming. All adults with TD reported moderate or maximal PA.

Overview of Analyses

Results are organized to address baseline group differences in gait patterns and amount of gait variability before addressing changes in gait patterns and changes in amount of gait variability in response to the different perturbation conditions. Finally, we compare amount of response to the single and double perturbation conditions. Although there were no hypotheses directly addressing baseline differences in gait patterns between the two groups, we have included this analysis first to describe the baseline gait characteristics of each group before studying how they adapted their gait in response to the different perturbation conditions. We need to know what gait patterns are changing from, not only how they are changing, to fully understand different responses between the groups.

Group Differences in Baseline

To examine baseline group differences in gait we used two one-way MANOVAs with 5 dependent variables in each. In the first, we focused on gait parameter means for percent stance and normalized stride length, velocity, frequency and step width values. In the second MANOVA we used variability measures of these gait parameters, SD of percent stance and *CV* of stride length, velocity, frequency and step width.

The one-way MANOVA for mean gait parameter values indicated a significant group difference (Wilks' Lambda [5, 22] = 4.51, $p < 0.01$, partial eta squared = 0.51). Follow up univariate analyses revealed that this overall effect was due largely to the fact that adults with DS walked slower (F[1, 26] = 10.38, $p < 0.01$) and took shorter (F[1, 26]

= 4.34, $p = 0.047$), wider ($F[1, 26] = 7.21$, $p = 0.01$) strides than their peers with TD (see Figure 3.1).

The one-way MANOVA with variability measures in baseline as the DVs did not show a significant difference between groups (Wilks' Lambda [5, 78] = 1.77, $p = 0.13$, partial eta squared = 0.10). However, we examined the follow up ANOVAs because of the literature showing group differences heavily biased toward step width. We observed a significant group difference in the variability of step width, showing adults with DS varied significantly less than their peers with TD ($F[1, 82] = 6.88$, $p = 0.01$). For the other aspects of gait, adults demonstrated similar levels of variability (see Figure 3.2).

Group Gait Adaptations to Perturbation Conditions

To examine composite differences in gait parameters across conditions we used a 2 (group) by 8 (condition) MANOVA with repeated measures on condition, Bonferroni correction for multiple comparisons and Huynh-Feldt correction for unequal variances. Dependent variables were percent stance, normalized stride length, velocity, frequency and step width values. The five gait variables were standardized to Z-scores, maintaining their relative ranges while placing them on the same scale. This allows comparison of changes across conditions of variables originally measured on different scales, with different amounts of fluctuation. Overall, the group main effect was significant (Wilks' Lambda = 0.55, $F[5, 22] = 3.61$, $p = 0.02$, partial eta squared 0.45), as was the condition main effect (Wilks' Lambda = 0.57, $F[35, 751] = 3.06$, $p < 0.01$, partial eta squared 0.11). The group by condition interaction was not significant (partial eta squared 0.03). Follow-up univariate analysis for the group effect revealed adults with DS demonstrated larger

step widths (F[1, 26] = 7.52, p = 0.01) and slower stride velocity (F[1, 26] = 7.01, p = 0.01) than adults with TD. Follow-up pairwise comparisons for the condition effect demonstrated participants, as compared to baseline condition, had lower stride frequency in the irregular surface and distracting sound combination condition (p = 0.046). This was the only significant shift in performance from the baseline condition, although Figure 3.1 illustrates that there were differences between conditions when some parameters increased from baseline in one condition and decreased from baseline in a different condition. There were also conditions where one group increased from baseline while the other decreased.

To test for group differences in the amount of variability in performance across all conditions, we used a 2 (group) by 8 (condition) MANOVA with repeated measures on condition, Bonferroni correction for multiple comparisons and Huynh-Feldt correction for unequal variances. Dependent variables were SD of percent stance and *CV* of stride length, velocity, frequency and step width. The multivariate group effect (Wilks' Lambda = 0.60, F[5, 22] = 2.96, p = 0.03, partial eta squared = 0.40) and condition effect (Wilks' Lambda = 0.61, F[35, 751] = 2.97, p < 0.01, , partial eta squared = 0.09) were significant. The group by condition interaction was not significant (partial eta squared = 0.03). Follow-up univariate analysis for group differences showed that the group difference was largely due to the fact that adults with DS showed more stride velocity variability (F[1, 26] = 4.54, p = 0.04) and close to, but not significantly less, step width variability (F[1, 26] = 3.18, p = 0.08) than adults with TD (see Figure 3.2c). Follow-up pairwise comparisons for the condition effect revealed that the overall condition effect was due

largely to the fact that adults produced more variability in stride frequency in the obstacle condition as compared to the baseline condition ($p = 0.02$).

Because we believe aspects of gait patterns such as we have addressed are not adjusted independently, but emerge as a synergy of outcomes as the system adjusts the limbs and feet to current conditions, we created two additional variables to represent overall system adaptations to perturbation conditions. We created a composite value, by condition, of the five standardized gait values as well as one for the five variability measures. The composite value is a numerical/statistical representation of *average* overall performance by condition, and was created differently than the typical additive process of a clinical composite score. Each composite was created by taking an average value of the five standardized, normalized values per condition, thus creating an overall description of the gait variables for each condition. These composite measures were helpful for understanding the overall condition effect on gait parameters, but not helpful in understanding overall condition effects on variability measures. As we show in Figure 3.3, overall shifts in the five gait variables were especially prevalent in the divided attention condition and irregular surface and distracting sound combination condition. The composite figure for variability measures, Figure 3.4, is misleading, though. The composite gives the impression that adults with TD were more variable overall; however this is a reflection of the effects of a large group difference in one direction for step width offset by small or no group differences in the other direction in amounts of variability of the four other measures. Adults with DS show much less step width variability than adults with TD, and similar to lower levels of variability in stride length, frequency and velocity and percent stance.

A further aspect of response to perturbation conditions we wanted to explore was change from baseline gait in response to the different conditions. This was again more difficult to see due to the complex nature of adaptations that were made. For example, direction of shift of variables was inconsistent across parameters and conditions, in some cases there was an increase from baseline and in others a decrease. In order to better visualize specific gait parameter and variability changes we created two new summative parameters. In Figure 3.5 we present the percent change from baseline to each perturbation condition for each of the five gait parameters, while Figure 3.6 is percent change from baseline to each perturbation condition for each of the five variability measures. Both figures illustrate the relative changes in a variable by condition, as well as the inconsistent nature of changes by variable and by group.

Single vs. Double Perturbations

Human sensori-motor systems contain redundancies to allow flexibility in perception-action capabilities, however there is an ultimate limit to our capacity to adapt. Because adults with DS already show adaptations with age during unperturbed gait, we anticipated they would show a greater amount of adaptation to a single sensori-motor perturbation than they do in unperturbed gait, and greater adaptations yet to double perturbation conditions, which were designed to create more challenge to the system than even the single perturbation conditions. We expected we would see less, if any, adaptations in adults with TD. To reflect the total amount of change in gait parameters, regardless of the direction of shift, we created a new summative change parameter. We calculated an absolute percent change from baseline to each perturbation condition for

each of the five gait variables. As we show in Figure 3.5, adults with DS and TD mostly adjusted stride frequency and percent stance in the same direction, while they tended to adjust step width, stride velocity and stride length in opposite directions. However, a shift in gait patterns is an adaptation, regardless of the direction of shift. Using an absolute change, regardless of direction of shift from baseline, allowed us to compare overall amount of change in gait parameters.

To compare the overall impact of single vs. double perturbations we calculated average values for each participant based on the absolute percent change values, one for the single perturbation level (conditions 2-6) and one for the double perturbation level (conditions 7 and 8). To test for differences we used a 2 (group) by 2 (perturbation level) ANOVA with repeated measures on perturbation level. Perturbation level main effect was significant ($F[1, 26] = 34.34$, $p < 0.01$, partial eta squared = 0.57), while the group effect ($F[1, 26] = 3.70$, $p = 0.07$, partial eta squared = 0.12) and the group by perturbation level interaction ($F[1, 26] = 2.10$, $p = 0.16$, partial eta squared = 0.08) approached, but did not reach, significance (see Figure 3.7). Follow up inspection of the means to understand the perturbation level effect revealed there were more overall adjustments to gait in the double perturbation conditions than the single perturbation conditions.

DISCUSSION

We had proposed that some of the conditions would create more challenge than others for maintenance of gait stability in adults with DS, and they would adapt by making larger adjustments in gait parameters and variability in more challenging conditions as compared to less challenging conditions. Our results are somewhat

surprising, though, in that all conditions elicited many inconsistent combinations of small adjustments in gait parameters and variability in both groups. Overall, however, gait parameter means for adults with DS were significantly different when compared to their peers with TD and they maintained stability enhancing adaptations used in baseline across perturbation conditions. Primarily, gait differences were due to the fact that they walked slower with wider strides than their peers with TD, similar to our previous results (Smith & Ulrich, 2008). During the divided attention, low light and obstacle conditions adults with DS adjusted their gait in ways uniquely different than their peers with TD, though both groups made specific adjustments. The uneven surface conditions affected both groups similarly. During the distracting sound single perturbation condition neither group substantially adapted their gait patterns, although they did make small adjustments.

The condition that elicited the most striking differential effect on gait patterns was the divided attention condition. During this condition, our anecdotal observation of adults with DS suggests to us that they were highly influenced by the rhythm of the counting component of the task, and tended to synchronize their stepping with their counting. This produced an increase in stride length and reductions in variability despite their focus on counting and not walking.

In the low light condition, adults with DS increased their walking speed and stride length while adults with TD did not. We believe adults with DS walked faster in this condition because darkness eliminated visual distractions. They were familiar with the path we asked them to walk, and knew that it was without obstacles or clutter. They could, therefore, focus on the task of walking and reach the end of the walkway quickly.

The obstacle condition also had a differential effect on performance of the groups. When asked to step over the obstacle as they walked, we subjectively observed more preparation in adults with DS. Some adults with DS would stop in front of the obstacle before crossing it, while others would look at the obstacle the entire time as they walked toward it and stepped over it. Adults with TD did not behave this way; they started walking, glanced at the obstacle as they got close to it, and then looked back up before or as they crossed it. In addition, both groups of adults demonstrated a significant increase in stride frequency and a trend to increase stride length variability. Interestingly, the group pattern of stride length variability appears to reverse in this condition. Although difficult to demonstrate statistically, adults with TD seem to show more stride length variability than adults with DS in the obstacle condition, and less stride length variability than adults with DS in all other conditions. To better understand the results from this condition, we looked more closely at the sequence of strides prior to stepping over the obstacle. On average, adults with DS showed a 5%, 8% and 9% change in stride length with each subsequent stride as they approached the obstacle. Adults with TD, on the other hand, approached the obstacle with a 2% and 3% change in stride length and then make a larger adjustment (13%) at the obstacle, leading to more stride length variability per trial compared to their peers with DS in this condition. These results are consistent with earlier work where we observed that adults with DS used extended preparation time and more gradual adjustments in stride length and percent stance while preparing to cross a 12-cm-high obstacle, as compared to their peers with TD (Smith & Ulrich, 2008).

Despite the differential performance of adults with DS in the conditions described above, overall adults in both groups showed inconsistent adjustments in gait

parameters and their variability across conditions. We know that in humans gait is a complex and very adaptable movement pattern with redundancies in options available for making adjustments. One can increase walking speed, for example, by increasing stride frequency, increasing stride length, or through some other combination of adjustment of these parameters. Due to the overall lack of patterns in shifts in gait parameters and amounts of variability, there were not significant group by condition statistical interactions. Participants' responses were not uniform within variables or conditions; we observed a variety of responses. There were, however, some robust effects evident. In some cases, these effects were more clearly observed when looking at the composite combination of variable adjustments by condition (the condition effect), such as in the divided attention, low light and obstacle conditions. In other cases they were identifiable at the level of the individual gait parameter, for example the consistent adjustment in stride length or variability of step width.

Although there are many possible adaptive responses, and the combination used may change from situation to situation, greater challenges do require a greater amount of overall adaptive changes. When amount of change in each variable, regardless of its direction, was incorporated into a summative measure both groups of adults demonstrated greater total amount of change in the double sensory perturbation conditions as opposed to the single sensory perturbations. This reflects the increased complexity of response required to adapt when multiple sensori-motor perturbations are present.

We did not see overall increased variability in the gait parameters of adults with DS as they adapted to the increasing challenge provided by the perturbation conditions as opposed to their relatively unchallenged peers with TD. Adults in both groups adapted to

the conditions with a complex mix of adjustments seen in gait parameter changes and variability. In some cases variability increased in response to perturbations while in others it decreased. Challenging sensory perturbations during walking did not necessarily lead to an increase in gait variability; performers had many complementary adaptive responses they could draw from. Although inconsistent across variables and conditions, adjustments in amount of variability were fairly constant between the groups, in that both groups tended to shift in the same direction in response to the perturbation conditions, and thus maintained patterns of group differences observed at baseline.

Although follow-up univariate analyses of the group differences in variability measures were mostly not statistically significant due to small differences, adults with DS appeared to show similar levels, if not more, variability in stride length, frequency and velocity than their peers with TD. Adults with DS, however, showed much less variability in step width than their peers with TD across all conditions even though step width variability was the highest for all five variables by far, for both groups. While the more common finding in research is increased variability in movement patterns in persons with DS as compared to their peers with TD (Latash & Corcos, 1991; Latash, Kang, & Patterson, 2002; Kubo & Ulrich, 2006; Smith et al., 2007), and increased step width variability in faller and non-faller older adults as compared to younger adults (Owings & Grabiner, 2004; Maki 1997), we observed this pattern does not hold for step width variability in adults with DS. Step width is more tightly controlled; they use a wider step width than their peers with TD to stabilize their center of mass as they walk and show here that they are less willing or less able than their peers with TD to allow step width to vary in response to changing external conditions affecting gait. Researchers have

shown in passive dynamic robots and in-vivo studies that step width is more actively controlled than step length to provide medial-lateral stabilization during walking (Bauby & Kuo, 2000; Kuo, 1999). Anterior-posterior control appears to be more passively controlled. Kubo and Ulrich (2006) reported wider step width from the onset of walking in toddlers with DS as compared to their peers with TD, and argued, as well, this occurs for purposes of increased mechanical stability (Kubo & Ulrich, 2006).

Another consideration when discussing a step width in persons with DS is the cerebellum. Brain imaging studies have shown children and adults with DS have smaller relative cerebellar volumes than age and gender matched controls (Aylward et al. 1997; Pinter et al. 2001; Raz et al. 1995). The cerebellum is involved in balance, coordination, motor control and motor learning. Known effects of cerebellar deficits include an increased step width/base of support, increased variability in foot placement and excessive or diminished response to perturbations (for review see Morton & Bastian, 2004). Although cerebellar volumes are disproportionately small in individuals with DS, they do not diminish significantly with age. Researchers using MRI in a longitudinal study of adults with DS stated that volume reduction in the cerebellum does not appear to be specifically responsible for the age-related decline in fine-motor control that is observed in adults with DS (Aylward et al. 1997). Other researchers using MRI found trends for shrinkage of the dorsolateral prefrontal cortex, anterior cingulate gyrus, inferior temporal and parietal cortices, parietal white matter, and pericalcarine cortex in adults with DS as compared to healthy controls and concluded that the pattern of selective cerebral damage in DS is different than the pattern of loss in premature aging or Alzheimer's disease (Raz et al. 1995). Researchers using voxel-based morphometry,

however, suggested that smaller areas of grey matter in the allocortex and association neocortex in adults with DS were due to alterations or loss of allocortical and neocortical neurons due to Alzheimer's disease type pathology (Teipel, Alexander, Schapiro, Moller, Rapoport, & Hampel 2004). In addition, in healthy community-dwelling older adults (*M* age 78.3 years), greater variability of step length was associated with greater prevalence of subclinical brain vascular abnormalities measured as MRI infarcts and white matter hyperintensities (Rosano, Brach, Studenski, Longstreth, & Newman, 2007). Taken together, these studies suggest that although brain changes in adults with DS likely contribute to their declining ability to sense and interact with the world around them, there are not gross changes in the cerebellum or motor areas of the brain that are specifically and directly responsible for changes in gait patterns and variability with age.

Although reaction times are known to be slower in persons with DS, there is some evidence to suggest that motor planning, as opposed to the actual motor response, may be more responsible for motor control difficulties in adults with DS. Results from a study of event-related potentials and reaction times obtained through an auditory oddball paradigm under passive and active motor response conditions showed that participants had particular difficulty with sensory discrimination when preparing a movement in response to a cue (Lalo, Vercueil, Bougerol, Jouk, & Debu, 2005). In a functional context, adults with DS showed earlier and longer periods of motor preparation (step length adjustment) before stepping over a visually apparent obstacle in their walking path (Smith & Ulrich, 2008). As we presented here, adults with DS walked faster when visual information was removed (low light condition). Taken together, these studies suggest that sensory integration and motor preparation takes longer in adults with DS than adults with

TD, and more sensory input, such as a busy visual environment, slows the process further.

Overall, adults in both groups adapted their gait in response to the seven different conditions we presented. Adults with DS adapted their gait by maintaining step width and step width variability similar to baseline and manipulating stride length, frequency and velocity. Although they showed adaptations, a few adults with DS demonstrated ultimate failure in their ability to adapt and remain stable; they experienced loss of balance while none of the adults with TD did. Three participants with DS experienced at least one loss of balance during the data collection. Out of a total of 463 walking trials by adults with DS, a loss of balance occurred in the following conditions (number of occurrences in parentheses): baseline (1), irregular surface (2), divided attention (2), distracting sound (1) or uneven surface/distracting sound combination (1) conditions. One participant was able to regain stability with a very large lateral step, while the other two required assistance from the spotter to avoid a fall to the ground. The spotter simultaneously steadied the back of the harness and the forearm of the participant. As participants wore a harness they would not have fallen to the ground, but we intervened once a fall was imminent to prevent it. We did not want participants to become upset and risk their being unwilling to continue with testing due to fear of falling.

In this study we showed that adults with DS are capable of making complex adaptations to sensori-motor perturbations during gait, however they are more likely to respond unsuccessfully than their peers with TD, with losses of balance that can lead to a fall. We do plan to further investigate the responses of fallers and non-fallers within our study and to explore variables that discriminate the groups. However, the simple fact that

6 out of the 14 adults with DS we recruited from the community had experienced a fall within the past 5 years is indicative of an increased fall risk in adults with DS. In addition, 5 out of the 14 adults with DS reported they were afraid of falling. Falling is not a problem in adults with TD between the ages of 35 and 65 years, fall rates are not reported in the literature until adults with TD reach their mid- to late-60's. None of the TD adults in our sample reported a recent fall or endorsed a fear of falling.

In our study, we observed that adults with DS pay a lot of attention to visual input while walking, to the point of being distracted, and may be more likely to fall in visually distracting environments. In addition, they are strongly influenced by rhythmical tasks, so singing, music and dancing may be good ways to encourage movement and physical activity. From a physical therapy and health promotion and wellness standpoint, prevention of falls needs to start early in life and be maintained across the lifespan for people with DS. Children and adults with DS should be engaged in activities that require multiple repetitions of perturbations to strengthen and reinforce the ease with which they access adaptive response options. This could be through targeted physical therapy interventions, or through community recreational activities such as bowling, dancing or tai chi. These are only suggestions of beneficial activities that involve dynamic movement and a controlled shifting of the center of mass, there are many other possibilities.

The effects that do stand out here, in spite of the complexity and variability of adjustments observed, are compelling and will lead to interesting and more focused future studies. Unique sets of studies created to investigate the differences in performance between divided attention and increased distraction vs. low light and decreased

distraction, as well as to further probe the influence of rhythmical tasks on gait performance, will help delineate the variety of results observed here. We observed similar responses of increased stride length and velocity in adults with DS in the divided attention and low light conditions, although in the divided attention condition they were more distracted in the low light condition they were less distracted. Our conversations with participants and their families and caregivers revealed that adults with DS were more likely to fall "when they were not paying attention", and the unintended rhythmical nature of our divided attention task added an additional aspect to the task beyond merely attentional focus.

In addition, it would be theoretically and practically valuable to explore differences in response to anticipated vs. unanticipated perturbations. Theoretically, stability can be defined as the ability to respond to a discrete perturbation while performing at a continuous steady state, for example the amount of time taken to recover the lower limbs to steady-state trajectories following an unexpected trip. Practically, some events known to increase the risk of falls in the healthy elderly are known and can be adjusted (i.e., low light levels, loose floor coverings or cords). But often, events occur unexpectedly and require a rapid adaptation to recover control and avoid a fall. Although the uneven areas of the irregular surface could not be visually identified, participants knew in advance that the surface was uneven, thus all of our perturbation conditions were anticipated. Adults with DS showed extended preparation in adjustment of stride length before crossing the obstacle, and we also observed that they looked at the ground more frequently than adults with TD in all conditions. Their increased preparation and attention is a strategy that would not be helpful in response to unanticipated perturbations and we

do not know how they would respond or what proportion of the time they would respond successfully and avoid a fall.

Table 3.1

Anthropometric Data for Adults with Down Syndrome (DS) and With Typical Development (TD)

	DS Mean (Standard deviation)	TD Mean (Standard deviation)
Age (yrs)	43.43 (7.25)	48.50 (7.56)
Height (cm)	155.00 (9.27)	166.75 (10.96)
Weight (kg)	73.96 (18.22)	87.04 (29.40)
Leg length (cm)	72.23 (5.30)	83.56 (7.33)
Height to leg length ratio	0.47 (0.02)	0.50 (0.03)

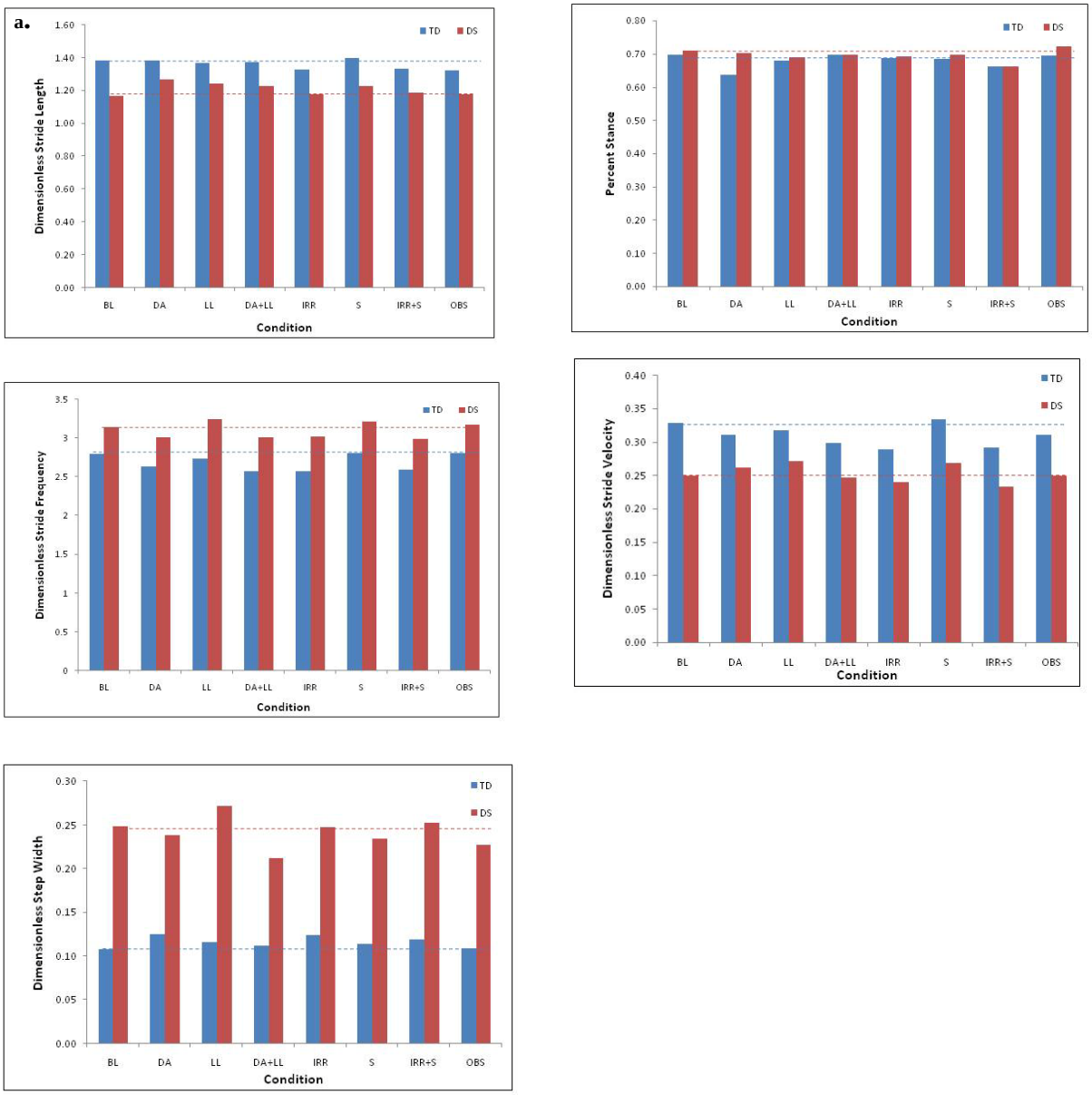


Figure 3.1. Dimensionless gait variables for adults with Down syndrome (DS) and adults with typical development (TD), each variable presented separately by condition. Horizontal dashed lines are a baseline value reference line. Conditions are: baseline (BL), divided attention (DA), low light (LL), divided attention and low light combination (DA+LL), irregular surface (IRR), distracting sounds (S), irregular surface and distracting sounds combination (IRR+S) and obstacle (OBS). Figure 3.1a is stride length, (b) is stride frequency, (c) is step width, (d) is percent stance and (e) is stride velocity.

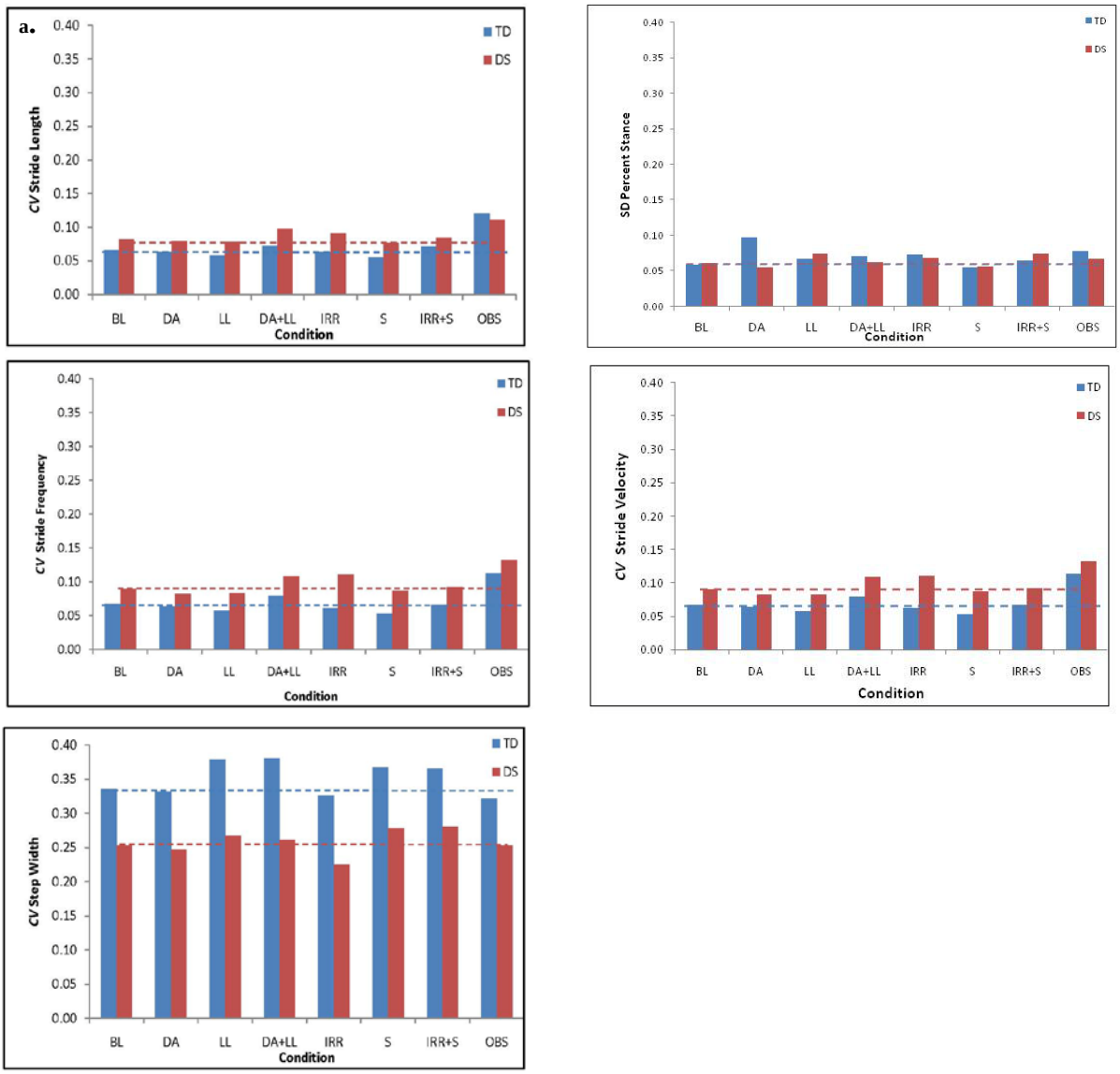


Figure 3.2. Variability measures for adults with Down syndrome (DS) and adults with typical development (TD), each variable presented separately by condition. Horizontal dashed lines are a baseline value reference line. Conditions are: baseline (BL), divided attention (DA), low light (LL), divided attention and low light combination (DA+LL), irregular surface (IRR), distracting sounds (S), irregular surface and distracting sounds combination (IRR+S) and obstacle (OBS). Figure 3.2a is *CV* stride length, (b) is *CV* stride frequency, (c) is *CV* step width, (d) is SD percent stance and (e) is *CV* stride velocity.

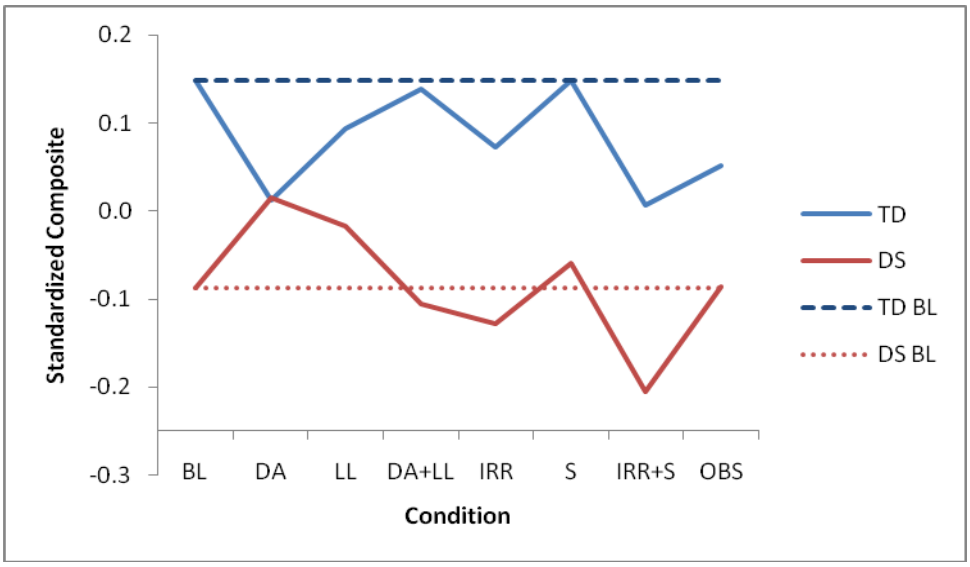


Figure 3.3. Composite of 5 standardized dimensionless gait variables, by condition, for adults with Down syndrome (DS) and typical development (TD). Conditions are: baseline (BL), divided attention (DA), low light (LL), divided attention and low light combination (DA+LL), irregular surface (IRR), distracting sounds (S), irregular surface and distracting sounds combination (IRR+S) and obstacle (OBS). Horizontal dashed lines are a baseline value reference line.

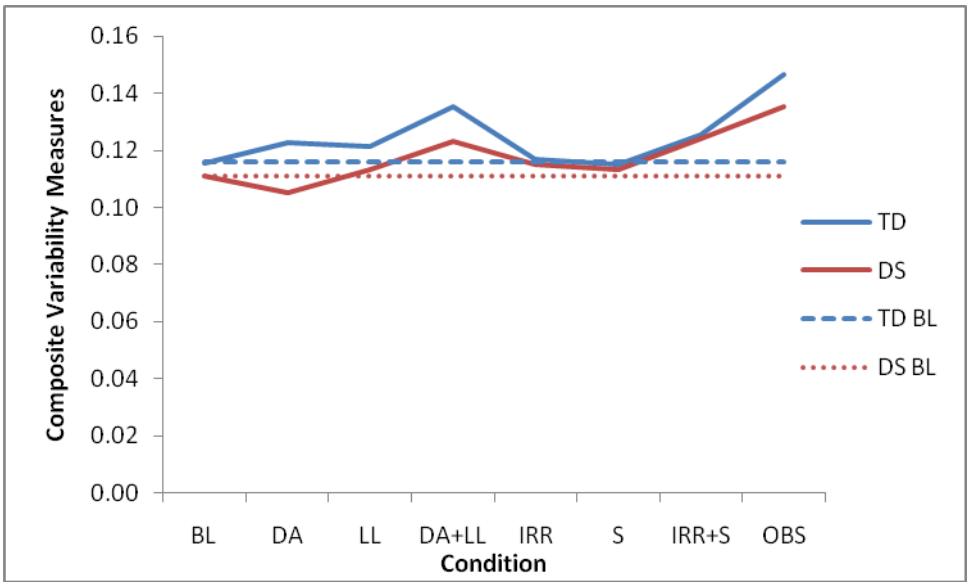
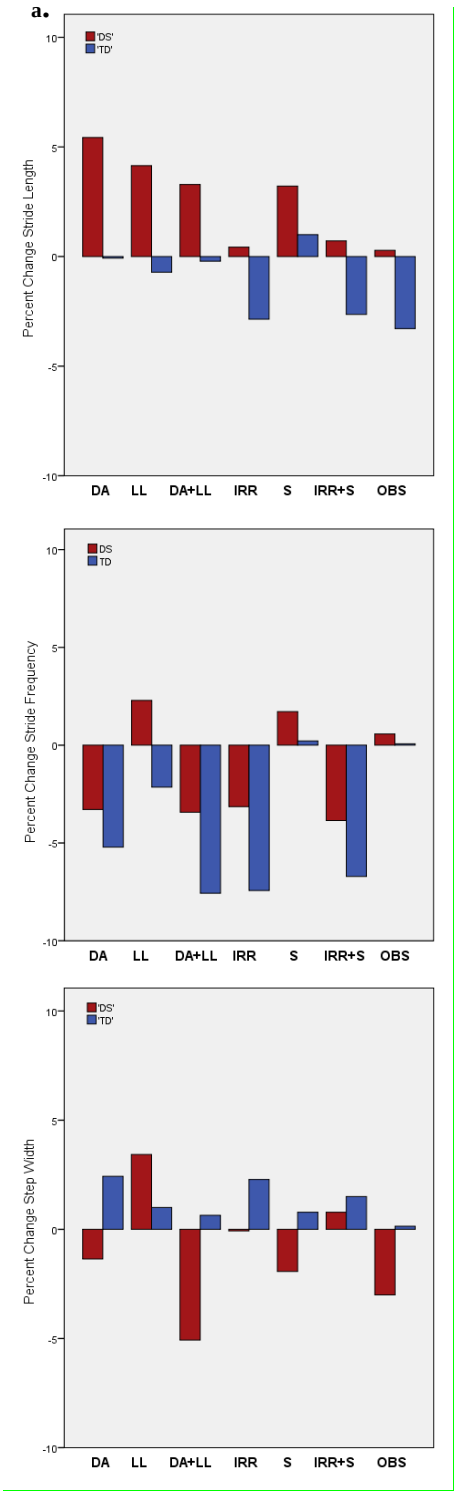


Figure 3.4. Composite of 5 variability measures, by condition, for adults with Down syndrome (DS) and typical development (TD). Conditions are: baseline (BL), divided attention (DA), low light (LL), divided attention and low light combination (DA+LL), irregular surface (IRR), distracting sounds (S), irregular surface and distracting sounds combination (IRR+S) and obstacle (OBS). Horizontal dashed lines are a baseline value reference line.



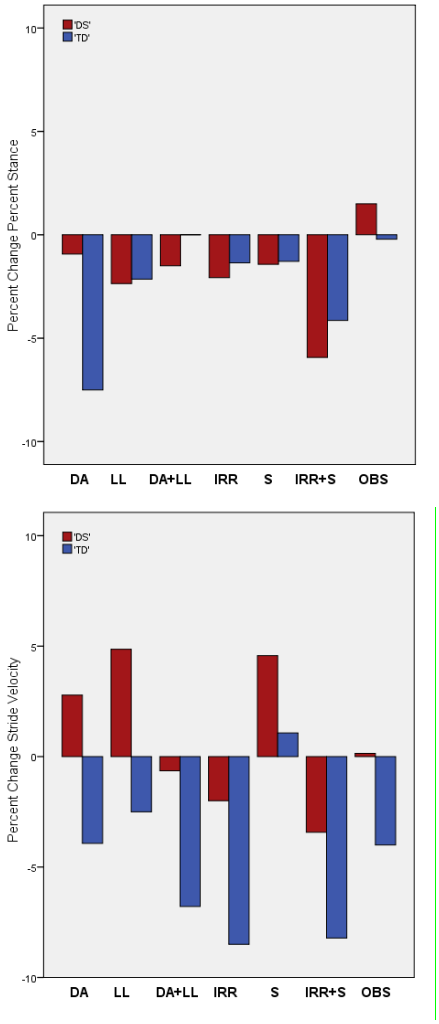


Figure 3.5. Percent change from baseline to perturbation conditions, for adults with Down syndrome (DS) and typical development (TD). Conditions are: divided attention (DA), low light (LL), divided attention and low light combination (DA+LL), irregular surface (IRR), distracting sounds (S), irregular surface and distracting sounds combination (IRR+S) and obstacle (OBS). Figure 3.5a is stride length, (b) is stride frequency, (c) is step width, (d) is percent stance and (e) is stride velocity.

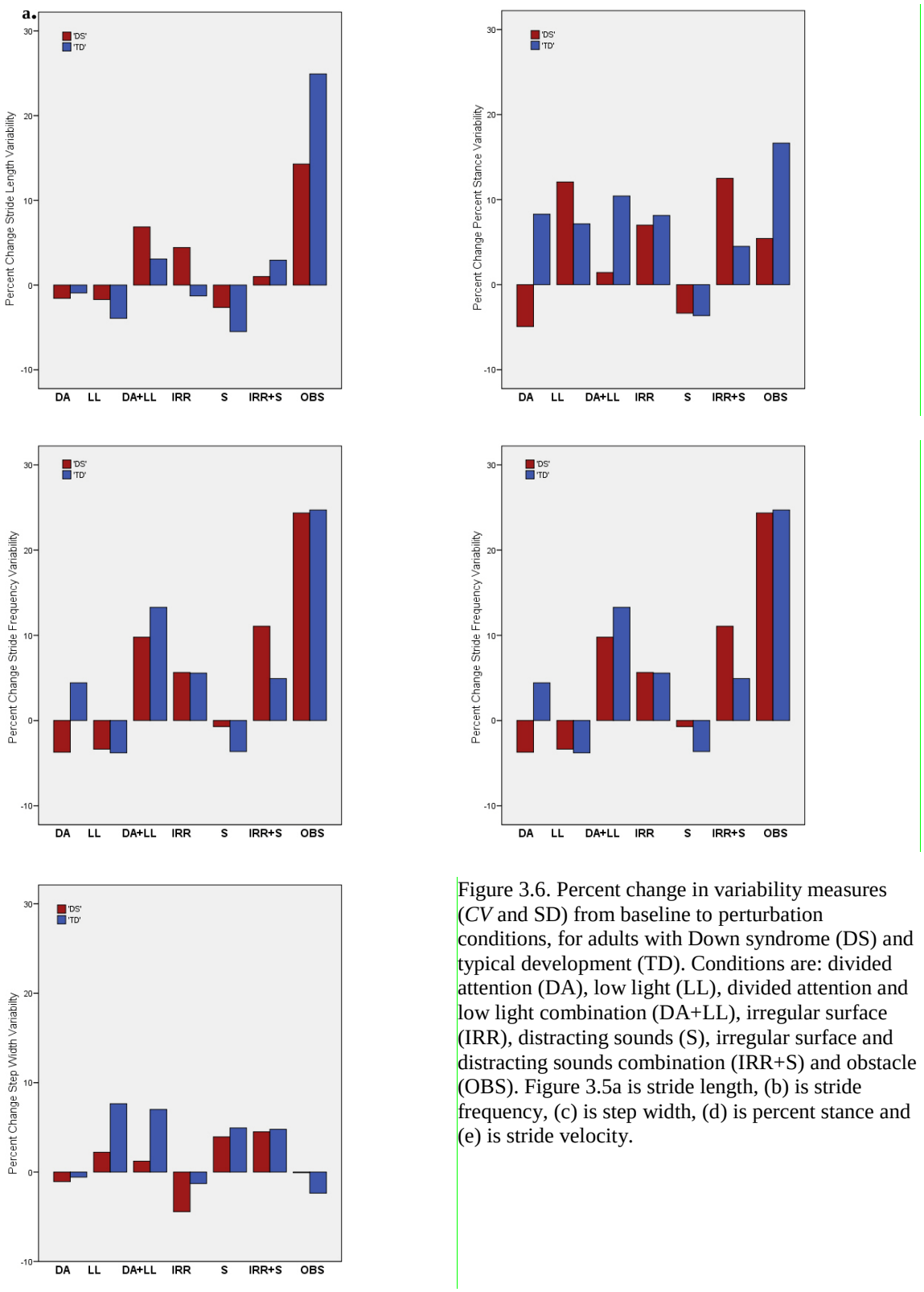


Figure 3.6. Percent change in variability measures (*CV* and SD) from baseline to perturbation conditions, for adults with Down syndrome (DS) and typical development (TD). Conditions are: divided attention (DA), low light (LL), divided attention and low light combination (DA+LL), irregular surface (IRR), distracting sounds (S), irregular surface and distracting sounds combination (IRR+S) and obstacle (OBS). Figure 3.5a is stride length, (b) is stride frequency, (c) is step width, (d) is percent stance and (e) is stride velocity.

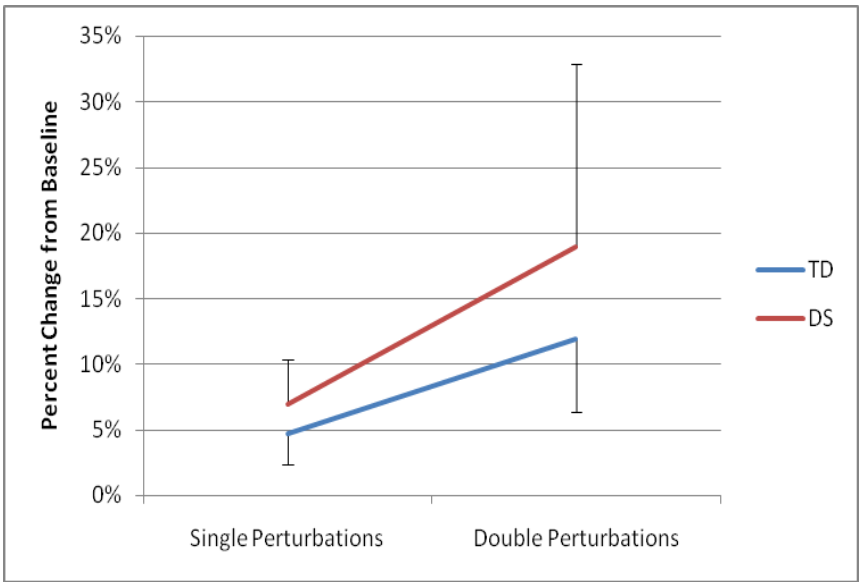


Figure 3.7. Average percent change in 5 gait variables from baseline to single vs. double perturbation conditions for adults with Down syndrome (DS) and and adults with typical development (TD).

APPENDIX 3.1

Divided Attention

Hollman and colleagues (2007) examined stride-to-stride variability in gait velocity in older adults (*M* age=81 years) as compared with middle-aged (*M* age=48 years) and younger (*M* age=25 years) adults during normal and dual task walking conditions. Participants spelled five-letter words in reverse while walking for the dual-task condition. Variability in stride velocity was increased in older participants compared with middle-aged and younger subjects. The authors conclude that gait changes observed indicate that cognitively demanding tasks during walking have a destabilizing effect on gait and may place older people at a greater risk of falling (Hollman et al., 2007). Other dual task conditions, subtracting 7 from 100 and 13 from 100 (attention-demanding tasks) and citing words starting with the letters “K” and “O” (verbal fluency task), also elicited increased stride length and stride time variability in healthy community-dwelling elders ages 70-82 years (van Iersel, Ribbers, Munneke, Borm, & Rikkert, 2007).

Moving beyond healthy older adults, a similar study compared performance of fallers and non-fallers, ages 65-85 years, in three different dual-task conditions. They listened to a story while walking and answered questions about it afterward, counted how many times two pre-specified words appeared a story, or walked while reciting out loud serial subtractions of 7 from 500. All conditions markedly increased swing time variability in the fallers, but not the non-fallers (Springer et al., 2006).

This Springer study showed increased variability in fallers, but not non-fallers, ages 65-85 years. The previously mentioned Hollman and van Iersel studies found

increased variability in general among older adults in their 70's and 80's, however they did not attempt to separate out fallers and non-fallers. It is likely, however, that there were fallers included in their studies, as 30% (Luukinen, Koski, Hiltunen, & Kivela, 1994; Tinetti, Speechley, & Ginter, 1988) to 52% (Berg, Alessio, Mills, & Tong, 1997) to 61% (Maki, Holliday, & Topper, 1994) of community-dwelling older adults reported a fall over a prospective one-year study period, with approximately two thirds of these falls occurring while walking (Berg et al., 1997; Luukinen et al., 1994). This is consistent with the previously discussed link between increased gait variability and increased fall risk in older adults.

Distracting sounds

Instead of an active attempt at divided attention, this is a test of whether or not the participant can block out the distracting nature of background traffic and indistinguishable voices. The audio track is 17 s long, and will be played on a loop at a moderate volume level (average 64 dB), as commonly experienced on a street. Although intermittent in nature, the track does not contain any startling sounds. Street sounds were chosen as they are environmentally realistic, and will avoid any entrainment of step frequency to a rhythm. Previous research with music with an even rhythm has shown that participants usually walk in tempo with the rhythm, and sometimes at double tempo or half tempo (Styns, van Noorden, Moelants, & Leman, 2007).

Uneven surface

Uneven surfaces are associated with falls in older adults (for review see American Geriatrics Society, 2001; NCOA Falls Free Coalition, 2005; Tinetti, Speechley, & Ginter, 1988). Despite this knowledge, little research has been conducted on walking on irregularly shaped surfaces. One group found healthy older women (*M* age 70 years) demonstrated greater step width and step time variability than young women (*M* age 22 years) on an uneven surface (Thies, Richardson, & Ashton-Miller, 2005), and adults with peripheral neuropathy who fell (*M* age 67 years) demonstrated higher step time variability than those who did not fall (DeMott et al., 2007). Another recent study found no age-related differences in gait parameter variability while walking on a surface consisting of squares of solid, compliant, rocky, irregular, slippery, and uneven surfaces all contained in the same walkway. However, the surface appeared to challenge both groups maximally as they both showed significantly increased step variability. In addition to demonstrating increased variability, healthy older adults (*M* age 74 years) walked more slowly with shorter steps than younger adults (*M* age 26 years) (Marigold & Patla, 2008).

Obstacle

Presence of floor rugs or general clutter is linked with falls in older adults (for review see American Geriatrics Society, 2001; NCOA Falls Free Coalition, 2005; Tinetti et al., 1988). There are multiple reasons for this association, and many studies have looked at characteristics of obstacle-related falls depending on whether or not the obstacle was visually apparent, whether there was contact with the obstacle to cause the fall, effects of the size of the object or how long the faller had to react (Brown, Doan, McKenzie, & Cooper, 2006; Chen, Ashton-Miller, Alexander, & Schultz, 1994; Hahn &

Chou, 2004; Pavol, Owings, Foley, & Grabiner, 1999; Weerdesteyn, Nienhuis, & Duysens, 2005).

In respect to the link between obstacles and gait variability, however, only one study has looked at the gait of healthy older (*M* age 71 years) and younger adults (*M* age 22 years) while they stepped over obstacles. In this study, older adults showed significantly greater step width variability than younger adults (Chen et al., 1991). In another study, it appears elderly adults with imbalance show more normalized stride length and step width variability than healthy elderly when crossing an obstacle; however the authors did not statistically test this result (Chou, Kaufman, Hahn, & Brey, 2003).

Low light condition

Older adults tend to rely more on vision than vestibular or proprioceptive input to maintain upright stance; when vision is removed, their static postural sway increases further (Speers et al., 2002). In addition, poor environmental lighting is related to falls (for review see American Geriatrics Society, 2001; NCOA Falls Free Coalition, 2005). However, light level (average 50 lux) showed no significant effect on any of the gait parameters when healthy older women (*M* 70 years) and young women (*M* 22 years) walked on an uneven surface (Thies, Richardson, & Ashton-Miller, 2005). Low light may have a destabilizing effect on adults with DS, however, who face greater constraints. In addition, the level of lighting in the Thies study may not have been low enough to adversely affect gait. There is not a consensus on what level of lighting is considered low enough to adversely affect gait, and it likely varies from person to person. We will use a

low level of evenly-distributed light at an average of 8.6 lux, allowing a participant to see the other end of the walkway but not to make out object details.

APPENDIX 3.2

We conducted extensive pilot work to determine camera set-up and camera and marker placement. Initially, I used 18 diodes, 9 on each side, including the head, arms and legs. However, after donning the harness and all 18 markers with wires attached and secured, participants indicated that the equipment felt very cumbersome. In addition, the wires become easily entangled and took an extended period of time to apply and secure despite our efforts to the contrary. Adults with DS have a limited attention span and it is important that we move the data collection along quickly and smoothly.

When using 18 diodes, the cameras had to be positioned in a more horizontal position in order to capture the position of the head and arms, thereby sacrificing some of the viewing area possible for the diodes on the feet and ankles. In turn, we lost some foot and ankle data at either end of the walking trial. In addition, it was difficult to monitor the collection of all 18 diodes during data collection. Based on these experiences, we decided that applying diodes to only the lower extremities will allow participants to be more comfortable in the laboratory setting, as well as promote optimal gait parameter data for the variables of interest.

APPENDIX 3.3

Formulas for Normalization

$$\hat{v} = \frac{v}{\sqrt{g\ l_O}}$$

$$\hat{l}_{STRIDE} = \frac{l_{STRIDE}}{l_O}$$

$$\hat{f}_{STRIDE} = \frac{f_{STRIDE}}{\sqrt{g / l_O}}$$

$$\hat{w}_{STEP} = \frac{w_{STEP}}{l_O}$$

where $\hat{v}$ (velocity), f_{STRIDE} (stride length), $\hat{f}_{STRIDE}$ (stride frequency), and $\hat{w}_{STEP}$ (step width) are converted gait variables, l_C is leg length (sum of thigh length and shank length) and g is acceleration due to gravity.

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CHAPTER IV
EFFECTS OF PRACTICE AND DIFFERENT WALKING SPEEDS ON LYAPUNOV EXPONENT AND APPROXIMATE ENTROPY VALUES IN PERSONS WITH DOWN SYNDROME.

ABSTRACT

To understand changes in Lyapunov Exponent (LyE) and Approximate Entropy (ApEn) values with changes in walking speed, we compared LyE of knee motion and ApEn of step width and length of preadolescents and adults with Down syndrome (DS) and typical development (TD) as they walked at preferred, faster and slower treadmill speeds. We also assessed the effects of treadmill walking practice on LyE and ApEn values of preadolescents with and without DS. ApEn of step width increased with increased walking speeds, otherwise neither walking speed nor practice had significant effects on LyE values or ApEn step length values. Increased ApEn step width values indicated less regularity in successive step widths at faster speeds. Participants with DS, however, demonstrated a smaller increase than their peers with TD indicating they maintain more control of regularity in step width than their peers with TD.

INTRODUCTION

Although more researchers are starting to use nonlinear measures of variability such as Lyapunov exponent (LyE) and Approximate Entropy (ApEn) to study differences

in walking patterns between different populations of interest (Buzzi, Stergiou, Kurz, Hageman, & Heidel, 2003 Jun; Dingwell, Cusumano, Sternad, & Cavanagh, 2000; Dingwell & Cusumano, 2000; Moraiti, Stergiou, Ristanis, & Georgoulis, 2007), only a few have investigated the effect of different walking speeds on LyE and ApEn values (Buzzi & Ulrich, 2004; Jordan, Challis, Cusumano, & Newell, 2009; Stergiou et al., 2004; Georgoulis, Moraiti, Ristanis, & Stergiou, 2006) and none have looked at the effects of task specific practice. Both tools measure aspects of performance that are likely to change with changes in speed or in response to practice; LyE measures the local stability of a variable of interest while ApEn measures the regularity of its pattern. Larger LyE values reflect less local stability while larger ApEn values represent less regular patterns (Stergiou et al., 2004). Values may be expected to shift in either direction, reflecting improvement or decay in performance as well as the unique attributes of the population of interest. Our goal was to compare LyE and ApEn values of preadolescents and adults with and without Down syndrome (DS) as they walked at different treadmill speeds, as well as to assess the effects of treadmill walking practice on LyE and ApEn values of preadolescents with and without Down syndrome.

In recent work, England and Granata (2007) investigated changes in LyE of ankle, knee and hip angles of healthy adult participants walking on a treadmill at comfortable, faster, and slower speeds. Their results showed LyE values were lower at slower than preferred walking speed and higher at faster than preferred walking speed, as compared to values at the preferred walking speed (England & Granata, 2007). Studying adults with anterior cruciate ligament (ACL) impairments, Stergiou and colleagues used LyE and ApEn to explore the dynamics of the flexion-extension angle of the ACL deficient knee,

which exhibits more locally stable (smaller LyE values) but more regular, less adaptable patterns (smaller ApEn values) than the participants' intact knee across different walking speeds. Their results showed LyE values did not change at 20% faster or slower treadmill speeds (Stergiou, Moraiti, Giakas, Ristanis, & Georgoulis, 2004). ApEn values, however, significantly increased with increased walking speed (Georgoulis, Moraiti, Ristanis, & Stergiou, 2006). These studies show different responses are possible across different populations, and we do not know if either of the patterns observed will describe the response of adults with DS.

We do have an idea, however, of how preadolescents with DS respond to being asked to change their walking speed away from preferred. When asked to walk on a treadmill at speeds faster and slower than preferred, preadolescents with DS showed decreased LyE and ApEn values for shank and foot segmental angles with an increase in speed. For the thigh segmental angle, however, preadolescents produced larger LyE values and smaller ApEn values as they progressed from slower, to preferred, to faster speeds. For shank and foot measures, but not thigh, these results suggest increased local stability and increased regularity of segmental angles at faster than preferred walking speeds in preadolescents with DS (Buzzi & Ulrich, 2004). The increase in local stability and regularity, however, could also reflect a decrease in adaptability of gait patterns. A pattern that is too rigid and regular is less adaptable. This is likely the case, as the increase in local stability and regularity is accompanied by an increase in stiffness and impulse values and, consequently, a less energy efficient walking pattern (Ulrich, Haehl, Buzzi, Kubo, & Holt, 2004). The combination of stiffening up and constraining

adaptability is a reflection of the novelty and challenge of the task itself, and should decrease with practice.

Stiffness values do, in fact, decrease with treadmill walking practice. Following four practice sessions of approximately 800 strides each, participants with DS and typical development (TD) reduced global stiffness and impulse values, however they did it by adjusting their gait in different ways. Following practice, participants with DS decreased step width at all speeds (slower than preferred, preferred and faster than preferred). They increased stride length greatly at slower than preferred speeds and less-so at faster than preferred speeds. Participants with TD did not adjust step width, and showed less change in stride length with changes in speed than their peers with DS (Smith, Kubo, Black, Holt, & Ulrich, 2007). While we have shown in this earlier work that stiffness and impulse values decrease and reflect changes in performance with treadmill walking practice, we do not know if the quality of movement patterns (as measured by LyE and ApEn values) is changed by the shift in performance that occurs with task specific practice.

Taken together, these studies suggest that changes in gait patterns and nonlinear measures with speed and practice are unique to the chosen variable and population. Here, we wanted to compare LyE of the displacement of the knee marker (chosen to represent the pendular motion of the lower extremity during walking) and ApEn values of step width and length of preadolescents and adults with and without Down syndrome (DS) as they walked at different treadmill speeds, as well as to assess the effects of treadmill walking practice on LyE and ApEn values of preadolescents with and without DS. Because both groups make adjustments to their gait patterns when walking at non-

preferred speeds, we propose that, preadolescents and adults with DS and TD, when walking slower and faster than preferred on the treadmill, will show less regular, less stable trajectories (higher ApEn and LyE values) of movement than at their preferred speed. In addition, for preadolescents with DS and TD, treadmill-walking practice will result in more regular, more stable trajectories (lower ApEn and LyE values) of movement as they learn to become more efficient at the task.

METHODS

Participants were 12 adults with DS and12 chronologically age-matched adults with TD (all 35-62 years of age) as well as 12 older adults with TD (ages 70-83 years). We recruited two groups of adults with TD because we wanted to be sure to provide an accurate comparison group for adults with DS, who show precocious age-related changes in gait (Smith & Ulrich, 2008). In addition, we tested 8 preadolescents with DS and 8 with TD (all 10-12 years). Participants signed an assent or consent form as appropriate, with consent for assenting adults and children provided by a legal guardian. The University of Michigan Institutional Review Board approved all procedures.

After we discussed all procedures to participants and those who accompanied them, we attached reflective markers (2.5 cm diameter) bilaterally at the temperomandibular joint, shoulder at acromion process, elbow at lateral humeral epicondyle, wrist at styloid process, greater trochanter, femoral condyle, ankle at 10 cm above lateral malleolus, heel at bony prominence and third metatarsophalangeal joint. We used a 6-camera Peak Motus real-time system (Peak Performance Technologies, Centennial, CO) to collect 3-dimensional reflective marker position data at a sampling

rate of 60 Hz while participants walked barefoot and performed 4-6 repetitions of walking at their preferred speed over a 5.3-m GAITRite mat (CIR Systems, Inc., Havertown, PA). We used GAITRite software to calculate the average walking speed of each participant, which we used to adjust the belt speed for the treadmill phase of testing. For the treadmill portion of the data collection, participants walked on a motorized treadmill (Parker brand, LET Medical Systems Corp., Miami Lakes, FL) for 30-s trials without holding onto the handle of the treadmill. Based on previous work in our lab, we operationalized comfortable treadmill speed for all participants as 75% of their self-selected overground speed (Smith et al., 2007; Ulrich et al., 2004). Participants performed 2-30 s trials each at 45%, 75% and 110% of their preferred overground walking speed, with trials progressing from slower to faster speeds.

Following the initial assessment of treadmill performance for preadolescents with DS and TD, we asked them to return to our lab and participate in four treadmill-walking practice sessions. Each practice session consisted of twelve 60-s repetitions of treadmill walking at each participant's 75% speed, approximately 800 practice strides per leg per session. Practice sessions were evenly spaced across 7 to 15 days. We conducted a post-test data collection session following the final practice visit (Smith et al., 2007).

For the purposes of this study we used the anterior-posterior and vertical displacement of the knee marker to determine LyE values and calculated ApEn values of step length and step width from the 3-D position of the heel markers. Please see Chapter II for a full description of pilot work, methods, and data analysis methods.

RESULTS

We used a linear mixed model to test effects of repeated measures because the approach is more robust with regard to the structure of variance of the variables. Therefore, mixed models can handle missing data points and unbalanced designs and are thus more powerful. We had some cases where data from one of the three speeds we considered missing at random. These data were missing due to technical reasons and not for reasons related to the performance of the participant. In all cases, we used a linear mixed model with an unstructured covariance model and repeated measures. Please see Bagiella et al. (2000) for more information (Bagiella, Sloan, & Heitjan, 2000).

Effects of Speed Perturbation in Adults

To test for effect of speed and group on LyE values, we used a 3 (group) by 3 (speed) linear mixed model with repeated measures on speed. We used a separate test for anterior-posterior and vertical direction values. For anterior-posterior LyE values, the group effect was significant ($F[2,28.5] = 5.21$, $p = 0.01$), while the speed effect and speed by group interaction were not. As we show in Figure 4.1, follow-up pairwise comparisons revealed the DS adult group had significantly higher LyE values than the TD adult group. Results for vertical direction LyE values showed the speed effect, group effect and speed by group interaction were not significant, as we illustrate in Figure 4.2.

To test for effect of speed on ApEn values, we used a 3 (group) by 3 (speed) linear mixed model with repeated measures on speed. The dependent variable for one test was ApEn step length, and ApEn step width for the other. For ApEn step length, none of the effects tested were significant (See Figure 4.3). For ApEn step width, the speed by

group interaction was significant (F[4,29.2] = 3.0, p = 0.04), as was the speed effect (F[2,29.2] = 6.37, p = 0.01). The group effect was not significant. Inspection of the means in Figure 4.4 and follow-up pairwise comparisons revealed that DS adults had higher ApEn values for step width than TD adults at the 40% speed (p = 0.02), followed by no difference at the 75% and 110% speeds.

Effects of Speed Perturbation in Preadolescents

To test for effect of speed and group on LyE values, we used a linear mixed model with repeated measures on speed, one for anterior-posterior direction values and another for vertical direction values. For both sets of LyE values, the group effect was significant (anterior-posterior direction F[1,14.3] = 9.1, p = 0.01; vertical direction (F[1,14.2] = 8.3, p = 0.01). None of the other effects tested were significant. As we show in Figures 4.5 and 4.6, preadolescents with DS had significantly higher anterior-posterior and vertical direction LyE values than their peers with TD.

To test for effect of speed on ApEn step length and width values, we used a linear mixed model with repeated measures on speed. The dependent variable for one test was ApEn step length values and, for the other, ApEn step width values. For ApEn step length, none of the effects tested were significant (See Figure 4.7). For ApEn step width values the speed effect was significant (F[2,12.5] = 6.2, p = 0.01), while the group effect and speed by group interaction were not. Inspection of the mean values in Figure 4.8 reveals ApEn step width values increased at faster treadmill speeds.

Effects of Practice in Preadolescents

To test for effect of practice on LyE values, we used a linear mixed model with repeated measures on visit to test for a visit effect, one for anterior-posterior direction values and another for vertical. For both directions, the group effect was significant (anterior posterior $F[1,13.4] = 25.7$, $p < 0.01$; vertical ($F[1,14.2] = 9.1$, $p = 0.01$), while the visit effect and visit by group interaction were not. As we show in Figures 4.9 and 4.10, preadolescents with DS had significantly higher LyE values than their peers with TD.

We used a separate linear mixed model with repeated measures on visit to test for effects of practice on ApEn step length and width values. For ApEn step length and width, none of the effects were significant. As we show in Figures 4.11 and 4.12, the variability within the DS group was very high for ApEn values at both pre and post-test.

DISCUSSION

Overall, preadolescents and adults with DS and TD showed robust resistance to changes in patterns of variability as a function of speed. Preadolescents with DS and TD also showed a lack of change in patterns of variability in response to practice. There were significant group differences in LyE values, but not ApEn values, which were maintained across different speeds and practice. Speed had a narrow and unique effect on ApEn step width in a similar direction for preadolescents and with a somewhat different outcome for adults.

ApEn values for step width increased with speed for both preadolescents and adults with DS and TD, indicating less regularity in successive step widths when walking

at faster speeds. Participants with DS, however, demonstrated a smaller increase than their peers with TD indicating they maintain more control of regularity in step width than their peers with TD, likely reflective of more active control of step width. Researchers have shown in passive dynamic robots and in-vivo studies that step width is actively controlled to provide medial-lateral stabilization during walking (Bauby & Kuo, 2000; Kuo, 1999). Across the lifespan, persons with DS use a wider step width than their peers with TD to stabilize their center of mass as they walk (Kubo & Ulrich 2006; Ulrich et al., 2004; Smith et al., 2007; Smith & Ulrich 2008). They actively control step width, and maintain more control of regularity in successive step widths than their peers with TD, allowing less change as walking speed increases.

We did not find changes in LyE values with changes in walking speed or practice of treadmill walking. There was some indication that the DS and TD groups responded differently to slower and faster speeds, as well as treadmill walking practice, but the differences were not robust enough to be significant. There were, however, group differences in anterior-posterior direction LyE values in preadolescents and adults and vertical direction LyE values in preadolescents. Participants with DS demonstrate higher LyE values than their peers with TD, indicating less local stability and in knee trajectories from stride to stride and more adaptability overall.

Similar to our findings, Stergiou and colleagues did not find a change in LyE values with a 20% increase or decrease in walking speed in participants with ACL impairment, although they were able to show differences as compared to the ACL intact knee (Stergiou et al., 2004). Other researchers, however, have found a decrease in LyE values with increased treadmill speed for shank and foot segmental angles in

preadolescents with DS and TD (Buzzi & Ulrich, 2004), or an increase in LyE of ankle, knee and hip angles in adults with TD at faster than preferred walking speeds (England and Granta, 2007). These studies, in three different populations, show three different results for LyE values of kinematic angle data as treadmill walking increases to a faster the preferred walking speed. Together these studies show that different systems vary more under some conditions than others, and where in the system adaptation emerges may vary.

When using the tools of ApEn and LyE, researchers need to perform pilot work to certify that they are choosing variables of interest that adequately reflect changes in behavior. In addition, it appears that LyE and ApEn values may be more sensitive to group differences in performance (i.e., DS vs. TD, ACL intact vs. deficient) than to variations of performance (i.e., increasing speed or effects of practice). It is also possible that between-group differences are just larger than within-group differences. This contention deserves further investigation for researchers interested in using LyE or ApEn to measure within-group changes in performance.

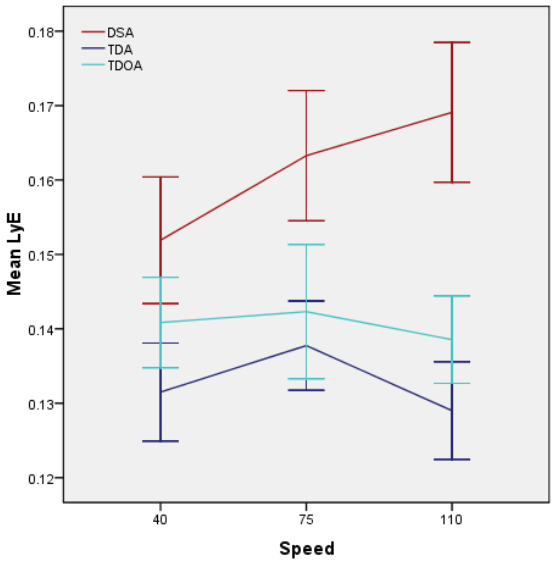

Figure 4.1. Anterior-posterior direction LyE values by treadmill speed. Speed set at 40, 75 or 110% of self-selected overground speed for adults with Down syndrome (DSA), adults with typical development (TDA) and older adults with typical development (TDOA).

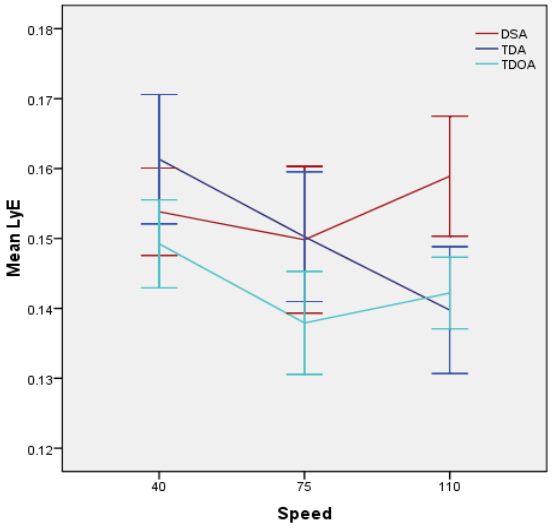

Figure 4.2. Vertical direction LyE values by treadmill speed. Speed set at 40, 75 or 110% of self-selected overground speed for adults with Down syndrome (DSA), adults with typical development (TDA) and older adults with typical development (TDOA).

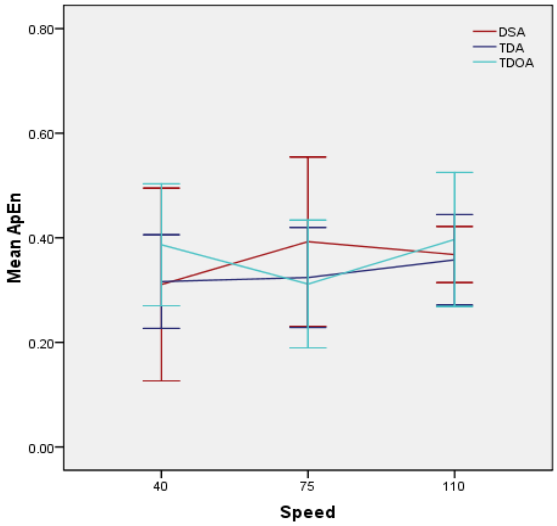

Figure 4.3. ApEn step length values by treadmill speed. Speed set at 40, 75 or 110% of self-selected overground speed for adults with Down syndrome (DSA), adults with typical development (TDA) and older adults with typical development (TDOA).

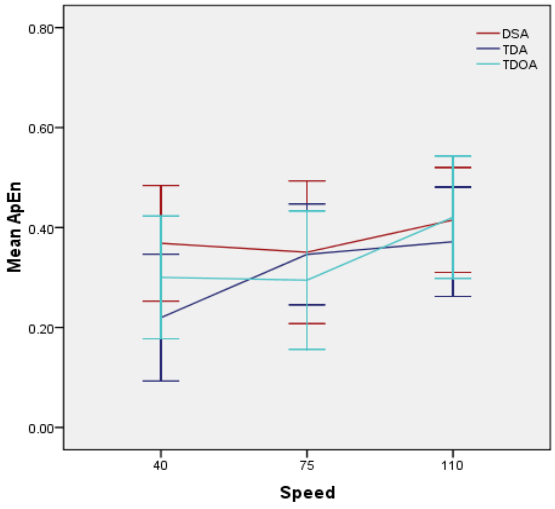

Figure 4.4. ApEn step width values by treadmill speed. Speed set at 40, 75 or 110% of self-selected overground speed for adults with Down syndrome (DSA), adults with typical development (TDA) and older adults with typical development (TDOA).

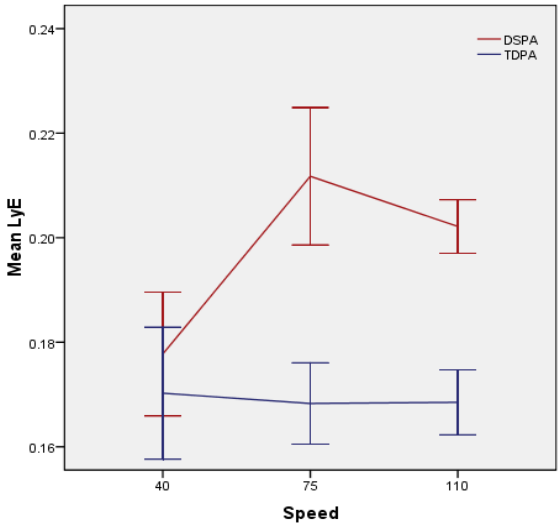

Figure 4.5. Anterior-posterior direction LyE values by treadmill speed. Speed set at 40, 75 or 110% of self-selected overground speed for preadolescents with Down syndrome (DSPA) and preadolescents with typical development (TDPA).

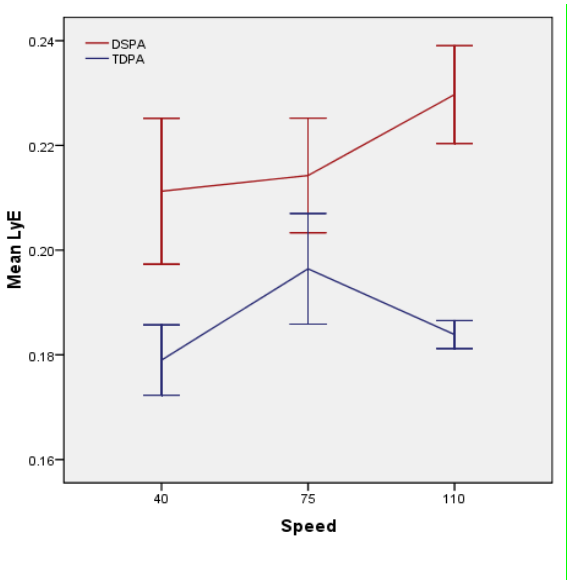

Figure 4.6. Vertical direction LyE values by treadmill speed. Speed set at 40, 75 or 110% of self-selected overground speed for preadolescents with Down syndrome (DSPA) and preadolescents with typical development (TDPA).

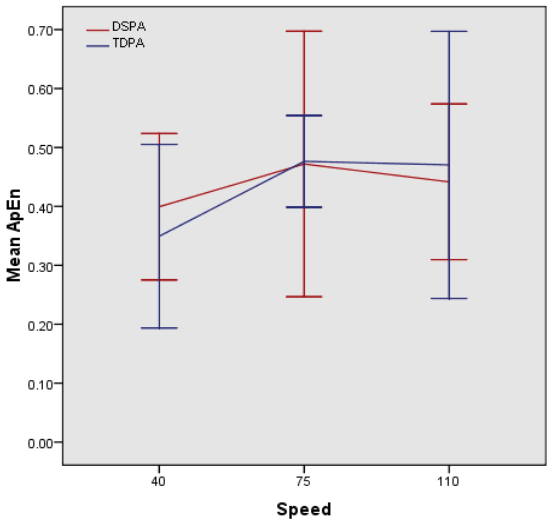

Figure 4.7. ApEn step length values by treadmill speed. Speed set at 40, 75 or 110% of self-selected overground speed for preadolescents with Down syndrome (DSPA) and preadolescents with typical development (TDPA).

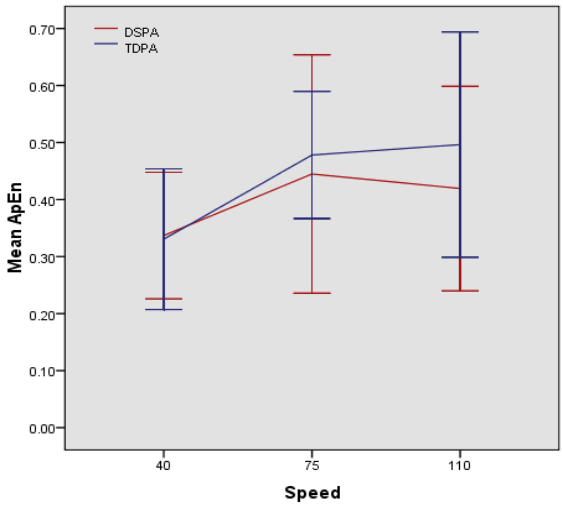

Figure 4.8. ApEn step width values by treadmill speed. Speed set at 40, 75 or 110% of self-selected overground speed for preadolescents with Down syndrome (DSPA) and preadolescents with typical development (TDPA).

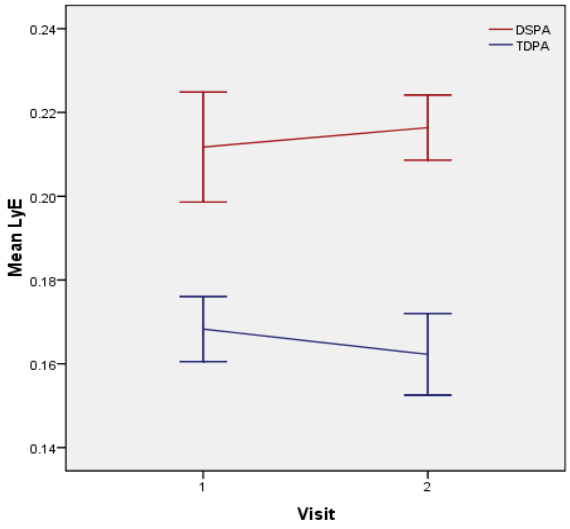

Figure 4.9. Anterior-posterior direction LyE values by pre- and post-test visit for preadolescents with Down syndrome (DSPA) and preadolescents with typical development (TDPA).

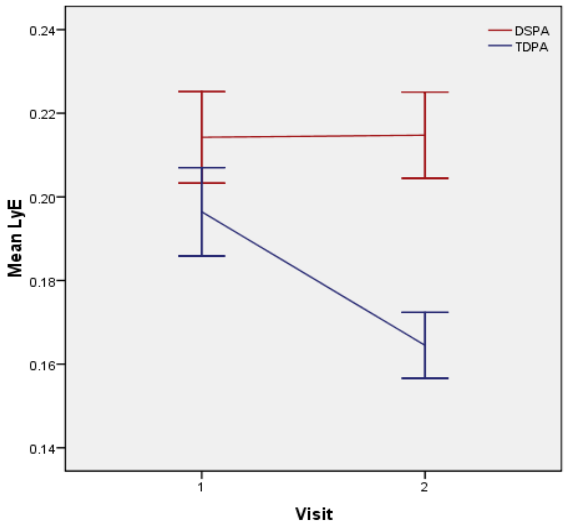

Figure 4.10. Vertical direction LyE values by pre- and post-test visit for preadolescents with Down syndrome (DSPA) and preadolescents with typical development (TDPA).

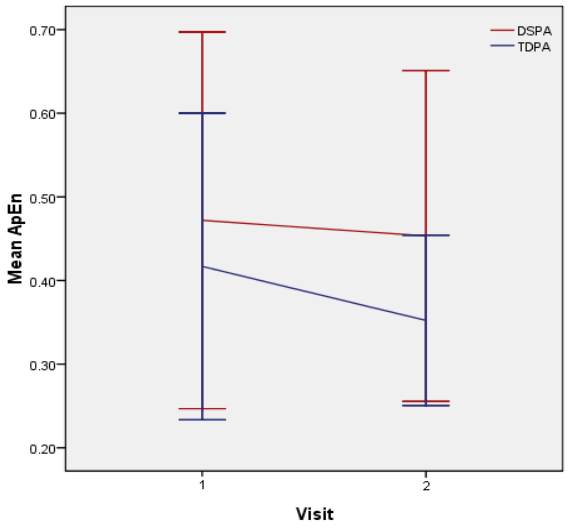

Figure 4.11. ApEn step length values by pre- and post-test visit for preadolescents with Down syndrome (DSPA) and preadolescents with typical development (TDPA).

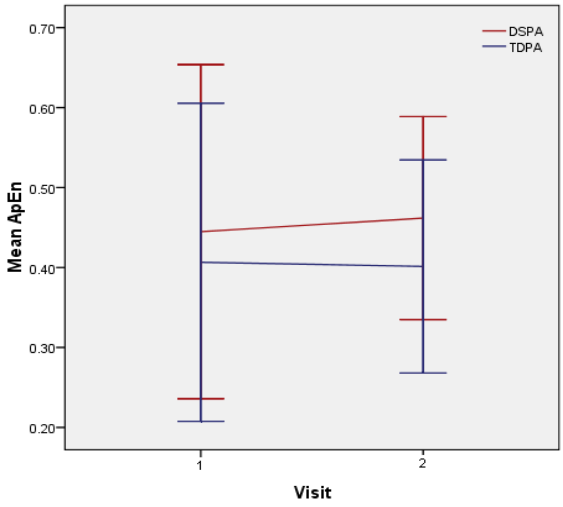

Figure 4.12. ApEn step width values by pre- and post-test visit for preadolescents with Down syndrome (DSPA) and preadolescents with typical development (TDPA).

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CHAPTER V
CONCLUSION

LIMITATIONS

One limitation common to all studies is measurement error. Determining the signal to noise ratio is always a consideration when analyzing human movement data, and it is impossible to fully separate the two components. Researchers must perform pilot testing and use appropriate filters for their data, or, in the case of nonlinear tools, use unfiltered data and consider all points as information and not "error". However, movement analysis systems never capture exact motion, so care must be taken to measure movement as accurately as possible. Maintaining and standardizing equipment and procedures for all data collections is one way to assure the most accurate data possible.

Prior to each data collection using PeakMotus equipment, we used a fixed 4-marker frame and dynamic 2-marker wand to set up a calibrated volume of 2.9 by 1.4 by 1.85 m. Acceptable summed measurement error for each calibration was set at <0.008 m. The known accuracy for the PeakMotus system is 0.2 mm for a 3-m field of view, and the maximal measurement error is 0.259 cm for a known 50 cm distance (Richards, 1999). Prior to each data collection using Northern Digital's Optotrak 3020 equipment, we used a defined 16-marker calibration cube to dynamically establish a viewing volume of

approximately 10 by 1.2 by 1.8 m. Known accuracy for the Optotrak system is as follows; for a known 60 cm distance between markers, the average standard deviation of the collected distance was 0.125 mm, with a range from 0.0047 mm to 0.68 mm. For a known 90 degree angle, average standard deviation of the collected angle was 0.020, with a range from 0.002 to 0.138 (States & Pappas, 2006).

Of additional concern for the older adult perturbation studies (using Optotrak) is the procedure of calculating gait parameters based on heel contact. It is possible that measurement error is higher at heel contact than during swing due to the impact forces and consequent skin movement experienced at heel contact. To explore this issue, I created figures similar to the exemplar Figure 5.1 showing that although the vertical position of the heel marker from 10 frames before and approaching 10 frames after heel contact is more variable than the analgous time frame before and after peak swing, displacement values a frame or two before and after both heel contact and peak swing are much more similar. Further, trajectories were not grossly different between the groups. Gait parameters were calculated based on heel contact and toe off events, and should have been accurate to the exact frame number. If there was a mistake, the error would likely be within a frame before or after the event, thus all errors should have been minimal and consistent between both groups of participants.

Limitations unique to the older adults with DS study include the lack of an assessment of cognitive ability, lack of standardized physical activity assessment and use of self-report of fall history. We used the Adaptive Behaviour Dementia Questionnaire, a screening questionnaire for dementia in Alzheimer's disease in adults with Down syndrome (Prasher, Farooq, & Holder, 2004). The screen was effective in identifying one

adult female with DS who was excluded from the study, as she did receive a diagnosis of dementia soon after participating. In part, the screen asked about ability to perform functional activities, which allowed us to collect this information and screen for dementia succinctly. The questionairre did not, however, assess cognitive level beyond a dementia/non-dementia classification. A more formal assessment of cognitive abilities would provide more detailed information about cognitive decline in relation to physical decline and fall risk. Similarly, physical activity was grossly classified as minimal, moderate and maximal based on self-report of employment and recreational physical activity. A standardized assessment, such as CHAMPS, would provide a more externally valid measurement of amount of physical activity (Stewart, Mills, King, Haskell, Gillis, & Ritter, 2001). In addition, when measuring both physical activity and history of falls, the use of self-report measures provides less accuracy than a prospective design. For example, if participants are told in advance about their falls being monitored and then followed up with weekly, they are less likely to forget a fall than if they are just asked, "Have you fallen in the last six months?".

GENERAL DISCUSSION

The mechanisms contributing to different gait patterns in persons with DS as compared to persons with TD, as well as differences between younger and older people with DS, are multi-factorial. A combination of physical and neuronal structure and function differences, and in adults the effects of aging, lead to the emergence of unique responses and behaviors.

Brain imaging studies have shown children and adults with DS have smaller relative cerebellar volumes than age and gender matched controls (Aylward et al. 1997; Pinter et al. 2001; Raz et al. 1995). The cerebellum is involved in balance, coordination, motor control and motor learning. Known effects of cerebellar deficits include an increased step width/base of support, increased variability in foot placement and excessive or diminished response to perturbations (for review see Morton & Bastian, 2004). Persons with DS are noted to have balance (Wang & Ju, 2002; Connolly & Michael, 1986) and coordination deficits (Latash, Kang, & Patterson, 2002). They typically show increased increased step width (Smith et al., 2007, Kubo & Ulrich 2006) and increased variability in movement patterns as compared to their peers with TD (Latash & Corcos, 1991; Latash, Kang, & Patterson, 2002; Kubo & Ulrich, 2006; Smith et al., 2007). The correlation between balance and coordination deficits and small cerebellums has also been noted in animal studies using a mouse model of DS (Costa, Walsh, & Davisson, 1999; Hyde, Crnic, Pollock, & Bickford, 2001).

Although cerebellar volumes are disproportionately small in individuals with DS, they do not diminish significantly with age. Researchers using MRI in a longitudinal study of adults with DS stated that volume reduction in the cerebellum does not appear to be specifically responsible for the age-related decline in fine-motor control that is observed in adults with DS (Aylward et al. 1997). Other researchers using MRI found trends for shrinkage of the dorsolateral prefrontal cortex, anterior cingulate gyrus, inferior temporal and parietal cortices, parietal white matter, and pericalcarine cortex in adults with DS as compared to healthy controls and concluded that the pattern of selective cerebral damage in DS is different than the pattern of loss in premature aging or

Alzheimer's disease (Raz et al. 1995). Researchers using voxel-based morphometry, however, suggested that smaller areas of grey matter in the allocortex and association neocortex in adults with DS were due to alterations or loss of allocortical and neocortical neurons due to Alzheimer's disease type pathology (Teipel, Alexander, Schapiro, Moller, Rapoport, & Hampel 2004). Taken together, these studies suggest that although brain changes in adults with DS likely contribute to their declining ability to sense and interact with the world around them, there are not gross changes in the cerebellum or motor areas of the brain that are specifically and directly responsible for changes in gait patterns such as a wider step width with age.

Although reaction times are known to be slower in persons with DS, there is some evidence to suggest that motor planning, as opposed to the actual motor response, may be more responsible for motor control difficulties in adults with DS. Results from a study of event-related potentials and reaction times obtained through an auditory oddball paradigm under passive and active motor response conditions showed that participants had particular difficulty with sensory discrimination when preparing a movement in response to a cue (Lalo, Vercueil, Bougerol, Jouk, & Debu, 2005). In a functional context, adults with DS showed earlier and longer periods of motor preparation (step length adjustment) before stepping over a visually apparent obstacle in their walking path (Smith & Ulrich, 2008). In our current study (Chapter III), adults with DS walked faster when visual information was removed (low light condition). Taken together, these studies suggest that sensory integration and motor preparation takes longer in adults with DS than adults with TD, and more sensory input, such as a busy visual environment, slows the process further.

Poor balance, decreased cerebellar volume and slower reaction times are present across the lifespan in persons with DS. In addition, adults with DS experience the physiologic effects of aging at a rate of physiological aging is nearly twice that of adults with TD (Nakamura & Tanaka, 1998). Declines in vision and hearing with increasing age have been documented, as well as increased incidence of thyroid dysfunction, cardiovascular dysfunction, obesity and arthritis (for review see Barnhart & Connolly, 2007). As discussed above, results from brain imaging studies do not point to a specific area of cell loss, but it appears that generalized brain atrophy and the multi-system decline of typical aging combined with the presence of a developmental disorder and its unique physical characteristics leads to decline in physical function earlier in life for adults with DS as compared to their peers with TD.

FUTURE STUDIES

As discussed in Chapter IV, future studies involve a prospectively-designed study of fallers and non-fallers with DS that addresses the lack of an assessment of cognitive ability, lack of standardized physical activity assessment and use of self-report of fall history. This study will be designed to test anticipated as compared to unanticipated perturbations, as the effects of unanticipated perturbations are likely much more detrimental to adults with DS. With our study, when they anticipated perturbations, they took longer and prepared more than their peers with TD and were able to successfully adjust most of the time. Our results, combined with anecdotal reports by participants and their families that they “need to pay attention” when they walk and other research on motor preparation and attention (Lalo, Vercueil, Bougerol, Jouk, & Debu, 2005) in adults

with DS suggest that unanticipated perturbations may be relatively more challenging than those that can be anticipated. In addition, an analysis such as “Return Path Analysis”, where one quantifies the time taken to return to the original trajectory after a perturbation, would be useful to look at speed of recovery of foot or center of mass trajectory as adults with DS respond to a perturbation.

It would also be beneficial to design an intervention study aimed at reducing fall risk in adults with DS. As discussed in Appendix C, adults with DS are increased risk of falling earlier in life than their peers with TD and this is likely amenable to intervention. Although exercise interventions are known to have many positive effects for children and adults with DS (see Barnhart & Connolly, 2007 for review), the effect of intervention on fall risk has not been studied.

For nonlinear analysis studies, it would be useful to explore the use of LyE and ApEn to measure the effects of interventions in children and adults with DS. How sensitive these measures are to changes in the quality of performance was only briefly addressed here in Chapter IV. In addition, for both measures of quality of performance and measures of change in performance, other dependent variables need to be considered. For example, the center of mass may be more descriptive of the system than our choice of pendular knee lower extremity motion. Center of mass could be represented by markers on the pelvis during gait.

CONCLUDING REMARKS

Overall, two themes emerge from the work presented here. The first theme is that preadolescents with Down syndrome (DS) and typical development (TD) are more

adaptive and flexible in their movement patterns as compared to their older and younger peers. Although the quantity of variability in walking patterns generally decreases from toddlers to preadolescents to adults, preadolescents with DS and TD demonstrate higher Approximate Entropy (ApEn) and Lyapunov Exponent (LyE) values than their older and younger peers indicating they have learned to use their variability to be optimally adaptive.

The exception to this general pattern, however, is step width variability, and this represents the second major theme of this work. As opposed to a decreasing trend in the amount of variability across the lifespan, preadolescents in both groups produce larger amounts of step width variability than their older and younger peers, which we propose represents preadolescents' efficient use of the passive pendular dynamics of walking. In addition, participants with DS produced smaller amounts of step width variability than their peers with TD at all ages, across different walking speeds, following practice and in response to stability-challenging perturbation conditions. This robust group difference may reflect that step width is more actively and tightly controlled in persons with DS; not only do they use a wider step width than their peers with TD across the lifespan to stabilize their center of mass as they walk (Kubo & Ulrich, 2006; Ulrich et al., 2004; Smith et al., 2007; Smith & Ulrich, 2008), they are also less willing or able to adjust step width.

The lifespan theme, that preadolescents with DS and TD are more adaptive and flexible in their movement patterns as compared to their older and younger peers, is a reflection of developmental processes and learning to control one's movements early in life and the effects of aging and a loss of control of movement later in life. Less stable

walking patterns can lead to falls in toddlers and older adults, but the effects of falls are certainly more detrimental in older adults than young children. Older adults have farther to fall to reach the ground and thus experience higher impact forces and are more likely to be injured. In addition, older adults who experience a fall often become afraid of falling. Fear of falling is fairly common among older adults and leads to changes in walking patterns (Maki, 1997; Rosengren, McAuley, & Mihalko, 1998). It might also lead to self-imposed activity restrictions and thus less experience responding to perturbations and a further decay in ability to respond to internal or external perturbations precipitating a fall.

When the older adults with DS were challenged to stabilize their gait in perturbation conditions, although they showed complex gait adaptations, 3 adults with DS demonstrated ultimate failure in their ability to adapt and remain stable; they experienced loss of balance while none of the adults with TD did. One participant was able to regain stability with a very large lateral step, while the other two required assistance from the spotter to avoid a fall to the ground. Combined with the fact that 6 out of the 14 adults with DS, ages 35-65 years, who we recruited from the community had experienced a fall within the past 5 years, we propose that adults with DS experience age-related increased risk for falls at an earlier age than their peers with TD. Falling is not a problem for healthy 35-65 year-old adults with TD.

Linear and nonlinear measures both reflected a lack of stability in the gait patterns of older adults with DS. Nonlinear measures showed adults with DS are less likely than preadolescents with DS to use variability in an adaptive way, and behavioral outcomes show adults with DS are more likely than their preadolescent peers to fall due to gait

instability. From a physical therapy and health promotion and wellness standpoint, prevention of instability and falls needs to start early in life and be maintained across the lifespan for people with DS. Children and adults with DS should be engaged in activities that require multiple repetitions of perturbations to strengthen and reinforce the ease with which they access adaptive response options. They need to experience and explore a rich repertoire of variability and behavioral strategies in order to obtain and maintain flexible yet stable solutions. In addition, we need to recognize that increased step width and decreased step width variability reflect a robust strategy for gait stability in persons with DS, and this is not a parameter we should expect, or attempt, to change directly with intervention. Decreases in step width and increases in step width variability may occur as a reflection of changes in behavior and increased stability, however the goal of intervention should be overall stability and not changing step width.

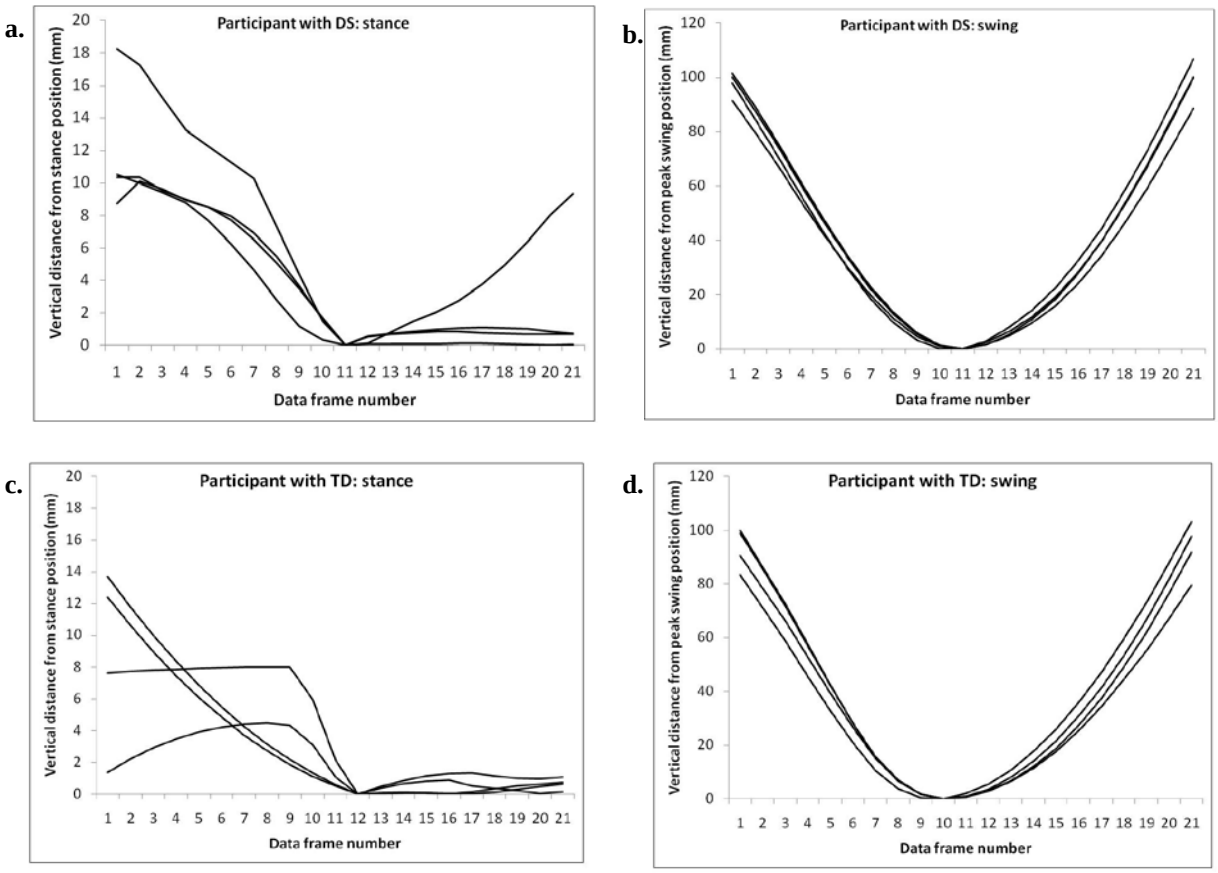

Figure 5.1. Exemplar figures of variability in heel marker vertical position around heel contact and peak swing for a participant with Down syndrome (top) and a participant with typical development (bottom). Vertical displacement was measured from the position of the heel marker 10 frames before and after heel contact and peak swing for four successive strides. All data were collected at 60 Hz. Figures 5.1a and (c) are 10 frames before and after heel contact. Figures 5.1b and (d) are 10 frames before and after peak swing. Although the vertical position of the marker from 9-2 frames before and 2-9 frames after heel contact is more variable than the analgous time frame before and after peak swing, displacement values are much more similar a frame or two before and after both heel contact and peak swing.

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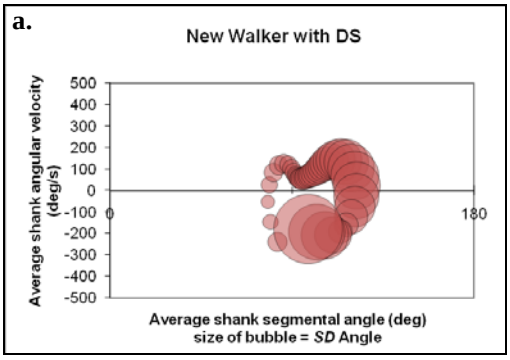
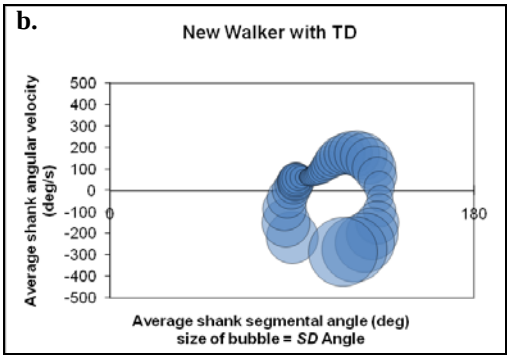
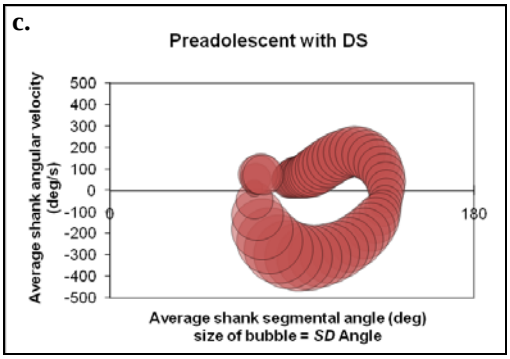
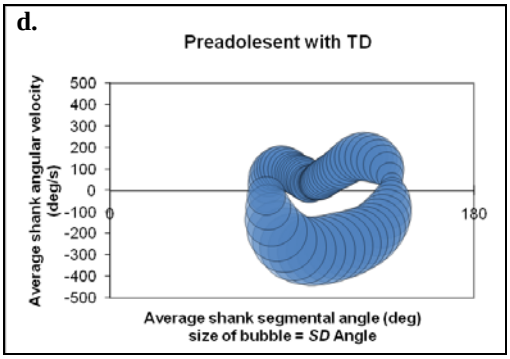
APPENDIX A

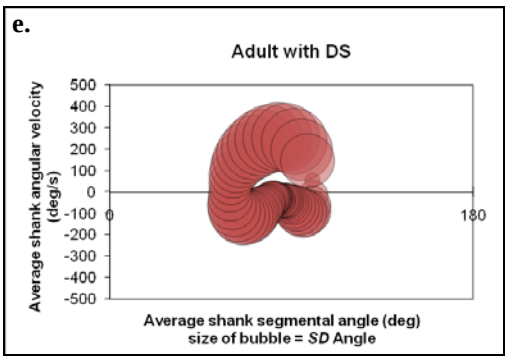
An additional way to explore variability in movement patterns across time is to plot a number of repetitions, one on top of another, and calculate a mean and standard deviation at each time point. We created phase portraits with standard deviation "rings" around each time point by plotting the mean and standard deviation of the shank segmental angle against the mean angular velocity of the shank segmental angle for three consecutive walking strides on the same graph. Plotting data in this manner allows the reader to see the amount of variability present and where in the stride cycle there is more or less variability across consecutive strides. The relationship of consecutive strides through time is ignored, however, as the order in which the consecutive strides were performed is not represented. What follows here are exemplar phase portraits for each group:











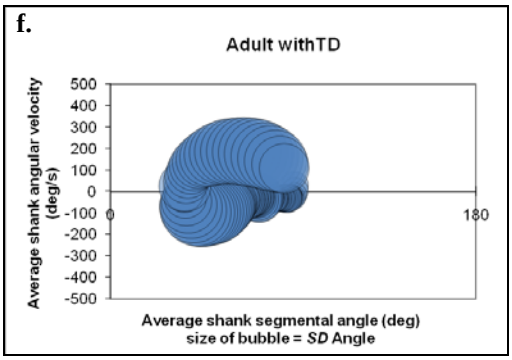
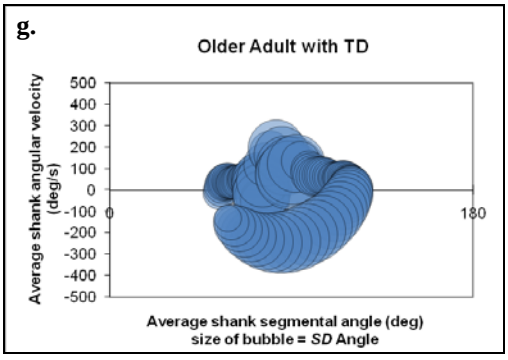


Figure A.1. The *x* axis is the average shank segmental angle (in degrees) and the *y* axis is average shank angular velocity (in degrees/second). The "ring" is the standard deviation of the shank segmental angle across three consecutive strides. Figure A.1.a and (b) are new walkers, (c) and (d) are preadolescents, (e) and (f) are adults and (g) is an older adults. DS = Down syndrome and TD = typical development.



APPENDIX B

Here I present the effects of walking speed and practice on Coefficient of Variation (*CV*) values of step length, stride length and step width for preadolescents and adults. Walking speeds are 40%, 75% and 110% of the self-selected preferred overground walking speed of each participant. Preadolescents were tested before and after task-specific treadmill walking practice.

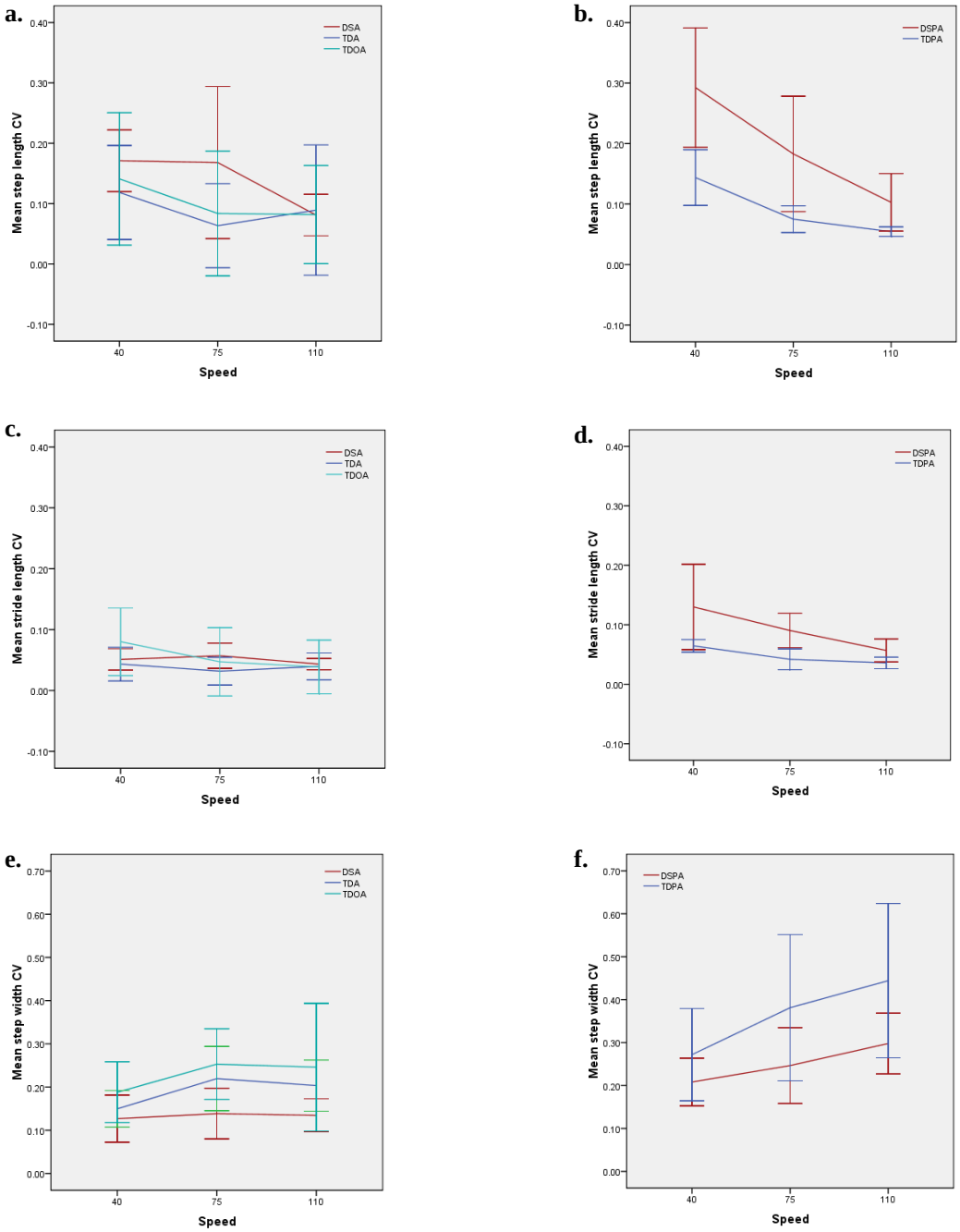


Figure B.1. Figures B.1.a and (b) are Coefficient of Variation (*CV*) of step length, (c) and (d) are *CV* of stride length and (e) and (f) are *CV* of step width. DSA = adults with Down syndrome, TDA = adults with typical development, TDOA = older adults with typical development, DSPA = preadolescents with Down syndrome, TDPA = preadolescents with typical development. Treadmill speed is on the *x* axis and represents 40, 75 or 110% of each participants' self-selected overground walking speed.

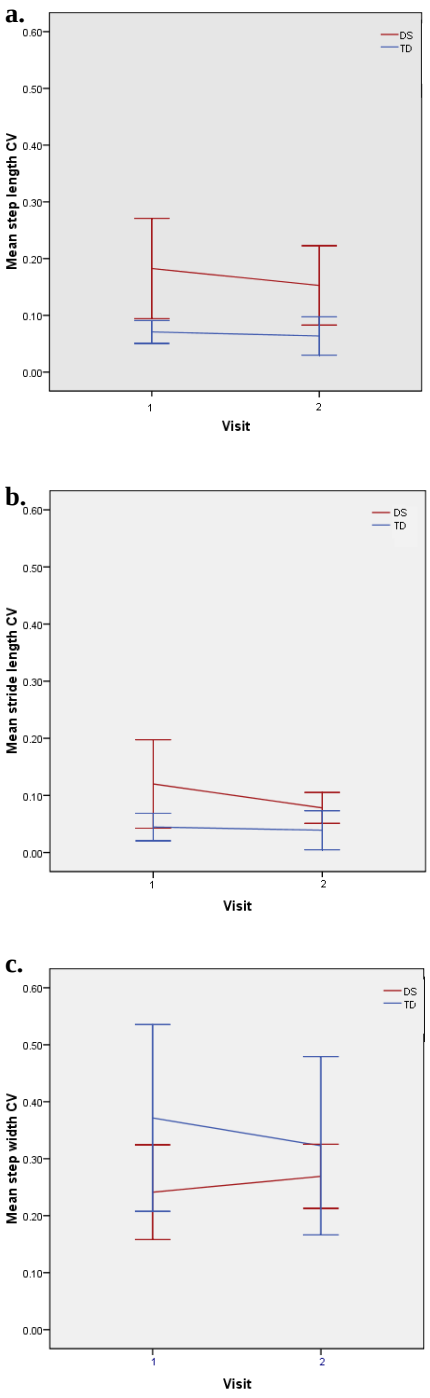


Figure B.2. Effects of practice on Coefficient of Variation (*CV*) values in preadolescents. Figure B.2.a is *CV* of step length, (b) is *CV* of stride length and (c) is *CV* of step width. Visit 1 is pre-test and visit 2 is post-test. DS = Down syndrome, TD = typical development.

APPENDIX C

For the purpose of my dissertation experiments was constrained to focus on variability in gait performance (quantitative and qualitative) in older adults with and without Down syndrome (DS). Because I believe these aspects of performance are also important to the increase in failures in gait (i.e., falls) that we see in aging populations, I also asked participants to report their history of falls and collected clinically relevant measurements that might relate both to my core variability measures as well as to fall incidence. To date, no reports of incidence of falls within the aging population with DS have been published but anecdotes and other examples of deterioration in gait variables earlier in life than peers with typical development (TD) suggests that rate of falls is relatively high. Within my sample of adults with DS the proportion of fallers was much higher than in the adults with TD. Adults with all TD reported that they did not have a history of falls, while six adults with DS reported a history of falls and eight reported no falls. Groups of six and eight were not sufficient to test relationships among variables. But, to use these data as pilot data for designing a more robust study between fallers and non-fallers with DS I examined this dichotomous variable in relation to other information I collected in my dissertation. These figures should be interpreted with caution and followed up with prospective studies designed to test specifically test them.

VARIABLES CONSIDERED

1) Age- From 30% (Luukinen, Koski, Hiltunen, & Kivela, 1994; Tinetti, Speechley, & Ginter, 1988) to 52% (Berg, Alessio, Mills, & Tong, 1997) to 61% (Maki, 1997) of community-dwelling older adults with TD reported a fall over a prospective one year study period, with approximately two thirds of these falls occurring while walking (Berg et al., 1997; Luukinen et al., 1994). Based on these findings, I anticipate older adults with DS are more likely to be classified as fallers than younger adults with DS.
2) Physical activity level and fear of falling- The gait characteristics of sedentary older adults with TD suggest that they adopt a more cautious walking style than active ones (Rosengren, McAuley, & Mihalko, 1998), as do TD older adults who are afraid of falling (Maki, 1997). Further, fear of falling can lead to self-limitation of physical activity (Deshpande, Metter, Bandinelli, Lauretani, Windham, & Ferrucci, 2008). I anticipate adults with DS who are more physically active on a regular basis will be less likely to endorse fear of falling and less likely to be classified as fallers.
3) Gait parameters- Older adult fallers with TD walk slower and take shorter strides than non-fallers (Guimaraes & Isaacs, 1980). I propose that fallers with DS will demonstrate different baseline gait parameters than non-fallers with DS.
4) Response to Peturbations- The irregular surface context elicits increased gait variability from fallers, but not non-fallers, with peripheral neuropathy (DeMott, Richardson, Thies, & Ashton-Miller, 2007). Divided attention

contexts elicit increased swing time variability in older fallers with TD, but not non-fallers (Springer et al., 2006). Uneven surfaces and clutter/obstacles are associated with falls in older adults with TD (for review see American Geriatrics Society, 2001; NCOA Falls Free Coalition, 2005; Tinetti et al., 1988). Based on these studies, and others, I propose adults with DS who are fallers will respond differently than non-fallers to some of the perturbations.

5) Clinical Screening Measures- I propose that, due to baseline differences in walking speed and balance scale performance between adults with DS and TD (Smith & Ulrich, 2008), cutoff scores for the Berg Balance Scale and Timed Up and Go best able to differentiate fallers and non-fallers with DS will be different than published values for adults with TD.

AGE

To test whether fallers were older than non-fallers I created Figure C.1. Fallers and non-fallers are evenly distributed across the age range.

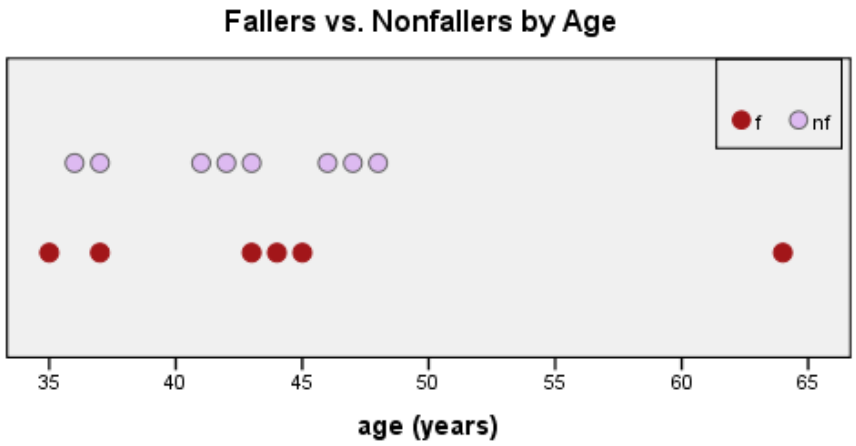


Figure C.1. Adults with DS stratified by age and fall history. Fallers are labeled with red markers and non-fallers with pink markers.

PHYSICAL ACTIVITY/ FEAR OF FALLING

Out of fourteen adults with DS, three reported minimal regular physical activity, eight reported moderate levels and three reported maximal levels. This variable needs to be investigated in a larger sample as the six fallers were evenly distributed across the physical activity groupings. It is difficult to relate physical activity levels directly to risk of falling, as high levels of physical activity may decrease fall risk, but conversely may expose at-risk persons to increased fall risk (Faulkner et al., 2009).

Five of the adults with DS endorsed a fear of falling. Four of them had history of falls, while the remaining one did not. In addition, there was one adult with DS who had a history of falls but reported he was not afraid of falling. Because self-reported fear of falling so closely reflects a history of falling in our current sample it is impossible to separate the effects of these two variables.

BASELINE GAIT CHARACTERISTICS

I show in Figure C.2 that fallers did not walk slower than non-fallers at their self-selected comfortable speed. Although I used dimensionless values to account for leg length differences between participants, mean absolute walking speeds were also not different between fallers and non-fallers, as follows (*M*(SD)): Fallers 0.68 (0.25) m/s, non-fallers 0.67 (0.18) m/s. Figure C.2 also shows that dimensionless stride length, stride time, step width and percent stance values were not different between fallers and non-fallers.

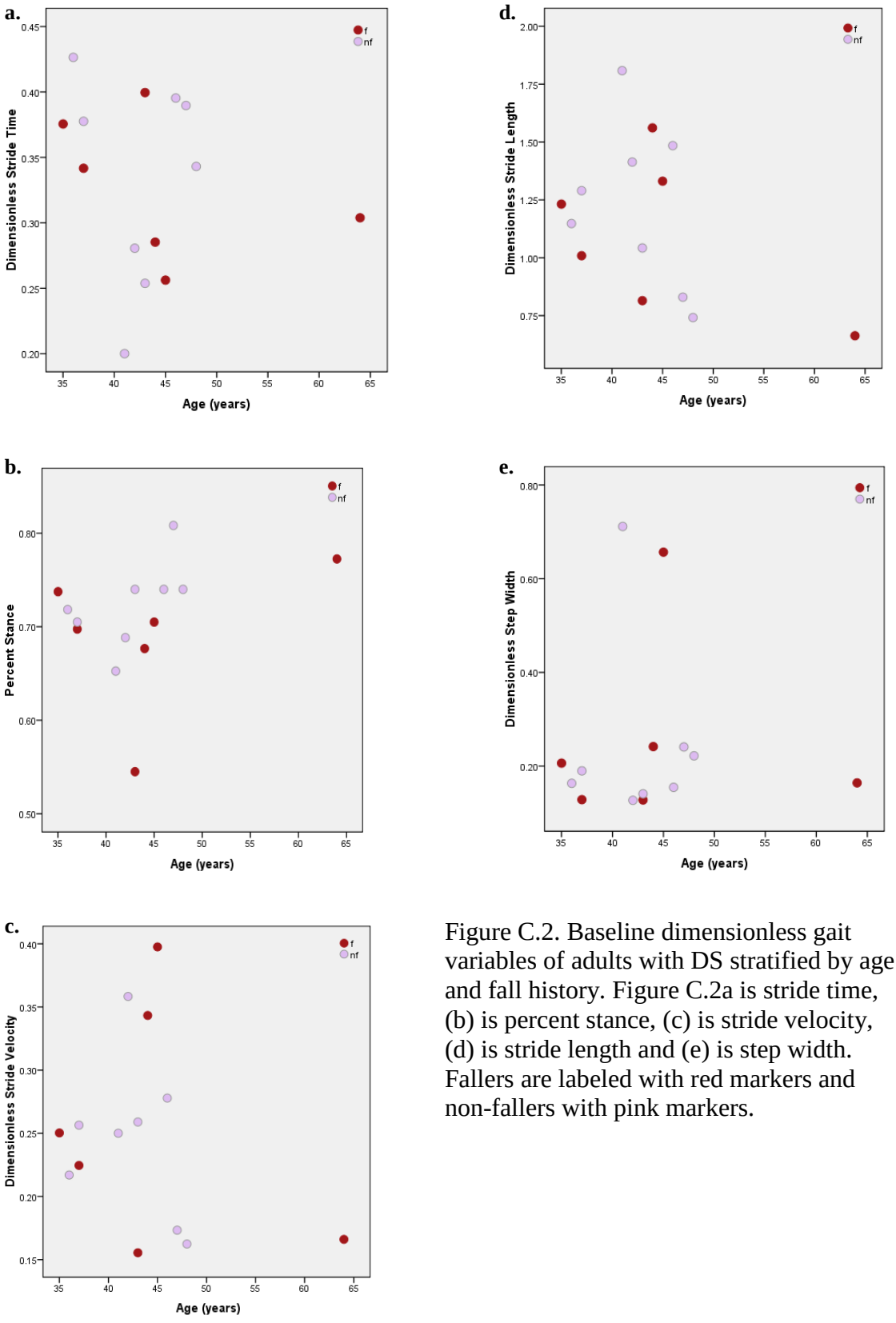


Figure C.2. Baseline dimensionless gait variables of adults with DS stratified by age and fall history. Figure C.2a is stride time, (b) is percent stance, (c) is stride velocity, (d) is stride length and (e) is step width. Fallers are labeled with red markers and non-fallers with pink markers.

RESPONSE TO PERTURBATION CONDITIONS

To visually examine responses to the perturbation conditions, I created figures showing percent change (increase or decrease) from baseline to each perturbation condition for each gait parameter (see Figure C.3) and for variability of each gait parameter (see Figure C.4).

Fallers tend to change their gait in the opposite direction of non-fallers. As Figure C.3 shows, in perturbation conditions, as compared to baseline, fallers tended to walk slower with increased stride frequency and percent stance and decreased stride length and step width. Non-fallers maintained walking speed or walked faster, with decreased stride frequency and percent stance, increased stride length and no change in step width.

In respect to changes in gait variability (Figure C.4), it appeared that fallers showed, in general, larger changes in increase or decrease of amount of variability in response to the perturbation conditions. The obstacle, irregular surface and irregular surface/sound combination conditions, in particular, evoked larger changes in gait variability in fallers as compared to non-fallers. As I show in Figure C.5, I noted that fallers demonstrated larger amounts of variability in stride length than non-fallers on the irregular surface, as well as in the irregular surface and sound combination condition. This finding is consistent with previous work that shows the irregular surface context elicits increased gait variability from fallers, but not non-fallers, with peripheral neuropathy, while walking on a level surface does not (DeMott et al., 2007).

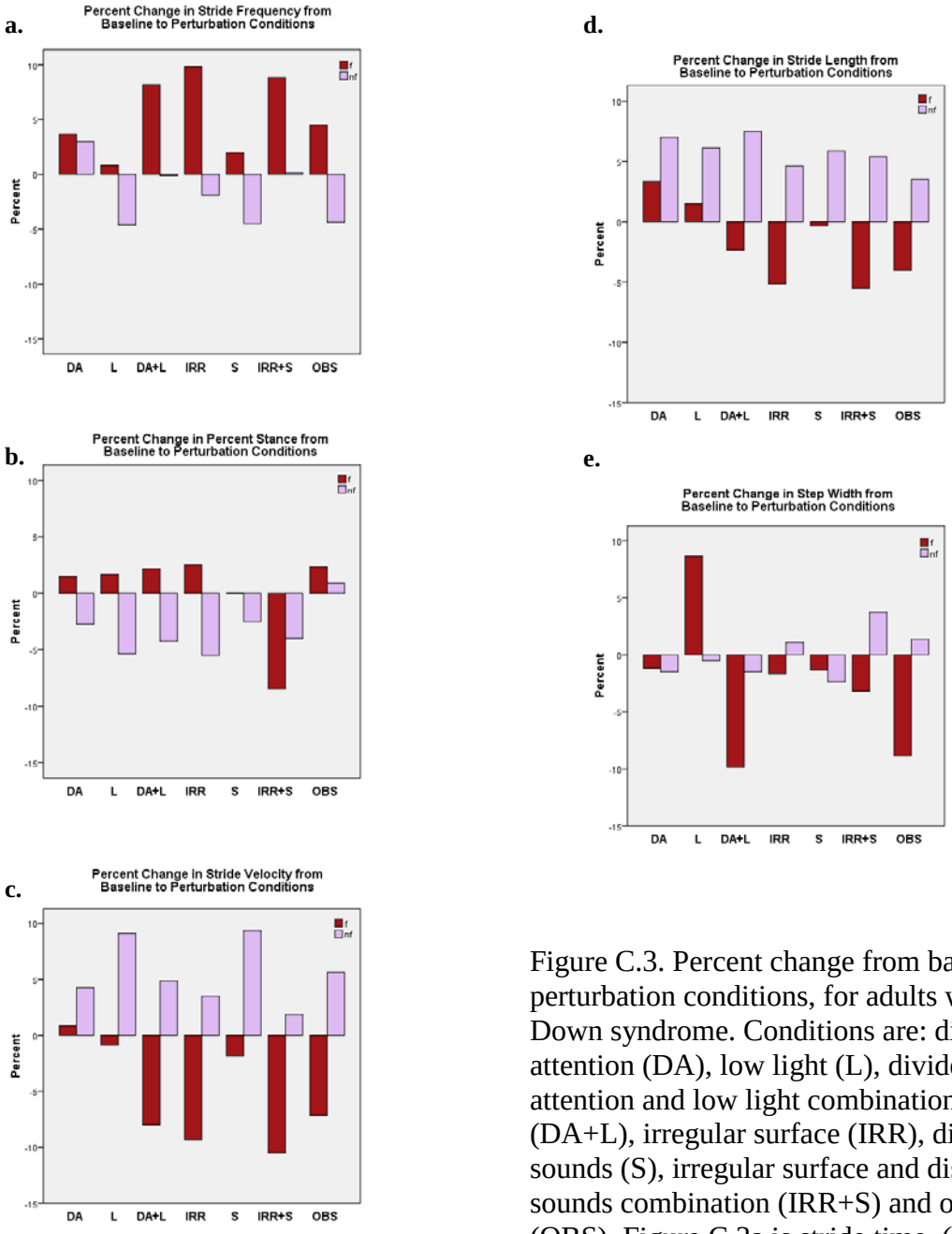


Figure C.3. Percent change from baseline to perturbation conditions, for adults with Down syndrome. Conditions are: divided attention (DA), low light (L), divided attention and low light combination (DA+L), irregular surface (IRR), distracting sounds (S), irregular surface and distracting sounds combination (IRR+S) and obstacle (OBS). Figure C.3a is stride time, (b) is percent stance, (c) is stride velocity, (d) is stride length and (e) is step width. Fallers are labeled with red columns and non-fallers with pink columns.

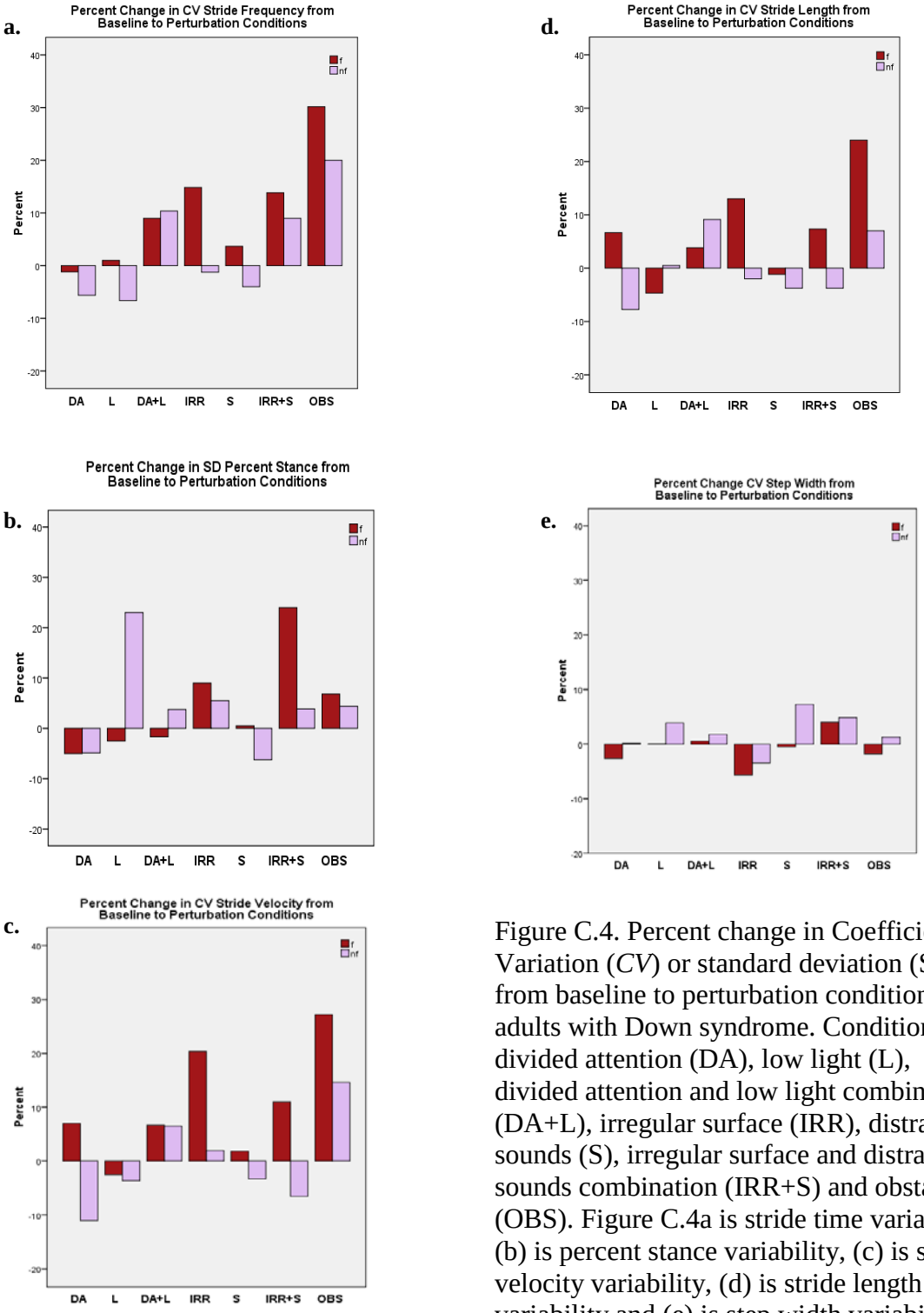


Figure C.4. Percent change in Coefficient of Variation (*CV*) or standard deviation (SD) from baseline to perturbation conditions for adults with Down syndrome. Conditions are: divided attention (DA), low light (L), divided attention and low light combination (DA+L), irregular surface (IRR), distracting sounds (S), irregular surface and distracting sounds combination (IRR+S) and obstacle (OBS). Figure C.4a is stride time variability, (b) is percent stance variability, (c) is stride velocity variability, (d) is stride length variability and (e) is step width variability. Fallers are labeled with red columns and non-fallers with pink columns.

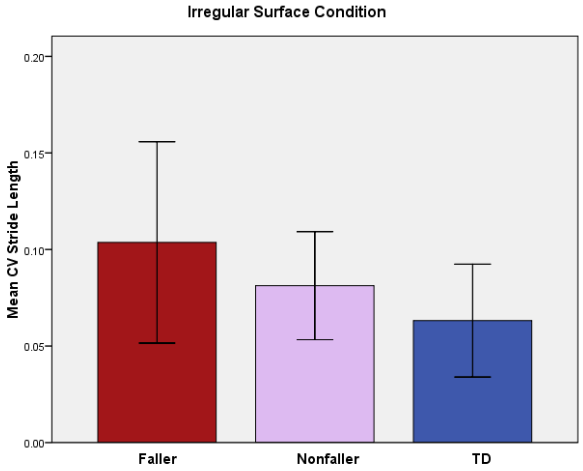


Figure C.5. Coefficient of Variation (*CV*) of stride length in the irregular surface condition for fallers with Down syndrome, non-fallers with Down syndrome and adults with typical development.

BERG BALANCE SCALE

Overall, as shown in Figure C.6, there were two observable effects influencing performance on the Berg Balance Scale, age and fall status. Older participants and fallers scored lower on the Berg, indicating poorer performance. Participants tended to lose points on the timed items, as well as when asked to stand on one leg. These results are similar to our previous findings, in a similar group of adults with DS (Smith & Ulrich, 2008). Our preliminary data indicate that age may need to be taken into account to figure out a sensitive and specific cutoff score for differentiating fallers and non-fallers.

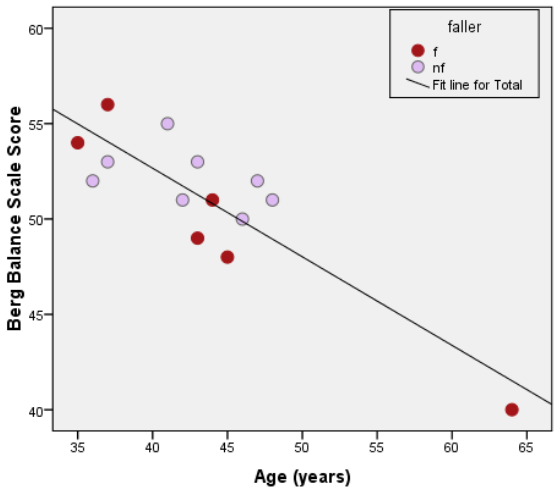


Figure C.6. Status of fallers (red markers) and non-fallers (pink markers) as a function of age and score on Berg Balance Scale.

TIMED UP AND GO

There were both age and fall status effects on performance of the Timed Up and Go (TUG), as shown in Figure C.7. Older participants and fallers took longer to perform the task, indicating poorer performance. To test the ability of the TUG to differentiate fallers and nonfallers, we used a one-way ANOVA to test for group differences in number of seconds taken to perform the task. Fallers took significantly longer to perform the test than nonfallers ($F[1,12] = 6.60$, $p = 0.03$), and we calculated a large effect size (Cohen's $d = 1.36$).

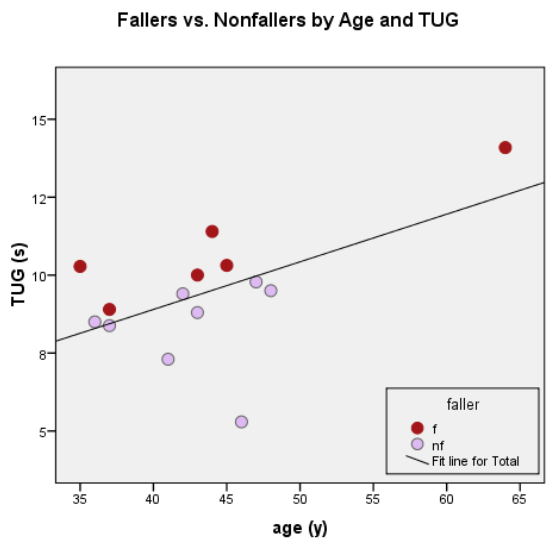


Fig C.7. Status of fallers (red markers) and non-fallers (pink markers) as a function of age and number of seconds taken to perform the Timed Up and Go.

DISCRIMINANT FUNCTION ANALYSIS

We used stepwise discriminant function analysis to test the relative contribution of the following variables on a function to discriminate fallers and nonfallers: Berg Balance Scale score, Timed Up and Go score and Coefficient of Variation of stride length in the irregular surface condition. Overall, the analysis was significantly able to discriminate fallers and nonfallers at the first iteration (Wilks' lambda = 0.6, $F(1,12) = 8.01$, $p = 0.02$). Our results showed the strongest discriminator was the Timed Up and Go, which alone correctly classified 86% of fallers. The Berg score and stride length variability on the irregular surface were not sufficiently able to discriminate fallers and non-fallers.

DISCUSSION

In general, I need to recruit a larger sample evenly distributed across the age range with fallers and non-fallers prospectively identified. I propose to follow up with prospective studies designed to test specifically test the following observations:

1) Baseline gait characteristics do not discriminate fallers from non-fallers, the task needs to be more challenging in order to see differences. When faced with perturbations, fallers tended to walk slower with increased stride frequency and percent stance and decreased stride length and step width. Non-fallers maintained walking speed or walked faster, with decreased stride frequency and percent stance, increased stride length and no change in step width. Results from the TUG, a clinical screening tool for fall risk, correlate well. The TUG also represents a perturbation to comfortable walking, as the participant has to plan and execute a reverse in walking direction.
2) Perturbation condition gait characteristics, but not baseline walking performance, discriminates fallers from non-fallers. All perturbations were effective to some degree in eliciting responses, which tended to be different between fallers and non-fallers. In particular, the obstacle and irregular surface conditions appeared to consistently discriminate fallers from non-fallers.
3) Unanticipated perturbations. Fallers show larger changes and extreme responses in amount of variability, particularly in response to the irregular surface. This may represent difficulty responding to unanticipated perturbation conditions, as the participants could not visualize where the surface was less stable. I would like to extend this work to test other unanticipated perturbations, such as sudden

obstacles in the walking path, slippery surfaces, loud noises and/or visual distractions. In addition, a comprehensive assessment such as the BESTest could help objectively delineate specific areas of difficulty. The BESTest follows a theoretical systems approach to evaluate six areas of balance performance: Biomechanical Constraints, Stability Limits/Verticality, Anticipatory Postural Adjustments, Postural Responses, Sensory Orientation, Stability in Gait (Horak, Wrisley, & Frank, 2009).

4) The TUG appears to discriminate fallers and non-fallers with DS, however the cutoff score for identifying an increased risk of falls in persons with DS needs to be investigated in a larger sample. A score of 14 seconds or greater indicates increased fall risk in older adults with TD (Shumway-Cook, Brauer, & Woollacott, 2000), but adults with DS routinely perform the task faster than this.
5) The TUG is able to discriminate fallers and non-fallers in our sample of six and eight in each group. A power analysis indicates a sample size of 19 in each group would have sufficient power to discriminate fallers and non-fallers based on irregular surface stride length variability. A sample of 20 in each group would not be unreasonable to recruit and would hopefully also allow further delineation of physical activity and fear of falling variables, in addition to variables of interest described above.

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