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Our view of certain gait disorders has changed with the development of new interventions for gait training. Recent gait research has suggested that humans do not walk with metronomic patterns, but with fractal patterns. Fractal patterns which are a common characteristic across nearly every human sub-system when healthy (e.g., gait, balance, heart rate, breathing rate, ect.). The patterns suggest that variability within a system is adaptive and healthy as opposed to the once held position that variability within a system was maladaptive. However, with the discovery of gait variability comes new questions about how to best help those who suffer from abnormal gait. One new area of research proposes that metronomes providing a variable stimulus, called fractal metronomes, could be used to redevelop adaptive patterns in clinical populations with abnormal gait. While immediate retention of these newly developed patterns has been shown immediately after and 5 minutes after a single session of training, the patterns revert back to pre-training levels after 24 hours. Like many other neuromuscular movements, a dosage effect may be associated with this type of training in order to see change. Longer-term retention is needed to ensure that these interventions have promise in helping patients with a pathology. Therefore, the goal of this thesis was to explore how seven days of training to a fractal metronome would impact the retention of new fractal gait characteristics. It was hypothesized that: (1) participants would exhibit a stronger coupling of their gait to the fractal stimulus with increased practice (i.e., assessed via

cross correlations across days) and (2) immediate retention (i.e., directly after training) and longer-term retention (i.e., 24 hours after training) would increase as a function of increased practice. Hypothesis 1 was supported by the observation that the cross-correlation between the metronome and subjects, as well as, within subjects increased across the seven days of training. However, that did not translate to immediate or longer-term retention, thus hypothesis 2 was not supported. It is important to note that embedded within the testing for hypothesis 2 was the observation that participants' fractal patterns got stronger during the training phase across the seven days, it was just not transferred to the overground walking that was used to examine immediate and longer-term retention. The results of this study suggest that fractal gait patterns can be strengthened with multiple days of training. However, future work should provide fractal gait training overground and then test retention overground to remove the confound of training on a treadmill and then retention testing overground.

DOSAGE EFFECT ON NEUROMUSCULAR RETENTION OF A FRACTAL GAIT PATTERN USING A VISUAL STIMULUS

by

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APPROVAL PAGE

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CHAPTER I

INTRODUCTION

"Walking is hard." This statement is not often heard amongst kids, teens, and healthy adults. It is not until aging or some pathology impairs our gait that we realize how much goes into the ability to walk. As researchers delve further into the science of gait they are unearthing new phenomena with respect to the variable nature of gait. With these new observations of gait variability come new interventions that could potentially help those with a maladaptive gait. The approach to gait training has been developing over the years and a relatively new way to potentially redevelop adaptive and functional gait is starting to be explored. The work of Hausdorff and others has shown that humans have fractal patterns within their gait cycle (Hausdorff, 2007; Rhea, Kiefer, Wittstein, Leonard, & MacPherson, 2014; Stergiou & Decker, 2011). Although variability is inherent in gait, young healthy adults exhibit more adaptive gait patterns (i.e., fractal patterns) within their gait cycle than when compared to adults with a maladaptive gait either due to age or pathology (i.e., Stroke or Parkinson's disease). The adaptive variability within healthy gait is demonstrated by the fractal patterns of the stride interval time. These fractal gait patterns have been shown to indicate a person's ability to adapt to the surface on which he or she is walking, hereby allowing researchers to objectively measure potential risk of falling (Rhea & Kiefer, 2014). Within the spectrum of gait variability, which will be discussed in chapter II, gait variability in the middle of the spectrum is considered healthy and adaptive, while gait variability on either side of the spectrum is characterized as maladaptive. For example, detrended fluctuation analysis (DFA) provides a measurement of gait variability ranging from 0.5 (reflecting random behavior) to 1.0 (reflecting persistent behavior). Both random and persistent gait present issues that increase fall risk. Young healthy adults have an average DFA value of 0.75, while patient's post-stroke are near 0.5 and patients with Parkinson's disease are near 1.0. This change in gait behavior reflects each person's ability to adapt to the environment, and both random and persistent patterns have been shown to be associated with fall-risk (Rhea & Kiefer, 2014). A gait intervention that focuses on redeveloping fractal gait characteristics would represent a novel approach to rehabilitation and potentially lead to less falls in older adults and pathological populations (Manor & Lipsitz, 2013; Rhea & Kiefer, 2014).

Research in this area began by simply showing that humans could synchronize their movement patterns to a fractal metronome. The fractal characteristics of the metronome were modified to have either persistent or random variability patterns within the prescribed timing structure, and participants showed that they were able to produce a range of fractal patterns when synchronizing to a stimulus with a simple finger tap (Stephen, Stepp, Dixon, & Turvey, 2008). This work was then extended to gait and participants were again able to synchronize with and produce both persistent and random patterns (Rhea & Kiefer, 2014). In a follow-up study, participants showed immediate retention of the new fractal gait patterns after the stimulus was turned off (Rhea, Kiefer, D'Andrea, Warren, & Aaron, 2014). This data suggested that further investigation was needed into whether subjects could reproduce the fractal pattern after a period of rest. However, a follow-up study showed that the effects of the single session of training started to wear off after 5 minutes post-training and completely wore off 24 hours after training (LoJaccono, Frame, & Rhea, 2015). These data suggest multiple training sessions would create a higher retention of the fractal gait characteristics. Each time the participant walks to the metronome constitutes a single dose. In order to stay consistent with the previous research that lead to this study (LoJaccono et al., 2015; Rhea, Kiefer, D'Andrea, et al., 2014; Rhea, Kiefer, Wittstein, et al., 2014), one dose was 10 minutes of walking to the fractal metronome and this training was repeated seven days in a row. In order to develop a novel intervention for populations who have elevated fall-risk, it is important to first understand the dosage effect of gait training on fractal gait characteristics in a healthy population.

The purpose of this thesis was to study whether fractal patterns in gait (specific to stride interval time) are retained when fractal gait training is provided to young healthy adults over seven consecutive days. Two hypotheses were tested:

Hypothesis 1: Participants would exhibit a stronger coupling of their gait to the visual stimulus with increased practice (i.e., assessed via cross correlations across days).

Hypothesis 2: Immediate retention (i.e., directly after training) and longer-term retention (i.e., 24 hours after training) would increase as a function of increased practice.

CHAPTER II

REVIEW OF THE LITERATURE

Overview

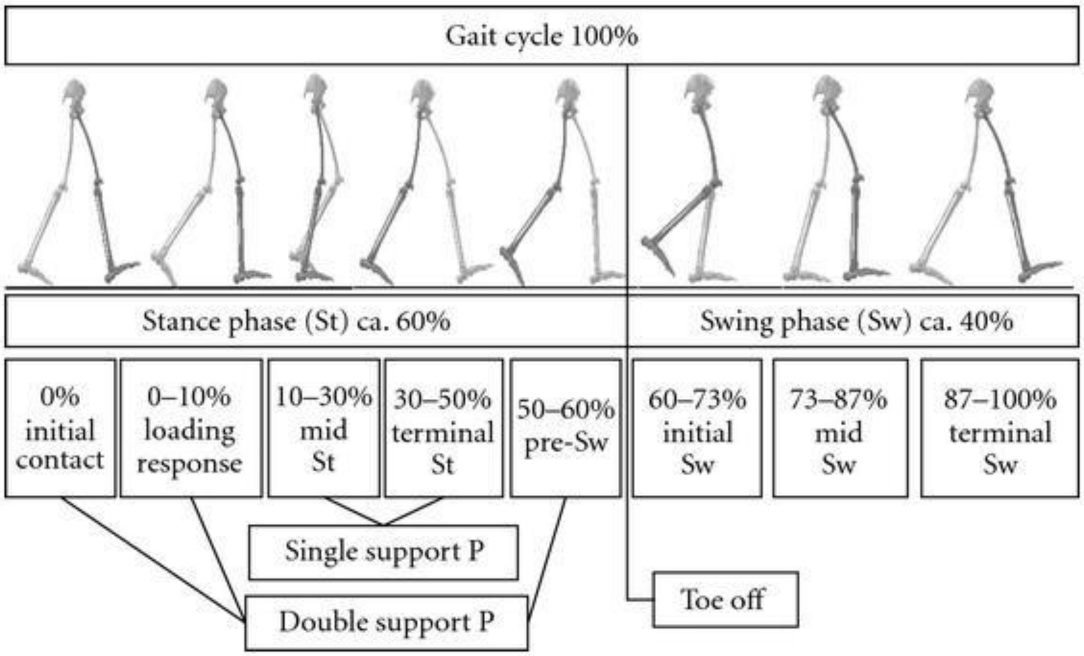
Among older adults, falls are the number one cause of fractures, hospital admissions for trauma, loss of independence, and injury related deaths (NIH Senior Health, "Falls and Older Adults", 2013). For this reason and others, scientists and researchers have been concerned with the phenomena that is human gait. The Gait Cycle portion of this chapter will document the research through which we have learned about our bipedal ambulatory ability. This section will demonstrate what we know about the basics of human gait. The understanding of how gait works at a basic level is necessary because when the ability to walk has been degraded due to age or pathology, the challenge for clinical professionals is to use this knowledge to redevelop gait patterns. From there the more contemporary scientific area of Gait Variability will be explored. The concept of gait variability explains just how much variation there is within step length, step width, cadence, and frequency. Furthermore, there is a range of healthy variation and on either side of that healthy variation there is variation that is linked to impairment. While a variety of metrics have been developed to quantify variability, Detrended Fluctuation Analysis (DFA) is a measurement tool that has been frequently used in the literature and is discussed in detail in this review. With the ability to measure variability researchers can quantify whether intervention techniques move the subjects' gait in the desired direction. The next section will further describe how researchers have tried to rehabilitate gait. It will explain how treadmill gait compares to overground gait and why both are important to this thesis. A gap will begin to appear in the literature when the research regarding fractal metronome is discussed. This study contributed to the literature by examining whether or not there is a dosage effect that occurs when trying to entrain a subject to a new fractal gait pattern over multiple days.

The Gait Cycle

A gait cycle consists of the motion from heel contact on one foot to heel contact on the same foot (Winter, 1991). Movements within gait happen in three planes: frontal, sagittal, and transverse plane (Vaughan, Davis, & O'connor, 1992). The frontal plane divides the body into two parts, the anterior and the posterior. The sagittal plane cuts the body into right and left halves. Lastly, the transverse plane goes through the body perpendicular to the two other planes, bisecting the body into top and bottom. Adduction and abduction occur within the frontal plane, flexion and extension occur within the sagittal plane, and all types of rotation occur within the transverse (Vaughan et al., 1992). During gait, the head and torso should remain upright for maximum balance. The torso and head should move the least when compared to the swinging extremities. The arms will move forward and backward in inverse unison with the legs (i.e., when the right arm is moving forward the right leg is moving backward) and the arms and legs mainly move within the sagittal plane. However, there is some rotational movement within the hips and shoulders that occur in the transverse plane.

The gait cycle can be broken down into the stance and swing phases. The stance phase is the time during which the reference foot is in contact with the ground and there are four components within the stance phase: Initial Contact (IC), Foot Flat/Mid-Stance (FF), Heel Off/Terminal Step (HO), and Toe Off/Pre-Swing (TO) (Winter, 1991). The alternate names for each stance phase refer to the terminology used in Figure 1. Figure 1 also shows the percentage of each portion of the stance phase. The stance phase can also be broken down into the single support and double support phases, which is when only one foot or both feet are in contact with the ground, respectively. The swing phase is the last phase when the foot is off the ground swinging to the next initial contact/heel contact. The timing and coordination of these phases/components have been recorded in order to develop normative data for human gait and to serve as a comparison in aged or pathological populations.

Figure 1. Healthy Gait Cycle Showing the Percentage of Time Spent within Each Phase.



Abbreviation Note: St is Step; Sw is Swing; P is percentage.

The muscles within our legs help us both drive through each cycle and recoil to begin another. The quadriceps muscles extend the knee and help absorb force during the time the foot is making contact with the ground (Hausdorff & Alexander, 2005; Winter, 1991). The hamstring muscles cause flexion at the knee joint and help pull the leg through the support stages. The gluteal muscle group controls the extension movement at the hip and provides much of the power needed to walk (Hausdorff & Alexander, 2005; Winter, 1991). Hip flexors during the swing phase help to pick the leg up and increase toe clearance. Muscles below the knee help to plantarflex, deliver power during toe off, and dorsiflex during the swing phase to also increase toe clearance. All of these muscles play their part to contribute to the fluid motion of the gait.

Role of Gait Variability

An area that is getting much more attention for how it relates to biological processes within humans is variability. Variability has now been examined within many different systems including postural sway (Petit, 2012), body temperatures (West, 2006), respiration rates and volumes (Peng et al., 2002), and gait dynamics (Hausdorff et al., 2001). Variability has allowed researchers to examine the fractal characteristics of these systems. The term fractal characteristics refers to the self-similar patterns within gait (Rhea, Kiefer, D'Andrea, Warren, & Aaron, 2014). Self-similar is a term used to describe how our steps are correlated to one another for example one may be exactly the same as step 100. The pattern with which a tree branches into smaller branches and smaller branches is often used to depict fractal characteristics. Each time a tree branches into a smaller branch it is similar to how the tree has branched before. The traditional metrics for measuring gross motor skills have been mean, standard deviation, and median values. These values aren't appropriate when measuring variability. Take postural sway measurement for example. When a subject is standing on a balance monitor he or she will sway in just about every direction, but summary metrics may not pick up on this variation. If someone sways a lot for the first 10 seconds and very little for the last 10 seconds, the mean and standard deviation of their balance behavior might look the same as someone who sways an average amount for the entire 20 seconds. Thus, examining patterns within the variability, in conjunction with the summary metrics provides a more holistic way to quantify human behavior.

The term gait variability refers to the differences from one step to the next concerning step length, step width, cadence, and swing time (Hausdorff et al., 2001). However, this variability exhibits particular patterns, similar to variation within heart rate or respiratory rates. In fact, it has been suggested that all healthy human sub-systems exhibit a specific variability pattern called pink noise and it is thought that this variability pattern allows for a favorable adaptive response when the system experiences a perturbation (Van Orden, Kloos, & Wallot, 2011). Relative to gait, variability itself is the reason we can walk on uneven surfaces, hike through the wilderness, or quickly change a step to accommodate to a new surface (Hausdorff, 2007). When our gait control breaks down due to aging or pathologies like stroke and Parkinson's disease, the fractal patterns in our gait degrade and our ability to adapt to each different surface we walk on is lessened (Hausdorff, 2007). For example, the transition from walking on hardwood floors to carpet presents a challenge to those who have degraded variability patterns. Thus, interventions focused on modifying variability patterns may show promise in improving the adaptive ability in a variety of populations. The first step in this line of research was to show that an external cue could be used to influence someone's variability patterns.

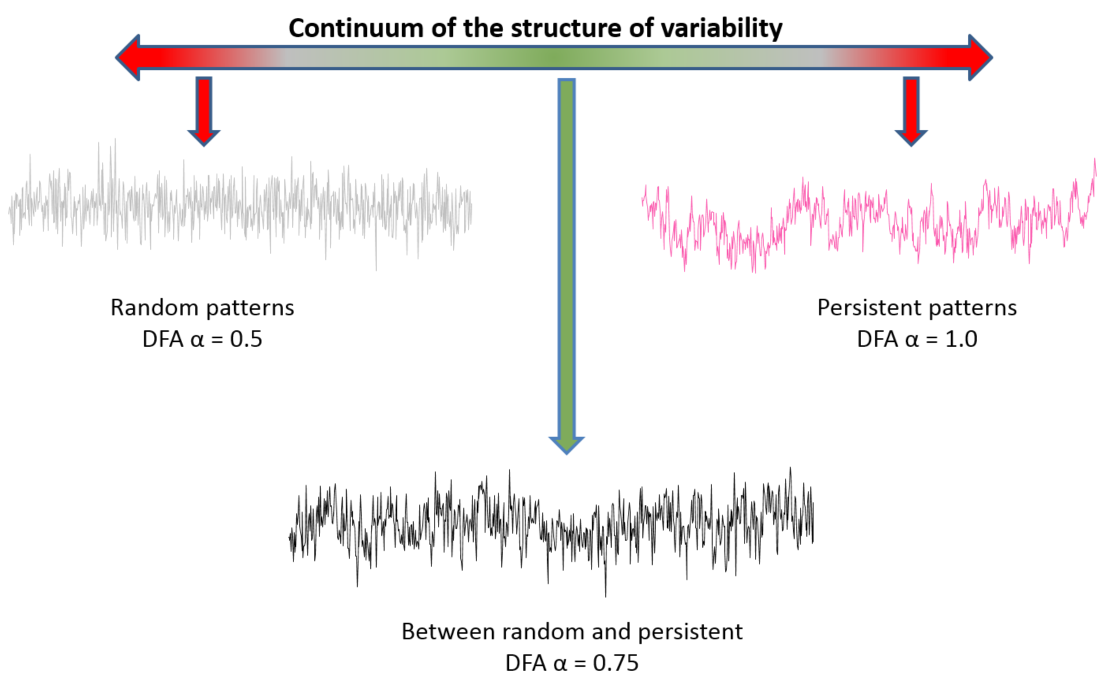
The ability to shift individuals up and down a spectrum of variability, with persistent/structured fluctuations on one end and unstructured/random temporal fluctuations on the other, could be used in clinical settings for gait training. As we age our gait variability becomes more random. Influencing stride intervals to become more persistent would help create a more adaptive healthy gait, due to a consistent but flexible pattern of movement (Hausdorff, 2007; Stergiou & Decker, 2011). A gait pattern with a healthy amount of variability is typical of an adaptive gait that can change course due to changes in the terrain. In clinical populations, one of the many goals of treatment is to improve gait adaptability. If the visual metronome can improve gait adaptability it could be used as a treatment for pathologies like stroke, Parkinson's, or Huntington's disease.

As numerous metrics have been utilized to explain variability within biological data sets, particularly in gait and balance there is one metric that specifically measures large data sets. Since the data sets in this study will have over 500 steps each, this literature review will focus on the metric best suited to measure those data sets: Detrended Fluctuation Analysis (DFA).

Detrended Fluctuation Analysis (DFA)

Even under the most constant of environmental situations, there are fluctuations in human gait cycles, defined as heel strike to heel strike. (Frenkel-Toledo et al., 2005; Hausdorff et al., 1996; Jordan, Challis, & Newell, 2007; Pailhous & Bonnard, 1992). While many metrics have been developed to quantify the patterns within gait variability, DFA has been repeatedly shown to discriminate between "healthy" and "unhealthy" systems. DFA is an analysis that makes use of the fact that a long-range (power-law) correlated time series can be mapped to a self-similar (fractal) process by simple integration (Hausdorff, 2007). By random-walk it is meant that there are no constraints on the subjects and that they are simply asked to walk as they normally do. Each integrated time series is said to be self-similar if the fluctuations at different observation windows, F(n), scale as a power-law with the window size n (i.e., the number of strides in a window of observation or the time scale). F(n) has a linear relationship with n so that F(n) is approximately equal to n^{α}. Alpha can be determined by calculating the slope of the line relating log F(n) to log n. Important to our study, Hausdorff (2007)points out that long range, persistent and fractal correlations are present if $.5 > \alpha \geq 1.0$. Relating back to previous studies, most humans walk at an α of 0.75 showing that humans do exhibit persistent fractal correlations within their gait. Graphical representations of fractal human gait often look like a version of sinusoidal graphs with varying peaks and valleys. Figure 2 shows the graphical representation of pink noise (persistence) and white noise (randomness).

Figure 2. Examples of Time Series Depicting Random (DFA α = 0.50), Between Random and Persistent (DFA α = 0.75), and Persistent (DFA α = 1.0) Patterns.



The mathematical steps begin with subtracting the average step from every step in the time series.

Figure 3. Calculation of Demeaning Data

$$y(k) = \sum_{i=1}^{k}[S(i) - S_{ave}]$$

From here the time series is divided into boxes (i.e., time scales). Those boxes are equal in length in order to compare them. "n" represents the length of each box. For a visual representation of this refer to figure 5. The data are typically separated into box sizes of 4 data points up to the large box size of 25% of the data length. In each box size, a line of best fit, $y_n(k)$, is computed across all boxes and each data point, y(k), is subtracted from

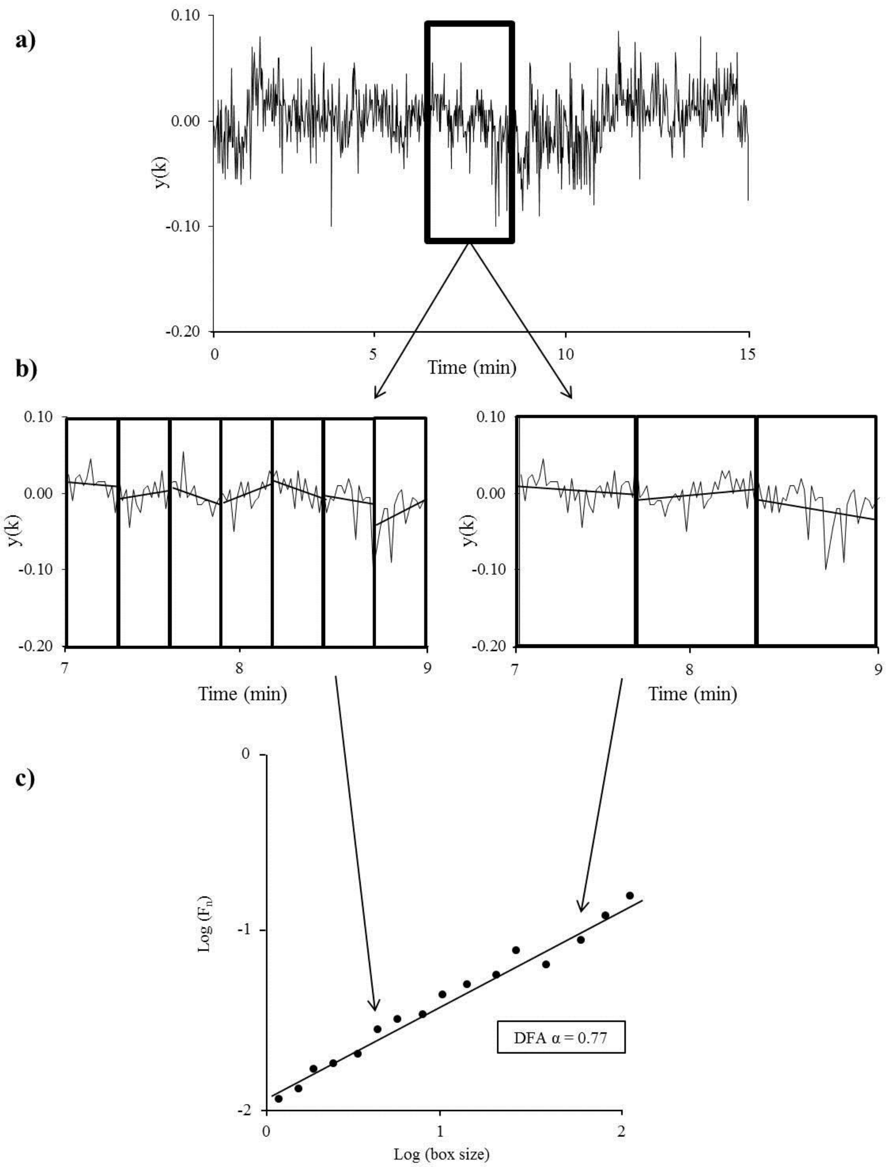
$y_n(k)$ to determine the residual variability. Next, a root mean square function is taken of the residual variability within each box at each box size using the following equation:

Figure 4**.** Root Mean Square Calculation for DFA

$$F(n) = \sqrt{\frac{1}{N}\sum_{k=1}^{N}[y(k) - y_n\,(k)]^2}$$

Each time scale is subject to this equation in order to give a relationship to F(n) or the average fluctuation as a function of box size. The data is then plotted on a log-log graph, with the log of the box size on the x-axis and the log of the residual variability within that box size on the y-axis. If similar scaling is occurring across all time scales, a linear relationship will emerge on the log- log graph. A line of best fit is applied to the log-log graph and the slope indicates the α, which indicates whether the time series shows persistence ($0.5 < \alpha < 1.0$) or randomness ($\alpha \leq 0.5$). The DFA process is illustrated in figure 5 (Rhea, Kiefer, D'Andrea, et al., 2014).

Figure 5. Log-Log Graph of Data Demonstrating Power Law Scaling



Overground vs. Treadmill Gait

Now that the gait cycle, gait variability and how gait variability can be quantified have been discussed, it is important to outline the differences between overground and treadmill gait. When studying overground gait, most research laboratories are only able to study 4-10 steps before the participant is outside of the data recording space. A treadmill provides a methodological advantage to the study of gait because the subject remains in a relatively stationary position while going through the gait cycle. Thus, a treadmill allows for recording strategies like electromyographic, kinetics, and kinematic analyses to be utilized over as many steps as possible only limited by the subject's stamina and the amount of memory on the computer (Altenmüller, Berger, Prokop, Trippel, & Dietz, 1995; Berger & Rokni, 1987; Gabel & Brand, 1994). This is important, because as outlined in the previous section, gait variability naturally emerges across hundreds of strides, so it is crucial to have the ability to record and analyze gait variability as it evolves throughout a long duration trial.

Although a treadmill offers some methodological advantages in the study of gait, much of the scientific research on gait has examined overground walking. Frenkel-Toledo et al. (2005) suggest that part of this reason is that treadmills exert an external cue upon the person walking. The belt does not stop even if the person stops walking. When it comes to speed or pacing, subjects do not have to think about what speed to select during overground walking as opposed to treadmills which need to be set at the beginning (Wall & Charteris, 1981). Another advantage generally attributed to overground walking is the choice of preferred walking speed which the subject self-selects (Sutherland, 1997). Often when individuals self-select a walking speed on the treadmill it is slower than their self-selected overground speed. Each subject is told to walk at a speed similar to when they are walking to class or walking with a purpose. Because the instructions do not change between the overground and treadmill conditions, the only difference is what the subject deems an appropriate speed based of the instructions. Some studies found a significant increase of the cadence and an associated decrease of the step length and the stance phase duration during treadmill walking in comparison to overground walking (Pearce et al., 1983; Strathy, Chao, & Laughman, 1983); others reported opposite effects, (i.e. a decrease of the cadence and an increase of the stance phase duration) (Greig, Butler, Skelton, Mahmud, & Young, 1993; Nelson, Dillman, Lagasse, & Bickett, 1971). In addition to these speed and stance differences there are some biomechanical differences when comparing treadmill gait to overground gait. Many of the findings from studies that observed muscle activation, hip flexion angle, and hip range of motion differences contradict each other on whether there are significant differences (Lee & Hidler, 2008). The authors found that knee joint kinematics and sagittal plane joint moments in general (with the exception of peak ankle plantar flexion) were significantly different between overground and treadmill gait. In support of Lee and Hidler, Alton, Baldey, Caplan, and Morrissey (1998) found that the treadmill condition significantly increased hip range of motion, hip flexion joint angle and cadence when compared to overground walking. It was also found that males especially increased their maximum knee flexion angle on the treadmill (Alton et al., 1998). In studying the knee moments Lee and Hidler (2008) found that the sagittal plane hip extensor moments in early stance and late swing were both greater during treadmill walking than during overground trials, whereas the peak hip flexion moment was significantly higher during treadmill walking. In short, when people walk on a treadmill they modify their muscle activation patterns and subsequently their joint moments and powers while maintaining relatively constant limb kinematics and spatiotemporal gait parameters (Lee & Hidler, 2008).

While the previously cited work shows that treadmill walking and overground walking are somewhat different, some studies have found there to be no significant differences in many of the biomechanical characteristics when walking on the two surfaces (Arsenault, Winter, & Marteniuk, 1986). Alton et al. found that in females the only significant difference was found in the maximum hip flexion angle, while the knee and ankle joint angles were similar. Chang, Shaikh, and Chau (2009) posited that gait speed was a confounding factor since self-selected gait speed is typically significantly faster in overground walking. Since the DFA α of stride time is used to compare gait variability, gait speed would be important to explore. However, when DFA α was plotted as a function of gait speed there was no significant correlation found between DFA α and the gait speeds. It was also found that when measuring variability there is no significant difference in the DFA α between overground and treadmill walking without a hand rail ($P>0.5$) (Chang et al., 2009). This information is promising because gait intervention programs that can be delivered on a treadmill offer efficacy in terms of space (less clinic space needed) and time (a single clinician can monitor more than one patient at a time if multiple treadmills are used). Those two factors allow any clinic that can afford a treadmill the ability to perform gait training of large distances that would otherwise have to involve an entire indoor track. While many authors continue to debate the differences between the two conditions, this study aims to add more information towards the relationship between overground and treadmill gait.

If variability is the main focus then how to best measure it. The two most common are DFA and the lyapunov exponent. One caveat of DFA is that it requires a lot of strides (> 500) to fully analyze gait (Damouras, Chang, Sejdić, & Chau, 2010). This often means that a treadmill is used to collect the large number of steps required. Some researchers have felt that a different statistical analysis requiring fewer steps or a smaller data set would be a more ecologically valid method. An analysis that could use fewer steps would not require a large laboratory or research gym or treadmill in order to get the required data for analysis. This would save the research team time and money. Dingwell, Cusumano, Cavanagh, and Sternad (2001) used the lyapunov exponent to measure the stability of variability patterns in gait. While DFA requires hundreds of steps, the lyapunov exponent requires fewer steps (i.e. 30 steps in Dingwell et al. (2001)) to get an accurate measurement of the variability patterns (Dingwell et al., 2001). For those reasons the lyapunov exponent is recognized by many as a valid statistic, but DFA was found to be more closely related to fall risk (Hausdorff, 2007). As one gets to either end of the DFA spectrum (0.5 or 1.0) the fall risk increases. With aging and pathology, the DFA α value drops toward 0.5 or more random and a DFA α value close 1.individuals have less adaptability which leads to more falls. Because the ultimate goal of this study is to add information about gait variability to help lead to interventions to reduce the risk of falls, DFA was chosen as the metric of interest. The next section will focus on how gait training is traditionally delivered in both overground and treadmill settings.

Gait Training

For quite some time, gait rehabilitation has focused on muscle strengthening exercises to help make up for the atrophy that commonly occurs in clinical populations. However, some pathologies disrupt the neural messages that are being sent to the muscles themselves. Parkinson's disease often causes degeneration of dopamine producing cells causing tremor, rigidity, postural instability, and bradykinesia (Spaulding et al., 2013). This can cause gait to worsen slowly over time. Since drugs that treat pathologies are not always effective and have a host of side effects, researchers have been experimenting with external cues to facilitate gait retraining. It is suggested that cueing can have a direct and significant effect on gait performance in many clinical populations, including people with Parkinson's disease (Picelli et al., 2010). Cueing, whether auditory or visual has been shown to improve gait cadence, stride length, velocity, and postural stability (Spaulding et al., 2013). Cues are a temporal or spatial stimulus to regulate movement often with some sort of rhythm.

Auditory cues are sounds that give the subject a signal to step to with the left or right foot. Some auditory stimuli make use of different sounds to represent the left and right stride. Most of the research has, until recently, used auditory cues that have metronomic qualities. The metronome used would be set a pace that the researchers deemed the optimal walking speed. In some studies the metronome was set to speeds 10% faster than the self-selected pace of the subject and another study has administered a metronome at 10% slower pace (Ledger, Galvin, Lynch, & Stokes, 2008). In both cases subjects increased and improved cadence, stride length, and velocity (Rubinstein, Giladi, & Hausdorff, 2002).

Visual cues include, but are not limited to, the use of laser pointers, adaptive glasses, or lines marked on the floor. In their most simplistic forms visual cues can be pieces of tape on a floor marking the length of each stride. In a meta-analysis, Spaulding et al. (2013) found that stride length was the only significantly improved characteristic within Parkinson's disease subjects. Some have hypothesized that the visual cues help patients regulate their stride with the added spatial information from the cue.

While these interventions have helped some patients with particular diseases such as Parkinson's, when asking an otherwise healthy subject to synchronize to an auditory metronome or a blinking visual metronome that is non-variable, subjects tend to produce a random and maladaptive walking pattern (Hausdorff et al., 1996). Subjects would be in a reactive state then switch to a proactive state. This changing of reactive to proactive and back and forth again would cause the DFA α value to decrease into the random end of the DFA spectrum (DFA $\alpha = 0.05$). Why does this occur? As stated above it has been shown that healthy human gait is not rigid or non-changing. Rather, it has variability as a functional component of the system. Thus, it seems asking a variable system (i.e. human gait) to synchronize to a non-variable metronome is a rather unachievable task that leads to random gait behavior. A more plausible way to modulate gait variability in humans is to use stimuli with variability characteristics that closely match that which is naturally observed in human gait. Thus, the next section will examine stimuli that been developed to have fractal characteristics for the purposes of gait training.

Gait Training with a Fractal Stimulus

Intricate variable patterns allow humans to adapt to their surroundings. Researchers realized that these variable patterns were fractal in nature and further studies have shown that fractal patterns exist in gait as well as many other different bodily systems (Yamamoto & Hughson, 1994). Cardiac and respiratory systems both demonstrate fractal patterns. Even nerve firings exhibit this behavior. It is due to this new understanding that researchers have studied the underlying factors that cause the fractal nature of the different systems. Within gait, these patterns not only reflect the coordination of many neuro-musculoskeletal components to generate a fluid walking motion, but also reflect sensorimotor modulation by proprioceptive and visual information (Glass & Chvala, 2001). One important facet is the visuomotor characteristic of gait. Our visual surroundings greatly impact how we move in space and coordinate the timing of our gait. Thus, stimuli that can prescribe different gait timing behavior, such as auditory and visual metronomes, have been used to probe the adaptive nature of human gait.

Fractal synchronization research originally began with finger tapping research by Stephen et al. (2008). The subjects were asked to tap a key on the keyboard in synchrony with each flash on the screen in front of them. This visual stimulus acted as a visual metronome and it was set to produce chaotic signals. The researchers looked for three aspects of the finger tapping behavior: (1) pure reaction, where each tap of the keyboard followed a signal by an average amount of time; (2) pure proaction, where the tap occurred before each signal by an average amount of time; and (3) pure synchrony, where both the tap and the signal happened at the same time (Stephen et al., 2008). None of the subjects fit perfectly in any of the three categories, as they all adopted a behavior that combined all three strategies. The researchers theorized that the subjects may be experiencing a form of entrainment. They found evidence that the subject exhibited a strongly anticipatory system that anticipated based on the statistical structure of the signals. This paper laid the foundation to study how humans synchronize to signals with variable timing. Prior to this paper, most timing synchronization research focused on using non-variable metronomes to probe human behavior. However, as stated previously, human biological systems are inherently variable, so using a variable stimulus represents a biological-like stimulus that could help further advance our knowledge of human behavior.

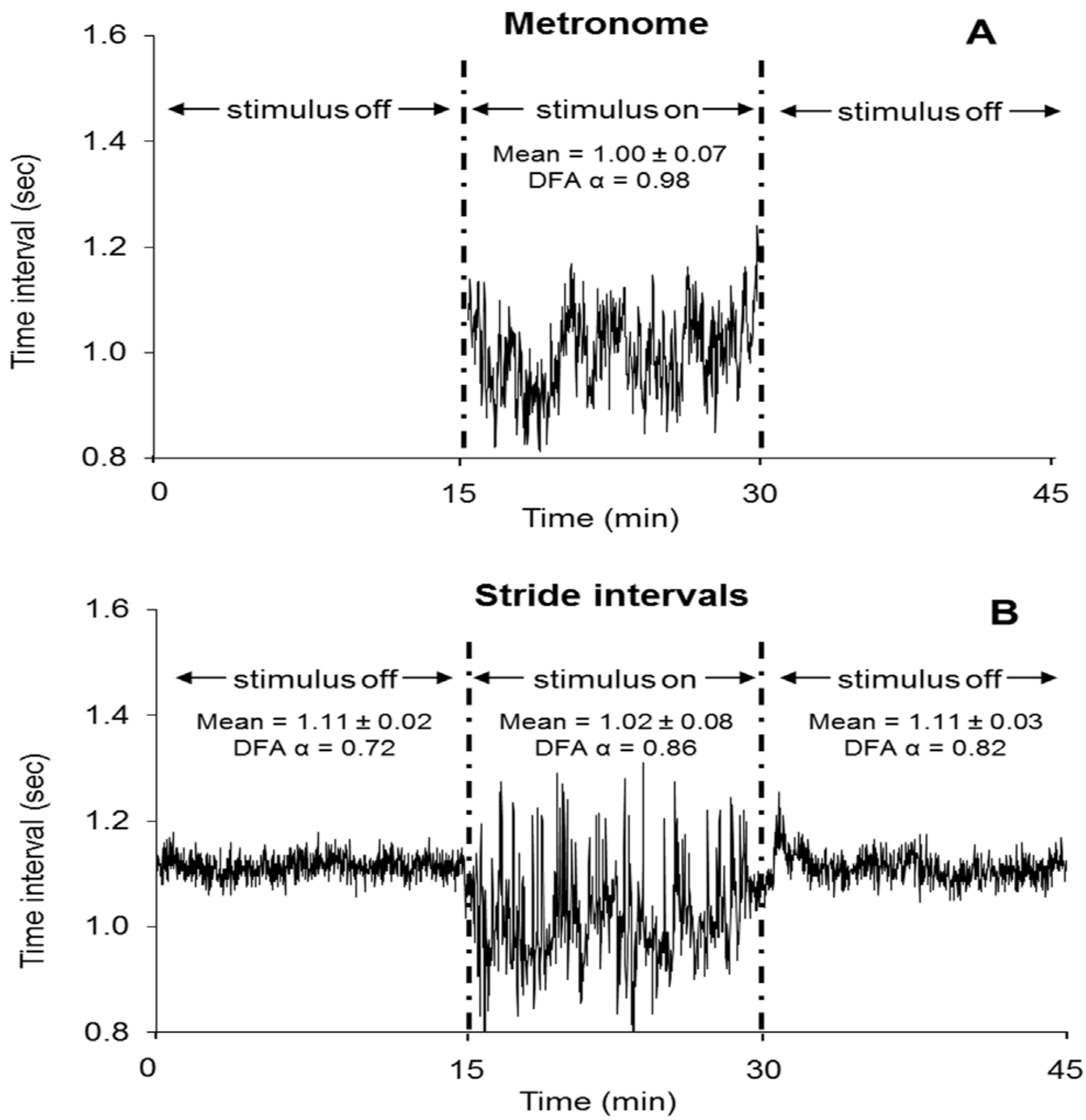
A logical extension of the Stephen et al. (2008) work was to determine if similar synchronization behavior occurred in gait. Some early studies employed an auditory metronome to modify locomotor timing behavior (Hove, Suzuki, Uchitomi, Orimo, & Miyake, 2012; Kaipust, McGrath, Mukherjee, & Stergiou, 2013). Hove et al. found that Parkinson's patients using the auditory metronome improved/increased the DFA α level within their gait pattern. A particular characteristic of Hove et al. that is important to our study is that it focused on overground walking. Rhea, Kiefer, D'Andrea, et al. (2014) used a visual metronome to more closely mimic the work of Stephen et al. (2008) to extend the research to gait. This was a proof-of-concept study to determine whether gait timing patterns that are not typically observed in young, healthy adults could be adopted when attempting to synchronize with a fractal visual metronome exhibiting either pink (i.e., persistent) or white (i.e., random) noise. The persistent metronome had a DFA α value of 0.98 and the random metronome had a DFA α value of 0.49. A flashing red box was used to give the subjects a visual cue to sync with the corresponding DFA α value. The subjects were instructed that every time the box flashed in front of them the right heel had to be in contact with the surface of the treadmill (Rhea, Kiefer, D'Andrea, et al., 2014). The subjects in this study demonstrated that they could indeed synchronize with a flashing metronome and the DFA α of their gait could be manipulated in a predicted manner. While all of the subjects did move along the continuum of DFA α, they did not perfectly synchronize with the metronome. Subjects were only able to get as high as 0.87 when the metronome was set at 0.98. When the metronome was set at 0.48 the subjects were able to get down to 0.60. A few postulates were put forth to potentially explain the lack of complete synchronization, which included how the stimulus was administered.

Rhea, Kiefer, Wittstein et al. (2014) conducted two experiments within the next study. The purpose was to not only determine that a fractal stimulus could be retained, but which type of visual stimulus could cause the most retention. The subjects were pushed in only one direction within this study. The persistent metronome was used due to the fact that most clinical populations demonstrate a more random or lower DFA α value than healthy individuals (<0.75). In line with the goal of creating an intervention for clinical populations, it was deemed best to push healthy individuals towards the persistent

(0.98) end of the spectrum. The idea was that if healthy individuals can be pushed towards persistence, then so could unhealthy populations.

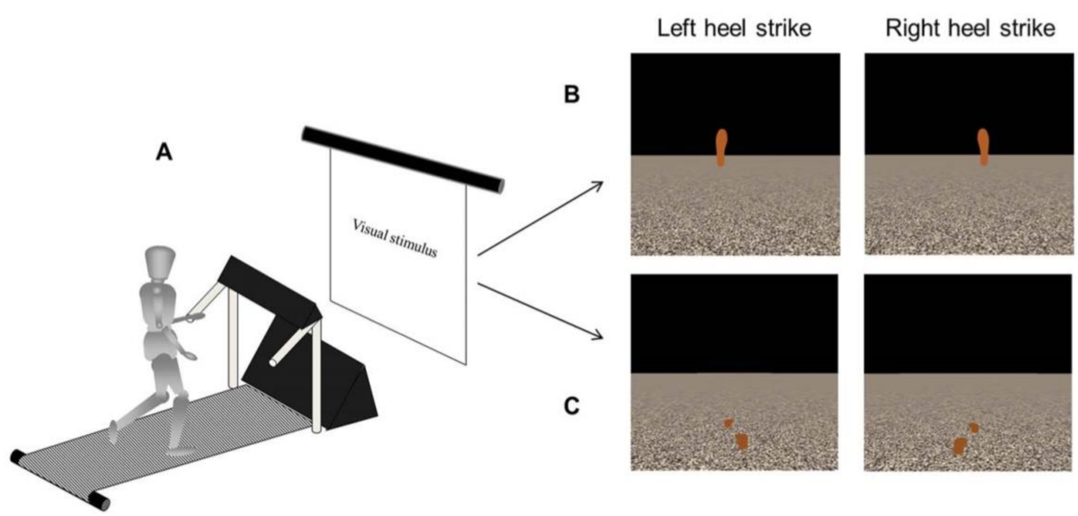
In experiment one, the subjects walked for 45 minutes continuously that consisted of three 15-minute phases. The first 15 minutes was at a self-selected pace without any visual stimulus (pre-synchronization phase). This 15-minute period would be considered the control for comparison in the second two phases. The second phase was the synchronization phase (sync phase) with the persistent visual metronome in order to push the individuals DFA α value towards 0.98. Lastly, the metronome was shut off for the third phase (post-synchronization) and the subject was instructed to walk normally again for 15 minutes. Experiment one demonstrated that the subjects walked with a significantly more persistent DFA in the post-synchronization phase than in the pre-synchronization phase, suggesting that 15 minutes of synchronizing to a fractal visual metronome leads to sensory motor reorganization of fractal gait patterns. These findings further bolster the findings of Hove et al. (2012), who showed that subjects were found to have significantly retained the DFA α value developed during training once the training had concluded. However, it should be noted in Rhea, Kiefer, Wittstein, et al. (2014) that the DFA α value achieved during training again fell short of the prescribed DFA α provided by the stimulus, which replicates the findings from Rhea, Kiefer, D'Andrea, et al. (2014). Figure 6 shows the time interval series of both the metronome itself (A) which is off during the first and last 15 minutes and the subject (B) whose patterns are displayed for all 45 minutes. The key aspect is to see how similar the patterns are for the subject in each 15-minute phase and how all of them compare to the pattern of metronome.

Figure 6. Time Series: Metronome and Subject. Adapted from Rhea, Kiefer, Wittstein, et al. (2014).



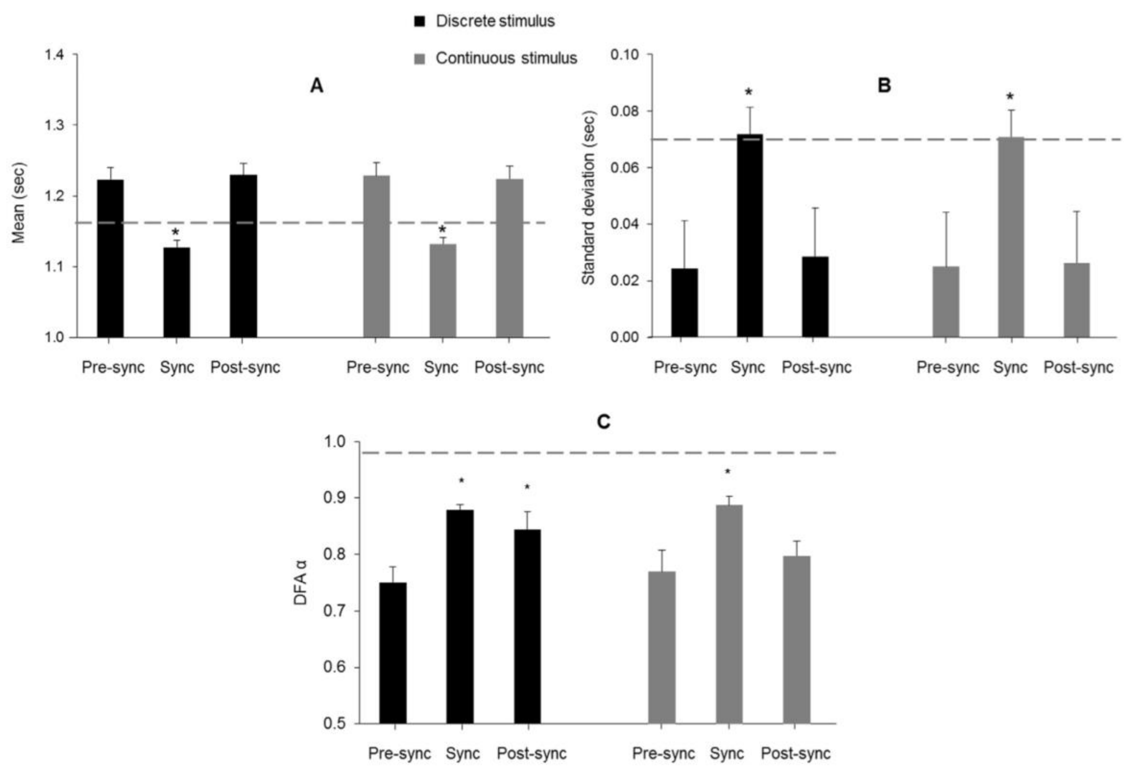
In experiment 2 of Rhea, Kiefer, Wittstein, et al. (2014), the researchers tested whether a fractal stimulus presented more continuously (explained below) would lead to a stronger synchronization and ultimately a higher DFA α value during the synchronization and post-synchronization phases. A series of left and right foot prints flashing at eye height of the subject was used as a discrete visual stimulus, which mimicked the stimulus used in experiment 1 of Rhea, Kiefer, D'Andrea, et al. (2014). Next, a continuous stimulus was developed that consisted of the same set of foot prints sliding down a virtual pathway that simulated how long each foot needed to be in contact with the ground. Figure 7 shows the how the visual stimuli in experiment 2 were administered.

Figure 7. The Treadmill Setup (A), Discrete Visual Stimulus (B) and the Continuous Visual Stimulus (C) used in Rhea, Kiefer, Wittstein, et al. (2014).



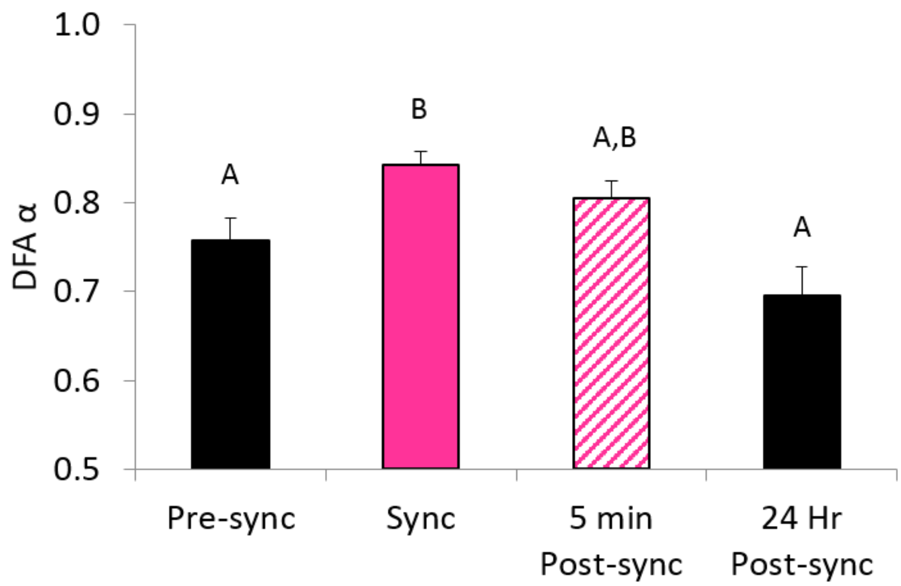
The key difference between the two set of foot prints was that the continuous set simulated the way the foot moved along the ground posteriorly while the other foot is moving anteriorly in the swing phase before heel contact. The footprint would disappear during the swing phase and reappear at the top of the screen at next heel contact. The same fractal pattern (DFA $\alpha = 0.98$) was used for the right foot print in both discrete and continuous with the left foot print appearing half way through each right foot phase. The fractal time series contained 500 data points that were bounded within 1.00-1.35 sec (mean 1.17 ± 0.07 sec). It was demonstrated that the difference between the discrete visual stimulus and continuous was not significant in terms of mean and standard deviation. However, with regard to the retention of the fractal pattern, the discrete stimulus did lead to higher retention than the continuous stimulus. Figure 8 shows the results from experiment 2 in Rhea, Kiefer, Wittstein, et al. (2014). The black bar graphs are referring to the discrete metronome and the grey bar graphs are referring to the continuous metronome. In graphs A (mean) and B (standard deviation) the discrete and continuous graphs are exactly the same. In graph C the pre-sync and sync are still the same but the post sync is where the main difference is seen. This is referring to the retention of the fractal gait that the subjects were administered while walking to the metronome in the sync phase. Because this was the main difference any study performed after with training to a visual metronome would be best suited to use the discrete metronome.

Figure 8. Mean (A), Standard Deviation (B), and DFA α (C) for Discrete and Continuous Visual Stimuli in Experiment 2 from Rhea, Kiefer, Wittstein, et al. (2014).



Rhea and colleagues followed up with a study to examine whether the immediate retention observed in Rhea, Kiefer, Wittstein, et al. (2014) was simply due to the continued rhythmicity of treadmill walking or truly due to neuromotor reorganization (LaJacono, Frame, & Rhea, 2015). To examine this, subjects (N=16) walked for 10 minutes at a self-selected pace during the pre-synchronization phase. Then the subjects were instructed to synchronize with the visual metronome for 10 minutes. The visual metronome produced right and left flashing footprints that exhibited a DFA α value of 0.98, just as in Rhea, Kiefer, Wittstein, et al. (2014). Immediately after the synchronization phase was over, the subject sat in a chair for a 5-minute wash out period. When the 5-minute rest was over the subject began the last 10 minute post-synchronization phase with no visual stimulus. Just as in the previous studies, DFA α was elevated during the synchronization phase. In the post-synchronization phase, DFA α declined to a level between the pre-synchronization and synchronization phases (Figure 7). This data indicates that even with a 5-minute wash out period the subjects retained some of the reorganized gait patterns from the fractal stimulus training. Since the DFA α value was not significantly higher from baseline to the retention phase, it suggests that there may be a dosage effect regarding the metronome training (sync phase) that wears off with time. Further, a subset (n=4) of the tested population was tested again after a 24-hour washout period and no retention of the fractal gait training was observed. That is, baseline gait behavior on day one and day two were not significantly different ($p < 0.05$).

Figure 9. Average DFA α Values for Each Phase.



These previous studies have shown that not only can subjects synchronize to a fractal visual metronome while walking on a treadmill, but that they will retain some of the metronome's variability after a 5-minute washout phase. Further studies are needed to examine that an individual can retain the metronome variability after long bouts of rest and that it can become entrained. There could possibly be a dosage affect leading to the retention of the fractal gait pattern. The next section examines factors related to neuromuscular training and retention that should be considered when developing a study examining the dosage effect of fractal gait training.

Dosage Effect on Neuromuscular Entrainment to a Visual Stimulus

Strength training is a form of neuromuscular gross motor movement training. In this thesis, I aim to use information about gross motor movement training to hypothesize what will happen when fractal gait training is provided over multiple days. The initial improvements seen within the first two weeks of any muscular strength training program are not due to change in the muscles but to change in neural recruitment (Deschenes et al., 2001). Neurons are learning to synchronize in order to produce a new movement. Rhea and colleagues have shown walking to a visual metronome does cause immediate and 5-minute retention, supporting the postulate of neural reorganization due to gait training (LoJacono et al., 2015; Rhea, Kiefer, Wittstein, et al. (2014). While there was some drop off in the performance after the 5-minute rest period, the DFA α values were still elevated above baseline. This shows that some retention is occurring. In a meta-analysis of the dosage effect within gait training Lohse points out, when treating stroke patients, more training is better and treatment type (visual cueing, auditory cueing, treadmill, overground, etc.) is not a determining factor (Lohse, Lang, & Boyd, 2014). This suggests that maybe after multiple training sessions with the visual metronome a significant retention may begin to develop. Within neuromuscular training there are four ways to change an exercise: frequency, intensity, time, and type. Since the type of gait intervention (visual cueing, auditory cueing, treadmill, overground, etc.) was demonstrated to be a non-factor by Lohse, the other three (frequency, intensity, and time) were left to be studied in terms of they affect fractal gait training. Frequency could be altered by having the subject train with the metronome over multiple days. Intensity could be altered but often this means cutting back rest periods or increasing the speed at which training occurs. Both of those options are not appropriate due to gait speed being self-selected by the subject and rest periods affect fatigue and retention. Time could be altered by having the subjects walk with the metronome for a longer duration in order to give them more experience with the metronome. To avoid confounding the effects of frequency, intensity, and time, I have elected to examine the influence of frequency (training over multiple days) for my thesis.

It has been suggested that it takes 300-500 repetitions to learn a new motor pattern and 3,000-5,000 repetitions to erase a former motor pattern and replace it with a new one (Schmidt & Lee, 2013). This suggests one could change his or her motor pattern even after long periods of moving a particular way. Thus, by increasing the frequency of fractal gait training to increase the repetitions, there is the possibility that the newly developed patterns could supersede the old patterns.

Clinical Motivations behind This Study

Since variability has become better acknowledged as a characteristic of gait that reflects adaptive ability and fall-risk, researchers have been looking at how pathologies translate to changes in gait variability. With Parkinson's disease, an increased stride variability has been shown to indicate a higher risk of falling (Frenkel-Toledo et al., 2005). The researchers used a treadmill to train gait rhythmicity compared to using a walker or free overground walking. They found that treadmill training reduced the variability in stride length causing the patients to become more stable while walking.

However, once the study was over it is undetermined if the subjects regressed back to their original DFA α levels. A study testing how one could cause retention of the new gait variability would help build the literature for a possible clinical intervention. Treadmill training in Parkinson's disease has been shown to increase gait speed, cadence, stride length and swing time. Frenkel-Toledo et al. (2005) suggests that not only do visual metronomes show favorable results with gait speed, cadence, stride length and swing time, but that visual and auditory metronomes to train internal cueing show promise as well. That is, these type of stimuli have the potential of favorably altering the internal mechanism of timing that leads to the observed gait characteristics (i.e., the response isn't a simple stimulus response behavior, but a reorganization of the mechanism driving the behavior). Both Frazzitta and Frenkel-Toledo, among others, agree that treadmill training with visual cues provides promising rehabilitation interventions for Parkinson's patients. Further, stroke is the number one cause of disability among older adults. Lohse et al. (2014) meta-analytic paper was designed to assess whether there is a specific amount of training that is required to improve the gait characteristics of stroke patients. In short, they were looking at dosage effect. The only difference between the control and experimental group was frequency and intensity of the treatments. Among the groups studied, the total time of therapy in the control groups was over half the amount of therapy time seen in the treatment groups (24 hours and 57 hours) (Lohse et al., 2014). Because time in therapy was the independent variable the differences seen between the control and experimental group would most likely be due to the time spent in therapy. Overall, the data suggests that there is a consistent dose response (more doses equal increased response) relationship between the time in therapy and improvement on clinical measures of function and impairment. Since the Lohse et al. (2014) paper was a meta-analysis, they included several different types of therapy. The authors found that type of treatment was not a significant factor in the dose-response relationship. This further supports the idea that changing the number of times an intervention is administered will add to the literature more than a study focused on the length of time in which the subject trains to a metronome in a single session. The findings of this thesis could help close the gap in understanding the amount of gait training needed to develop and retain a more adaptive gait pattern, which could then be extended to aging and pathological populations. However, it is important to first determine if an increased frequency in fractal gait training elicits the desired results prior to testing aging and pathological populations. Thus, this thesis will focus on a young, healthy population.

CHAPTER III

OUTLINE OF PROCEDURES

Participants

Twenty-three participants were recruited. The demographics and data from all participants is presented in Appendix A. However, four participants were shown to be non-responders to the training via an outlier analysis (see details below). The demographics for all participants included in the analyses (N=19) are presented in Table 1 of the manuscript. Participants self- reported that they did not have any neuromuscular/structural injuries or pathologies that cause abnormal biomechanics, and they must had normal or corrected to normal vision (glasses, contacts), and were not pregnant.

Instrumentation

Ambulatory Parkinson's Disease Monitoring or APDM (Portland, OR) movement hardware/software was used to record gait kinematics. Specifically, the Mobility Lab software from APDM was used with the three sensor set-up to record lower limb gait and balance kinematics. APDM sensors are a combination of accelerometers, gyroscopes, and magnetometer that are synchronized to derive gait and balance characteristics during static and dynamic movements. The three sensor set-up used for this thesis placed one sensor around the waist and one around each ankle, as prescribed by the APDM manual specific to Mobility Lab. Data are collected by each sensor at 1280 Hz and fused together to derive gait and balance characteristics using a patented procedure. Mobility Lab was chosen over other gait tracking technology due to its portability, reliability, and validity. The APDM Mobility Lab has been shown to be a valid (McConnell & Silverman, 2015) and reliable (Mancini et al., 2012) tool to measure gait kinematics. For example, no significant difference was found in the seven gait variables measured by GAITRite (a common gait assessment tool) and Mobility Lab (McConnell & Silverman, 2015). GAITRite and APDM are significantly matched in their ability to measure many important gait variables. a Pearson correlation analysis showed significant correlations between cadence (p<0.001), gait cycle time (p=<0.001), and double limb support % of cycle (p=0.026) (McConnell & Silverman, 2015). According to McConnell and Silverman, Mobility Lab may be the most suitable for both clinical and research use as it offers objective data combined with established clinical measures and more favorable usability factors compared to GAITRite.

While the APDM equipment is capable of recording a wide variety of gait kinematics (see Appendix B), stride time was the variable of interest for this thesis since the participants were asked to match their stride time to a visual metronome. Walking speed was also recorded with the APDM equipment to test for differences between treadmill and overground walking speed.

Procedure

On day one, participants first signed the consent form and then filled out a previous medical history questionnaire. For the gait testing and training, a pre-testing / training / post-testing design was used within each day, with each phase lasting for 10 minutes each day (30 total minutes per day). All three phases were completed in succession and the participants were asked to come seven days in a row to perform these three phases each time. The pre-testing phase consisted of walking overground around a 62m track in a gymnasium, which was used as a baseline every day. The training phase consisted of walking on a treadmill to the fractal visual metronome that was used in Rhea, Kiefer, D'Andrea, et al. (2014) (i.e., the flashing footprints). The post-testing phase concluded each day overground walking in the gymnasium (same set-up as the pre-test). The post-training phase was used as a within-subject measure for immediate retention of the metronome and compared to the next day's pre-test phase to test for 24 hour retention. The subject came in at the same time for all 7 days. A 30 minute period before or after the original start time was the accepted window for starting on subsequent days. For all days the participant was instructed to walk at a self-selected pace. The participants were asked to maintain a consistent speed in their overground walking throughout the days as best as possible with respect to the original directions. During the training phase, the subjects were asked to synchronize as best they could to the visual metronome in front of them. The visual metronome was displayed on a screen 2 meters in front of the treadmill. The timing of the visual flashes were set to a DFA α level of 0.98 or otherwise known as pink noise. Participants' preferred treadmill walking speed was measured prior to testing on day one and this speed was used for all treadmill training throughout the seven days. In order to obtain the preferred treadmill walking speed, the treadmill was started at 0 m/s and speed was incrementally increased until the participant verbally indicated that speed was their normal pace. Then, the participant was started at a speed which was too fast (2.0 m/s) and incrementally slowed until they verbally indicated that speed was their normal pace. If the two speeds were within 10% of each other, the average of the two speeds was set as the preferred walking speed. If there was more than 10% difference in the speeds, the participant completed the speed selection process again. With every subject the self –selection process never exceeded to attempts to obtain speeds within 10% of each other.

Data Collection and Analysis

Stride times from the APDM Mobility Lab were downloaded from the software and imported into Matlab (Mathworks, Natick, MA) where a custom script was used to compute DFA α for each phase and day. Further, cross-correlations were computed in Matlab comparing the sync phase each day to the time series prescribed by the metronome.

Although 23 participants completed the study, 4 participants were classified as non-responders to the training. The non-responders were identified as any participants who were more than two standard deviations below the group peak cross-correlation values on day seven on the training, indicating they were not able to synchronize with the metronome even after seven days of training. Appendix C shows the cross-correlation profile for all 23 participants (19 responders and 4 non-responders). Data presented in the manuscript are for the 19 responders.

To address hypothesis 1, two separate repeated measures ANOVAs were run on the cross-correlation data. The first one was run on the peak correlation for each participant across days in order to determine if their coupling to the metronome got stronger across the seven days. The second one was run on the standard deviation of cross coupling across participants across all time lags of interest (-20 to 20) to determine if participants were converging on a common coupling strategy across days. To address hypothesis 2, a three phase (pre-testing / training / post-testing) × seven day repeated measures ANOVA was used to examine DFA α changes across the study. Alpha was set at 0.05 for the ANOVA tests. For both hypotheses, significant ANOVA test were followed up with Bonferroni-corrected paired-samples *t*-tests to further probe the data to address each research question.

CHAPTER IV

MANUSCRIPT

Targeted for the journal Gait & Posture

Introduction

Intricate variability patterns evident within gait allow humans to adapt gait to environmental demands as needed, and these patterns exhibit a particular self-similar quality that has been termed fractal (Hausdorff, 1995). A consistent finding over the past two decades is that fractal patterns are present the gait of a young healthy adult, but aging or pathology can weaken the fractal patterns (Rhea & Kiefer, 2014; Stergiou & Decker, 2011). This weakening of the fractal gait patterns has been related to fall-risk (Hausdorff, 2007), so researchers have postulated that strengthening of fractal gait patterns may be a strategy to curb fall rates in at-risk populations (Manor & Lipsitz, 2013; Rhea & Kiefer, 2014). One way to alter fractal gait patterns is to provide a fractal stimulus to which participants could synchronize their movement.

Fractal synchronization research began with a finger tapping study (Stephen et al., 2008). Participants were asked to tap a key on the keyboard in synchrony with each flash on the screen in front of them. This visual stimulus acted as a visual metronome and it was set to produce fractal signals with varying strengths. This was the first paper to show that fractal patterns in human movement could be systematically altered using a fractal stimulus. A logical extension of this work was to determine if similar synchronization behavior occurred in gait. Some early studies employed an auditory metronome to modify gait timing (Hove et al., 2012; Kaipust et al., 2013). Rhea, Kiefer, D'Andrea, et al. (2014) used a visual metronome to more closely replicate and to extend their (Stephen et al., 2008) work to gait. This study showed that fractal gait patterns in young healthy adults could be either strengthened or weakened, depending on the structure of the fractal visual stimulus, during 15 minutes of treadmill walking. A key next question was whether the newly adopted fractal gait patterns would be retained after the training. Rhea, Kiefer, Wittstein, et al. (2014) showed that the new fractal gait patterns are indeed retained immediately after the 15 minute training, supporting previous work with an auditory stimulus (Hove et al., 2012).

While fractal gait training appears promising, it should be noted that the retention characteristics of this type of training are relatively unknown. For example, 15 minutes of training led to strengthened fractal gait patterns in the post-test immediately after the training, but the strength of the patterns began to drop back down to the pre-training levels after the post-test (Rhea, Kiefer, Wittstein, et al., 2014). In patients with Parkinson's disease a similar observation was reported in that while fractal patterns could be altered during training, 24 hour retention was not seen (Hove et al., 2012). In another study, four days of fractal gait training were shown to increase the strength of the fractal gait patterns, but retention was not assessed in this study (Uchitomi, Ota, Ogawa, Orimo, & Miryake, 2013). Thus, the effect of multiple days of fractal gait training on immediate and longer-term retention is unclear. Further, it is unknown whether fractal gait training on a treadmill transfers to overground walking, which is important to know not only from a motor learning perspective, but from a practical perspective in order to help identify the efficacy of this type of training for use in rehabilitation settings.

The purpose of this project was to determine whether fractal gait patterns are retained and transferred to overground walking when treadmill fractal gait training is provided to young healthy adults over seven consecutive days. Two hypotheses were examined. First, participants would exhibit a stronger coupling of their gait to the visual stimulus (i.e., a stronger training effect) with increased practice. Second, immediate retention (i.e., directly after training) and longer-term retention (i.e., 24 hours after training) would increase and be transferred to overgound walking as a function of increased practice.

Methods

Participants

Twenty-three participants were recruited. However, four participants were considered to be non-responders to the training and were excluded from analyses. Non-responders were defined as participants who were more than two standard deviations below the group peak cross-correlation values on the last day of training, indicating that they were not able to synchronize with the metronome even after seven days of training. Thus, data presented in paper are for the 19 responders (age: M = 22.0, SD = 2.47 yrs; height: M = 172.74 cm, SD = 11.14 cm; Male = 8; Female = 11). The demographics for the 19 participants are presented in Table 1. Participants did not have any neuromuscular/structural injuries or pathologies that might cause abnormal biomechanics, they had normal or corrected-to-normal vision (glasses, contacts), and they did not report being pregnant.

Instrumentation

Ambulatory Parkinson's Disease Monitoring or APDM (Portland, OR) movement hardware/software was used to record gait kinematics. Specifically, the Mobility Lab software from APDM was used to record lower limb gait kinematics. APDM sensors are a combination of accelerometers, gyroscopes, and magnetometers that are synchronized to derive gait and balance characteristics during static and dynamic movements. A three sensor set-up was used, with one sensor placed one inch above the bell button and on the front of each ankle, as prescribed by the APDM manual specific to Mobility Lab. Data were collected by each sensor at 1280 Hz and entered into the APDM software to derive gait and balance characteristics using a patented procedure. The APDM Mobility Lab has been shown to be a valid (McConnell & Silverman, 2015) and reliable (Mancini et al., 2012) tool to measure gait kinematics. While the APDM equipment is capable of recording a wide variety of gait kinematics, stride time was the variable of interest for this project since the participants were asked to match their stride time to a fractal visual metronome. Walking speed was also recorded with the APDM equipment to test for differences between treadmill and overground walking speed.

Procedure

On day one, participants first signed the consent form and then filled out a previous medical history questionnaire. Next, participants' preferred treadmill walking speed was measured and this speed was used for all treadmill training throughout the seven days. In order to obtain the preferred treadmill walking speed, the treadmill was started at 0 m/s and speed was incrementally increased by the researcher until the participant verbally indicated that speed was their normal pace. Then, the participant was sped up to a walking pace that was too fast (2.0 m/s) and incrementally slowed until they verbally indicated that the speed was their normal pace. If the two speeds were within 10% of each other, the average of the two speeds was set as the preferred walking speed. If there was more than 10% difference in the speeds, the participant completed the speed selection process again. All subjects were able to self-select a walking speed with no more than two tries.

For the gait testing and training, a pre-testing / training / post-testing design was used within each day, with each phase lasting for 10 minutes (30 total minutes of walking per day). All three phases were completed in succession each day and the participants were asked to visit the lab at the same time (±30 minute starting time each day) seven days in a row and perform these three phases each time. The pre-testing phase consisted of walking overground at their preferred walking speed around a 62m track in a gymnasium. The training phase consisted of walking on a treadmill while synchronizing their stride time to a fractal visual metronome. The post-testing phase consisted of overground walking in the gymnasium (same set-up as the pre-test). The post-training phase was used as a within-subject measure for immediate retention of the metronome and compared to the next day's pre-test phase to test for 24-hour retention. The participants were asked to maintain a consistent speed in their overground walking throughout the days as best as possible.

During the training phase, the participants were asked to synchronize their walking to the visual metronome that was displayed on an iPad directly in front of them (Figure 10). The visual characteristics of the metronome were identical to the one used in experiment 2 of Rhea, Kiefer, Wittstein, et al. (2014). In short, the visual metronome consisted of right and left footprints that flashed in the middle of a moving virtual environment. The timing of the appearance of the footprints was set to a strong fractal pattern (DFA $\alpha = 0.98$), with a mean stride time of 1.17 ± 0.07 sec (Figure 11). Participants were asked to be at right heel strike when the right footprint appeared and vice versa.

Figure 10. The Visual Metronome that was Provided on an iPad in front of the Participant.

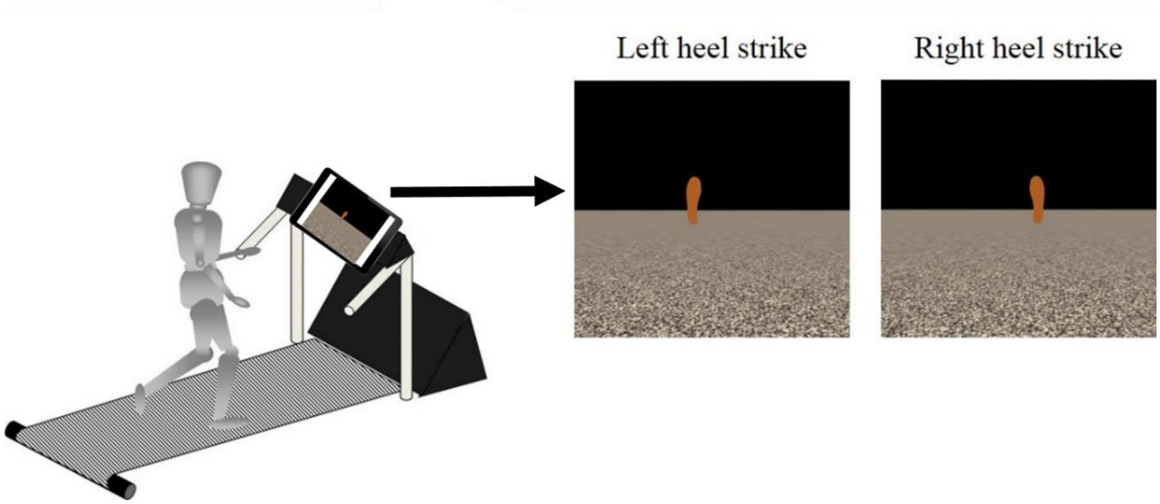
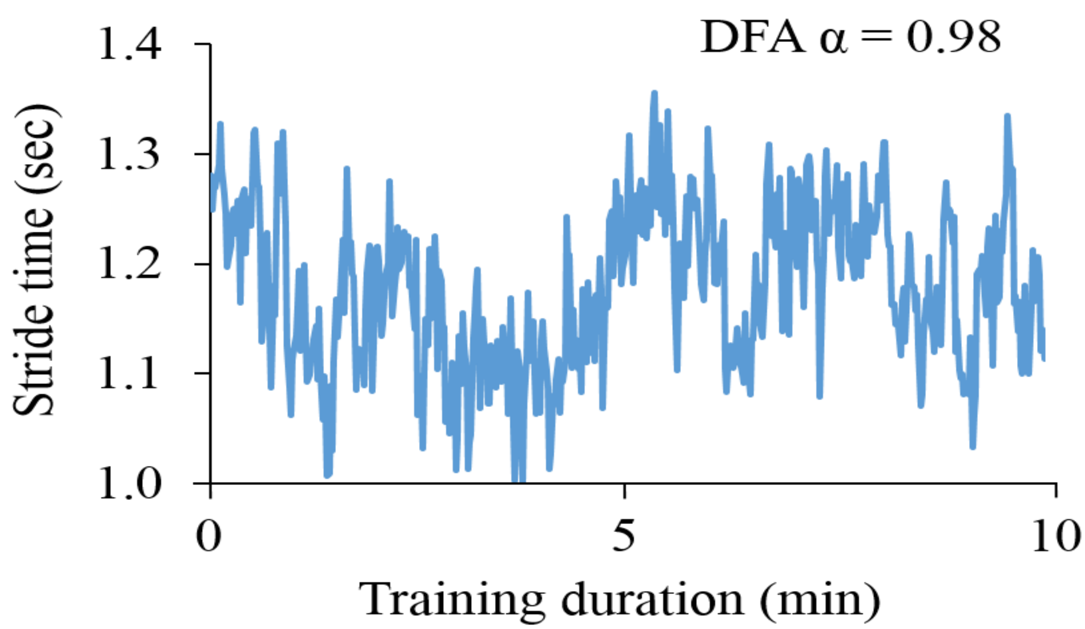


Figure 11. Fractal Time Series Prescribed the Stride Time Intervals for the Participant.



Data Collection and Analysis

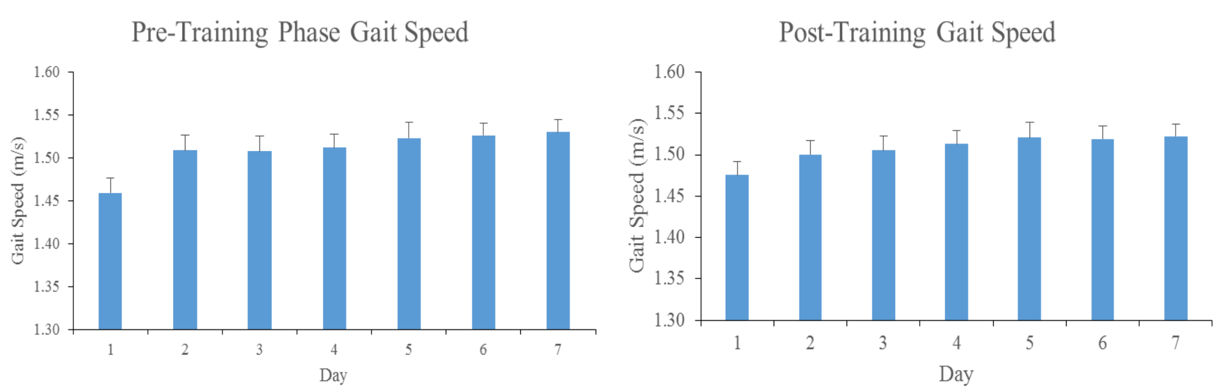
Stride time from the APDM Mobility Lab were downloaded from the software and imported into Matlab (Mathworks, Natick, MA). Fractal patterns were quantified using detrended fluctuation analysis (DFA), which provides a scaling exponent (α). DFA α for gait stride time series typically range from 0.5 (weak fractal patterns) to 1.0 (strong fractal patterns) (Hausdorff, 2007). A custom Matlab script was used to compute DFA α for each phase and day. Further, cross-correlations were computed in Matlab comparing the training phase of each day to the time series prescribed by the metronome.

To address hypothesis 1, two separate repeated measures ANOVAs were run on the cross-correlation data. The first one was run on the peak correlation, or how correlated the subject's steps were with the foot print metronome, for each participant across days in order to determine if their coupling to the metronome got stronger across the seven days. The second one was run on the standard deviation of cross-correlations between participants across time lag of interest (-20 to 20) for the seven days. The average number of steps the participant was ahead or behind the metronome's foot prints was plotted on the x-axis and determined the x coordinate of the peak correlation score. This was effectively a measure of bandwidth across the cross-correlation profile to determine if participants were converging on a common coupling strategy across days. To address hypothesis 2, a three phase (pre-test / training / post-test) × seven day repeated measures ANOVA was used to examine DFA α changes across the study. Alpha was set at 0.05 for the ANOVA tests. For both hypotheses, a significant ANOVA test was followed up with Bonferroni-corrected paired-samples *t*-tests to further probe the data to address each research question. A walking analysis was done to measure gait speed by day and phase to determine whether changed across training.

Results

In our walking speed analysis a phase × day interaction was observed for walking speed (m/s), $F(12,216) = 3.51$, $p = .02$, $\eta^2 = .16$. This interaction was driven by the observation that the training phase gait speed did not change across days (M = 1.28, SD = 0.07), but a slight increase was observed across days in the pre-training phase (day 1: *M* = 1.45, *SD* = 0.09; day 7: *M* = 1.53, *SD* = 0.08) and the post-training phase (day 1: *M* = 1.47, *SD* = 0.08; day 7: *M* = 1.52, *SD* = 0.07).

Figure 12. Gait Speed for Pre-Training and Post-Training Phases across Each Day.



Hypothesis 1: Participants would exhibit a stronger coupling of their gait to the visual stimulus with increased practice.

Cross-correlation profiles for each day are illustrated in Figure 12. A main effect of day on the peak cross correlation was found, $F(6,108) = 10.3$, $p < .001$, partial $\eta^2 = .37$. Follow-up t-tests indicated that the max cross correlation significantly increased from day 1 ($M = .56$, $SD = .22$) to day 2 ($M = .67$, $SD = .17$). No other significant changes across subsequent days occurred (all $p > .05$). With respect to the standard deviation across time lags, a main effect of day was found, $F(6,240) = 121.2$, $p < .001$, partial $\eta^2 = .75$. Follow-up t-tests indicated that the SD across time lags significantly changed with each successive day of training, generally decreasing (with the exception of comparing days 2 /3 and 6/7). Mean ±SD for days 1-7 listed in order: day 1 ($M = .12$, $SD = .06$), day 2 ($M = .08$, $SD = .04$), day 3 ($M = .10$, $SD = .05$), day 4 ($M = .09$, $SD = .05$), day 5 ($M = .05$, $SD = .03$), day 6 ($M = .04$, $SD = .02$), and day 7 ($M = .05$, $SD = .03$) (all $p \geq .004$).

Hypothesis 2: Immediate retention (i.e., directly after training) and longer-term retention (i.e., 24 hours after training) would increase as a function of increased practice.

DFA α values are presented in Figure 13. The phase × day interaction was significant, $F(12,216) = 2.38$, $p = .007$, partial $\eta^2 = .12$. This interaction was driven by the training phase across days, with DFA α generally increasing across the training. DFA α values for each day are as follows: day 1 (M =.81, SD = 09), day 2 (M = .86, *S*D = .06), day 3 (M =.88, SD =.06), day 4 (M =.88, SD =.05), day 5 (M =.90, SD =.05), day 6 (M = .90, SD =.05), and day 7 (M = .92, SD = .04). No changes in DFA α across days were observed in the pre-training ($p = .15$) or post-training ($p = .81$) phases.

Figure 13. Cross-Correlation Graphs. The Gray Lines Represent Each Participant and the Black Line is the Average among All Participants. Panels A-G Represent Days 1-7, Respectively.

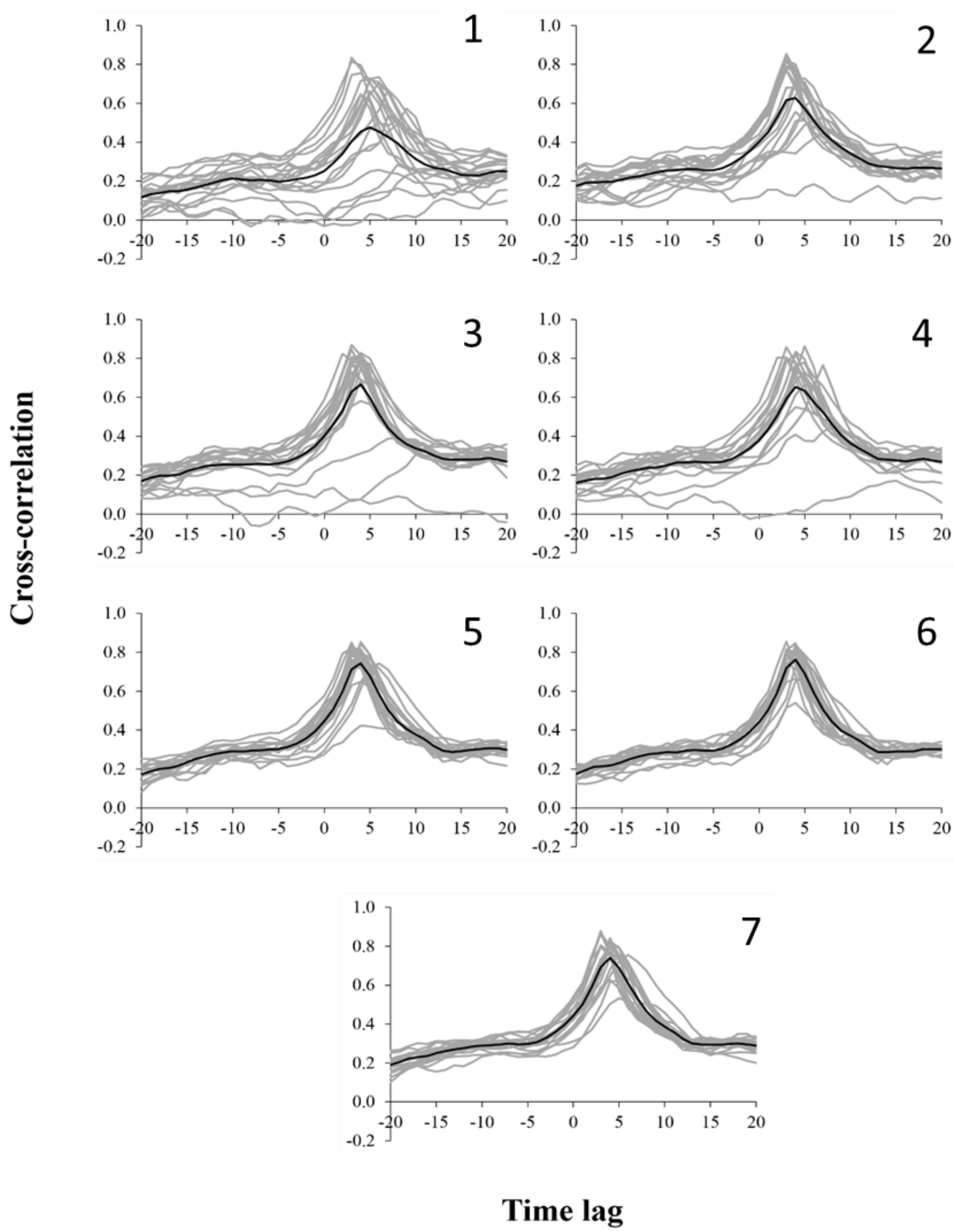
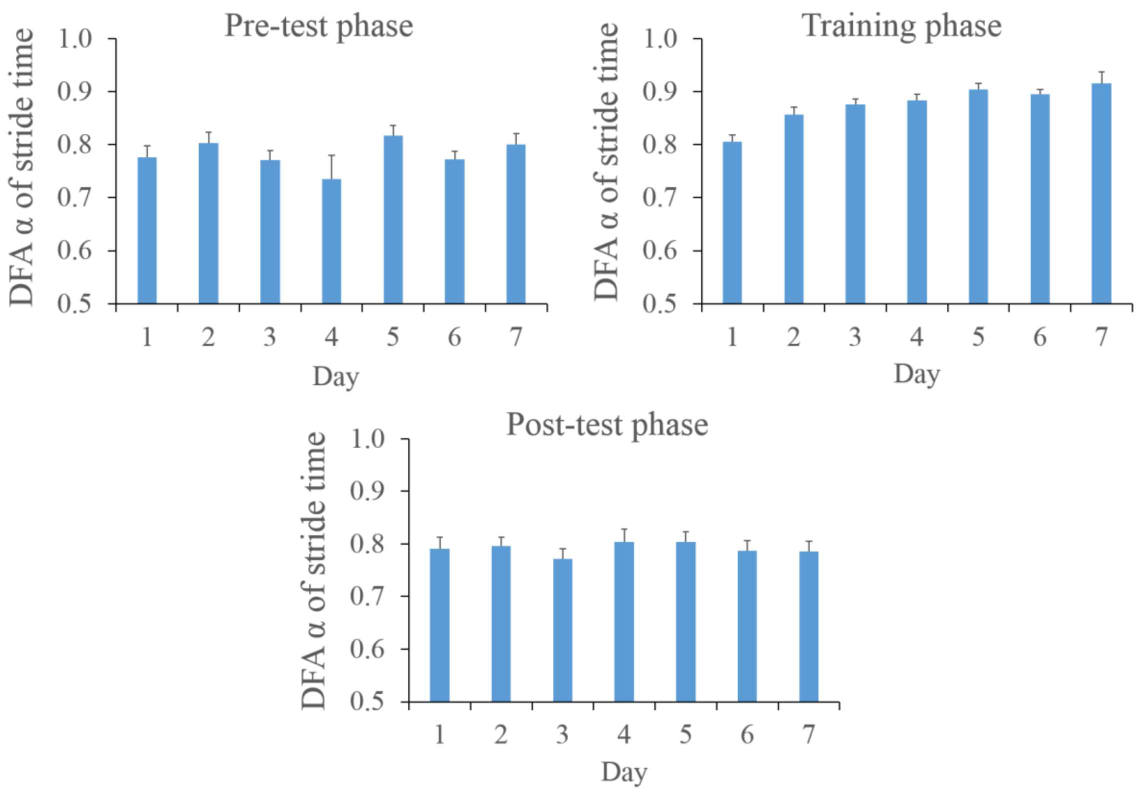


Figure 14. Average DFA α Values for Each Phase by Day.



Discussion

This purpose of this study was to explore whether seven days of training to a fractal stimulus will increase a person's ability to couple with that stimulus and to determine whether fractal gait characteristics are retained and transferred to overground walking following multiple days of fractal gait training on a treadmill. We found that participants did significantly couple better to the fractal stimulus after seven days of training, which supports hypothesis 1. Further, we found that there was no retention of the fractal stimulus either immediately following the training or 24 hours after the training, which does not support hypothesis 2. This study contributes to the literature by showing that fractal gait patterns can be strengthened by multiple days of fractal gait training. This study also demonstrates the need for further investigation of immediate and long-term fractal gait retention, and the transferability of these patterns.

We hypothesized that participants would show a stronger coupling with the stimulus after seven days of training, which was supported by both an increase in the peak cross-correlation within subjects across days and a decrease in the SD across time lags between subjects. The former suggests that participants were able to more tightly couple with the fractal metronome with training, while the latter shows that participants were converging on a common behavior with respect to their synchronization to the fractal metronome. This suggests that there may be a learning effect when training over multiple days to a fractal stimulus, supporting the work by Uchitomi et al. (2013). Further, these results are in line with what other gait training studies have found in that a higher dosage of training positively effects gait (Lohse et al., 2014). The results of our study suggest that subjects converged on a behavior that was synchronized with the fractal metronome. This suggests that the subjects became so familiar with the metronome across days that they began to anticipate when the metronome would flash, supporting the strong anticipation framework put forth by Dubois, Butz, Olivier, and Pierre (2003) and further explored by Stephen et al. (2008). Unlike previous work in this area, our data is the first to use a cross-correlation approach to examine how synchronization behavior to a fractal metronome changes over multiple days of training. Now that this profile has been used in young healthy adults, a similar approach can be adopted with clinical populations to outline the motor learning process using fractal stimuli.

For the second hypothesis, the results show that there was no immediate retention or 24-hour retention of the fractal gait behavior adopted during the training phase. This is inconsistent with Rhea, Kiefer, Wittstein, et al. (2014) where immediate retention was found when the participant stayed on the treadmill during the post-testing phase. LoJaccono et al. (2015) also showed immediate retention as well as retention after the participant sat for 5 minutes before getting back on the treadmill to begin the post-testing phase. In both studies, immediate retention was found when subject stayed on the treadmill. This suggests that there may be differences between the treadmill and overground conditions that are causing a disconnect between the training and post-training phases. Thus, fractal gait training may be context specific with respect to the training environment.

While there were many physical gait characteristics that were not significantly different between the overground and treadmill conditions, the data of the current study suggests that some differences exist, otherwise retention would likely have been observed, as shown by previous work in this area. For example, a treadmill provides a smaller ground reaction force than overground gait (White, Yack, Tucker, & Lin, 1998). A smaller ground reaction force may lead to less salient feedback about foot position during the gait cycle, so a task learned on the treadmill may not be transferred to overground gait due to different ground reaction force profiles. Further, the continuous belt of the treadmill propagates a movement that is outside of the body. The treadmill will not stop even if the subject does. This continuous movement may cause a sensory difference between the two conditions. Also, the self-selected gait speed may have been different enough during overground gait to contaminate any learning that occurred on the treadmill. Previous work has shown that DFA α of stride time intervals does change with different gait speeds (Jordan et al., 2007) so not precisely controlling for different walking speeds on the treadmill and overground may have influenced our results. If the day one pre-training gait speed was sued for the speed in the treadmill training phase this effect may have been nullified. Overall, our data suggest that fractal gait training on a treadmill may not a plausible mechanism for altering fractal gait characteristics overground. Future studies should focus on using overground walking during all testing/training conditions in order to see if the immediate and/or 24 hour retention improves as a function of the environment. Future studies could also adopt an auditory metronome, as it will provide a more feasible way of administering a fractal metronome while walking overground.

In conclusion, this study shows that with more training a participant can more strongly couple to fractal metronome. This study also shows that there is much more to learn about gait training to a fractal stimulus. With the end goal of a gait intervention for those at higher risk of falling, an intervention that incorporates the dosage effect observed in this study and an appropriate fractal stimulus that can lead to retention will potentially be the a highly effective tool for clinicians and physical therapists alike. Future studies should focus on using overground gait during testing/training. Further, future work should also determine whether the intensity and duration, in conjunction with the frequency, of fractal gait training influence motor learning and retention.

CHAPTER V

DISCUSSION

The literature regarding fractal gait training is fairly new within the realm of gait training in general. Nonetheless, it has been established that both fine and gross motor movements can be entrained to a fractal stimuli and that subjects can be moved up and down the spectrum of DFA α scores. As the literature on fractal gait increased a possible training intervention gap began to form. The overall goal of creating a way for the aging and pathologically impaired to regain adaptive gait became more than theoretical.. Currently, fractal gait training presents a plausible method for potentially reducing fall risk. However, it is important to understand the motor learning and retention characteristics in a healthy population prior to deploying this training to a clinical population.

This study builds upon the previous research by Rhea and colleagues that explores the use of a discrete fractal metronome to train subjects to walk with a new fractal gait pattern. This study showed that participants more strongly coupled to the metronome after multiple days of training, but the newly developed fractal gait patterns were not transferred to overground. The data adds to the postulate of Lohse et al. (2014) that the frequency of training is the most influential on gait. It also adds to the literature on a fractal stimuli showing that a training effect exists, which has never been shown in young health adults before. Lastly, this study suggests that changing the environment between the training and retention phases may hinder the retention that was demonstrated in previous studies in this area.

Next, benchmarks need to be established so researchers can predict retention of a fractal stimulus with a relatively high level of certainty for healthy individuals. If factor associated with retention can be better understood, then determining how long the new behavior persists before the effects of training begin to diminish will be important to note. As we move forward, the ability to capture gait kinematics wirelessly and remotely will help future research from being constrained to labs and research buildings. Improvements in technology will help researchers collect information about moving around overground in the real world and less time will be spent deciding whether treadmill data is generalizable to the everyday environment. Further studies are needed to test smartphone accelerometers and other portable devices in order to determine their validity in recording and probing fractal gait training.

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APPENDIX A

DEMOGRAPHICS FOR PARTICIPANTS WITH OUTLIERS

Table 1. Demographics (mean $\pm$ SD) for All Participants who Completed the Study (N=23).

Age (yrs)	**Height (cm)**
22.39 ± 2.54	172 ± 10.30

APPENDIX B

APDM MEASURES

Table 2. All Data that was Recorded with the APDM System. Only Stride Time was Analyzed Due to the Research Questions Posed in this Thesis.

Data derived from each limb individually	**Variables derived from both limbs**
Stride length (m)	Stride time (sec)
Stride velocity (m/s)	Percent of time in double support phase (%)
Percent of time left limb is in swing phase (%)	Percent of stride length asymmetry (%)
Percent of time right limb in swing phase (%)	
Percent of time left limb in stance phase (%)	
Percent of time right limb in stance phase (%)	
Shank range of motion (deg)	
Knee range of motion (deg)	

APPENDIX C

CROSS-CORRELATION GRAPHS WITH NON-RESPONDERS

Figure 15. Cross-Correlation Graphs with the Responders (N=19) and the Non-Responders (N=4). The Four Non-Responders are the Four Participants at the Bottom of Panel 7 that Hover Around Zero for All Time Lags.