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THE EFFECT OF METRONOME PACING ON GAIT IN HEALTHY SUBJECTS

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The effect of metronome pacing on gait in healthy subjects

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Summary

The complex process of gait is rendered partially automatic by central pattern generators (CPGs). To further our understanding of their role in gait control, we adapted the paradigm of anti-phase, or syncopated, timing from research into simpler movements performed to an auditory stimulus. This project compares in-phase and anti-phase gait in healthy subjects. To provide a context for our results, it was necessary to review the literature on in-phase gait and summarize the findings. An overview of its effect on the gait of healthy subjects has not previously been conducted, although metronome-paced gait is used for rehabilitation and investigating gait timing.

Briefly, the review results are as follows. Auditory cueing increased step/stride rate in four out of five studies with older subjects, but in none of the three with younger subjects. Stride rate variability decreased in the two studies with young subjects who were instructed to synchronize to the beat, perhaps because the metronome's cue acted as a temporal 'anchor point' for each step. However, the single study reporting this measure in older subjects found an increase. Step width increased in half of the treadmill studies, but none of the overground ones, suggesting a cumulative effect of the attentional demands of synchronizing gait while on a treadmill. Time series analysis of gait parameters revealed that cueing usually decreased the long-range correlations. The α exponent was the most sensitive parameter reported, decreasing toward anti-persistence in almost all cued-gait studies (including two in which subjects were not instructed to coordinate their steps with the beat). These results confirm that simply synchronizing to a metronome disrupts normal gait patterns, although the mechanisms and their interactions still need to be elucidated. The research phase of the project compared in-phase (IN) and anti-phase (ANTI) gait. We expected gait to be less disrupted during ANTI trials at preferred speed, when the facilitating effect of CPGs would be strongest. We also hypothesized that these trials would be more difficult for older subjects. The measures step time variability, jerk index, and harmonic ratio quantified gait perturbation, while the time difference between beat and heel strike was used to quantify how well the appropriate temporal relationship was maintained for the two conditions.

Unsurprisingly, achieving anti-phase gait proved more difficult than in-phase for both groups. However, none of the measures indicated that is it less challenging at preferred walking speed. Furthermore, the gait of older subjects was no more perturbed than that of younger subjects; in fact, the former seemed to walk much less awkwardly in the ANTI trials. Exit interviews suggested they were also much more optimistic about their performance. Performance measures, however, revealed that when older subjects successfully matched the pace of the beat, they unwittingly synchronized to it. They were unable to time their steps to occur between beats. Thus the temporal relationship of their steps to the beat was the same in the IN and ANTI conditions. Younger subjects, who visibly struggled more during ANTI trials, were able to walk in syncopation. This

result suggests not only that cognitive resources beyond those available to the older group are required to successfully resist the synchronizing pull of the beat, but also that awareness of their poor performance was unavailable to them.

While it is not at all clear that CPGs per se were involved in this age-related difference, it is nevertheless also clear that this study has produced new insights into the workings of gait control. Why is this search for specific evidence of CPGs important? Although CPGs certainly exist, and contribute to human locomotion, in many respects they remain inside a ‘black box’. Their interaction with conscious control is complex, and little is known. For populations at risk of falling, particularly the frail elderly, understanding how these neural circuits work (and cease to work) will eventually help us exploit them to improve and maintain mobility-- and independence, and quality of life. To this end, research that sheds light on these obscure neural circuits is worth undertaking.

Introduction

In this thesis I investigate a particular type of rhythmic movement, gait, under the novel condition of anti-phase movement, in which subjects step at the same velocity as a steady auditory cue, timing each step so that the heel strikes the ground exactly midway between two beats. First, relevant previous research is presented, to provide a background of what is known about human timing and motor control generally, and gait specifically. The methods and instrumentation which have been used are evaluated. Second, a review of the 'state of the art' of in-phase, metronome-paced gait facilitates an informed understanding of the anti-phase gait protocol. Third, the anti-phase gait project is presented. Finally the implications of this work are discussed. In addition to calling attention to what we can learn about the role of central pattern generators (CPGs) in gait, consideration of future work emphasizes the role that metronome-paced paradigms can play in increasing our understanding of gait control mechanisms, with the goal of developing methods to preserve or restore functional gait and the concomitant quality of life.

The initial research question was 'Is anti-phase gait possible?' However, it would be simplistic to say that such a general question is not likely to yield any new information of value. Certainly the immediate relevance of a reply may not be clear; after all, there are plenty of ways to make gait challenging for people without asking them to walk precisely opposite the beat, if general rehabilitation is the goal. There are also plenty of simpler ways to quantify people's ability to handle attentionally demanding tasks while walking.

The hope has been to identify some aspect of anti-phase gait that indicates a facilitating influence of CPGs. CPGs are considered to facilitate even non-standard gait-related movements such as obstacle avoidance (Lacquaniti et al. 2012) and backward walking (Thorstensson 1986). Moreover, healthy, mature humans are certainly highly trained at walking at their normal pace, which is partly determined by CPGs (West and Scafetta 2003, Yakovenko et al. 2005). Clearly, since we are deducing an influence of CPGs in humans indirectly, their role can only be indicated when other known influences fall short of explaining specific results. To this end it is necessary to consider all of these possible influences. Gait is complex, and so are we; a null hypothesis that all differences between in-phase and anti-phase gait are due to factors such as attention or anchoring would, hopefully, serve to highlight some other, less easily explained difference.

Chapter One

Background

Rhythmic movement has been studied in a variety of contexts. Foremost among them have been: a) neurophysiology research, from functional studies to brain activation studies using functional magnetic resonance imaging (fMRI), positron emission tomography (PET) and scalp surface electroencephalography (EEG) to better understand cognitive timing mechanisms during rhythmic movement; b) motor control research to investigate how we activate, and control, rhythmically consistent movements; c) rehabilitation research; and d) gait research in healthy subjects and patient populations.

Neurophysiology

Research has sought to locate the structures responsible for motor control and rhythmic timing, and understand exactly how they lead to functional, coordinated movement. This vast topic was approached from the specific viewpoint of pathology. Historically, many important advances have been made by comparing functional deficits in patient populations with specific brain anomalies.

The basal ganglia (BG) are a heterogeneous group of nuclei at the base of the forebrain that form a complex structure, richly connected to the cortex and thalamus, among others (see Figure 1).

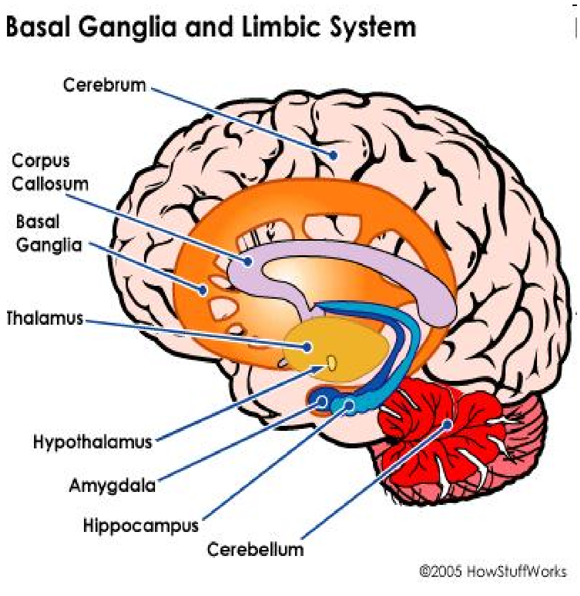


Figure 1 Basal Ganglia

Parkinson's Disease (PD) is a degenerative disease that attacks the basal ganglia (BG). Because movement disorders are frequently the most salient feature of the disease, the BG were initially considered to be involved primarily in motor control. We now know that they are important for many disparate functions, from memory and learning to attention, planning and reasoning (Stocco et al. 2010). Figure 2 demonstrates how the inhibitory and excitatory effects of the BG are affected in PD.

Green arrows- excitatory (+) glutamatergic pathways
Red arrows- inhibitory (-) GABAergic pathways
Turquoise arrows-dopaminergic pathways, excitatory (direct pathway) and inhibitory (indirect pathway)
Note that disinhibitory pathways are excitatory on the feedback to the cortex, while dis-disinhibitory pathways in effect are inhibitory.

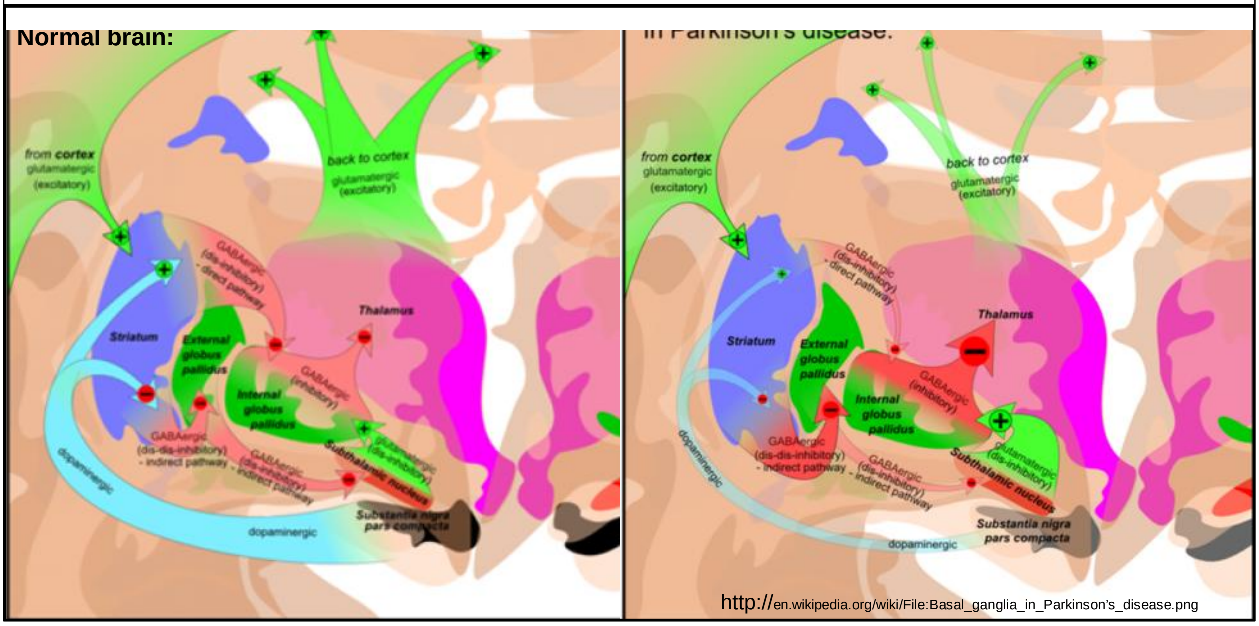


Figure 2 BG pathways: normal (L) & PD (R)

It is known, furthermore, that the BG play a role in executing rhythmic movements, specifically when they're syncopated, or anti-phase (Mayville et al. 2002). Byblow and Stinear (2006) reported that "syncopation with respect to a regular external beat requires greater excitability of inhibitory networks that impact upon the involved muscle representation, than the more stable synchronisation pattern." Ivry and Spencer propose a gated threshold model, in which the BG, intrinsic to decision-making processes, functionally inhibit signals which do not exceed the threshold at a given point in time (2004). With BG atrophy, decreased dopamine production raises the threshold, and motor control is compromised. Allen and McKinnon found that PD patients with impaired rhythmic movement ability also displayed abnormalities in the accompanying oscillatory neural signals (2010). Similarly, PD patients were worse at synchronized finger tapping, and demonstrated increased inhibitory activity of the pallidum, when 'off' their dopaminergic medication (compared to 'on'); increased cerebellar activity suggests that the timing tasks were executed, albeit less well, by this structure. Thus the movement impairments in PD are partly central in origin.

BG are involved in many neural pathways, comprising both excitatory and inhibitory feedback loops connected to a multiplicity of other brain structures. Even in healthy aging, brain structures may display some dysfunctional changes. There is evidence that impairments seen in PD patients are echoed in the healthy elderly (Beste et al. 2009). Thus we can expect that highly challenging timing tasks may highlight deficiencies in elderly subjects similar to those we would see in pathological populations.

While PD suffers struggle with balance and gait (Hausdorff 2009, Bovonsunthonchai et al. 2013, Paul et al. 2013), as we have seen the BG are not specific to gait or even movement. In contrast, CPGs are specifically involved in rhythmic repetitive movements, with locomotion being the primary example. In fact it is not unreasonable to suggest, in line with Takakusaki (2013), that CPGs are responsible for automatic gait patterning, while the BG play a role in gait when conscious attention is allocated, as when gait is initiated, when corrections need to be made or when conditions become more challenging.

Rehabilitation studies

Metronomes have been extensively used in gait research and rehabilitation. Walking in time to the beat, has been shown to restore-- or at least improve-- patients'abnormal gait parameters by reducing gait variability (Stegemöller et al. 2009; Thaut et al. 1996) and increasing gait speed (Howe et al. 2008) in persons with Parkinson's disease (PD), and increasing gait symmetry in stroke patients (Roerdink et al. 2011). These improvements are thought to increase stability and equilibrium, promoting independent living and quality of life (Hausdorff et al. 2007).

Simple movement studies

Although many types of paced movement have been studied, finger tapping is the most common, and is the only one that will be considered here. Compared to unpaced tapping, paced tapping is less temporally variable (Sasaki et al. 2011), due to an effect known as 'anchoring': the steady beat provides a strong reference point for a repetitive movement, reducing variability (Beek 1989, Byblow et al. 1995, Roerdink et al. 2008). The effect is particularly strong when the beat coincides with a salient reference point (Byblow et al. 1995), which in finger tapping is making contact with the tapping surface. Curiously, tapping is also jerkier when it is synchronized to a beat, which Balasubramaniam et al. (2004) attribute to the fact that the movement is being consciously manipulated and corrected to conform to the timing.

As is typical of successfully synchronized movements, in finger tapping the tap slightly precedes the beat (Repp 2011, Madison and Merker 2004, and Balasubramaniam et al. 2004) although the tapper perceives them as occurring simultaneously. The reason for this time lag is not entirely clear, but it has been attributed to different processing times for the different sensory modalities involved (Repp 2011). This phenomenon is known as negative asynchrony or negative phase shift.

Studies exploring anti-phase finger-tapping have found that temporal variability is higher for anti-phase than in-phase, although jerkiness is unchanged (Balasubramaniam et al. 2004).

Furthermore, untrained subjects cannot tap in anti-phase faster than approximately 1.7-2 Hz without transitioning to in-phase tapping (Repp 2005, Byblow and Stinear 2006). According to Ko et al. (2011), typical step frequencies are 1.83 Hz for men and 1.88 Hz for women, suggesting that it may be impossible to perform such a difficult task as walking in anti-phase since the pace is already equivalent to a challenging anti-phase tapping pace.

We hypothesized that, like anti-phase finger-tapping, anti-phase gait is possible but difficult, and would be more temporally variable, jerkier, and less consistent than when performed in time with the beat. We further hypothesized that due to the facilitating influence of CPGs, anti-phase gait would be less perturbed at preferred speed than at other speeds.

Chapter Two

Review of Metronome-Paced Gait

The contents of this chapter have been submitted for publication: Mayberry KJ, Hausdorff JM, Chiari L, "A systematic review of the effect on gait of auditory cueing", Hum Mvmt Sci.

Introduction

Bipedal gait has long been acknowledged as a form of locomotion that, while deceptively simple and repetitive, is also complex and malleable. Walking typically requires almost no conscious attention, and can be described as simply putting one foot in front of the other. Nevertheless, toddlers making their first steps may fall if they are suddenly distracted, and even adults engrossed in conversation may slow their pace to devote more mental energy to the discussion. As gait research has probed the mechanisms of our uniquely human form of propulsion, we have learned that gait is partly automatic, in that it is apparently partly controlled by subcortical neural networks known as central pattern generators (CPGs). This automaticity was dramatically demonstrated by Dimitrijevic's 1998 study in which electrical stimulation of the spinal cord in paralyzed subjects elicited a primitive gait. However, gait is also consciously controlled. It requires attention and utilizes corrective feedback whenever necessary, as when conditions are non-ideal. These two processes, one occurring without conscious control and one specifically comprising cognitive mechanisms, are strongly inter-related. Moreover, young, healthy subjects have attentional resources in abundance to allocate to both processes (Yogev et al. 2005). Thus the properties of each process usually reveal themselves only when something goes wrong. This situation is common in pathologies, or when the system is overloaded, such as during dual task conditions. Cognitive mechanisms may also be revealed in healthy older adults, when less attention is available even while more attention may be required due to growing physical limitations.

Current research seeks ways to examine gait, often by breaking down the processes or challenging the system itself. This is where auditory cueing plays a role. Numerous studies have explored how gait is affected by auditory cueing, which can be defined as a beat (usually at a consistent tempo) with which footsteps are to be synchronized. Generally, this research can be divided into two types. Some studies investigated the mechanisms of motor control of gait using cueing, and others applied the cueing paradigm as a rehabilitative technique. By far, the majority of work has been accomplished in the latter area. For example, auditory cueing has been shown to help restore gait symmetry in stroke patients (Thaut et al. 2007). Its use is also associated with gait improvements in movement disorders, such as cerebral palsy (Kwak et al. 2012), and neuro-degenerative diseases, such as Parkinson's disease (Hausdorff et al. 2007, Lim et al. 2005, Rochester et al. 2005), and Huntington's disease (Thaut et al. 1999). Interestingly, its benefits for dementia patients are not clearly documented; Wittwer et al. recently reported detrimental effects of cueing on patients with Alzheimer's disease (2013a). However, there is evidence that healthy older adults can benefit from this type of rehabilitation, an important consideration since this population may be at risk of falling as their gait becomes increasingly unstable (Sheridan & Hausdorff 2007). As efforts continue to identify those most at risk, rehabilitation programs are being developed to restore or maintain healthy gait patterns. There is reason to believe that these programs increase stability during activities of daily living, reducing the risk of falls with all the attendant complications and comorbidities (ibid.). Auditory-cued gait frequently plays a part in such programs.

The first avenue of scientific exploration mentioned above seeks to learn more about how gait is controlled and how it is disturbed. If a person walks at a comfortable pace, does a steady beat at the same rhythm have an effect? One obvious difference between cued and uncued gait is that the former is a dual task paradigm, since the subject must not only walk but time his step to the beat. Possible effects could be due to attentional considerations, either the increased cognitive challenge of divided attention or the decreased cognitive load due to facilitation; or more specifically, due to the externally generated rhythm which might entrain, or interfere with, normal locomotor patterns. Clearly identifying the ways in which cueing affects gait could yield insights about subcortical CPGs and attentional mechanisms, which in turn could lead to the development of more effective rehabilitation techniques, for example to improve stability in the frail elderly at risk of falling.

Interestingly, few comparisons have been made between cued and uncued gait in healthy populations. Furthermore, the results of the studies that do exist have never, to our knowledge, been considered in their entirety or subjected to rigorous examination, since many of the studies included healthy subjects for control purposes only. The aim of the present review is to fill that void by presenting the findings of a literature search, with the primary objective of ascertaining what is known about the effect of auditory cueing on gait in the absence of pathologies or other complicating factors.

One such factor would be varying gait speeds: to keep the paradigm simple, we evaluated only preferred or 'natural' gait speed. This speed generally requires minimal energy expenditure (Zarrugh & Radcliffe, 1978) and manifests a compromise between optimal mechanical power and mechanical efficiency (Umberger & Martin, 2007). Walking at this speed is typically more stable and adaptable (Jordan, Challis, & Newell 2007) and more consistent, exhibiting a higher harmonic ratio (Brach et al. 2011). Additionally, natural gait in healthy subjects requires a minimum of attention, particularly for maintaining gait rhythmicity and stride variability (Yogev et al. 2005). By selecting only those studies evaluating unconstrained gait, we are maximizing the automaticity of the natural gait patterns in the uncued condition.

Methods

The following online databases, PubMed, Web of Science, CINAHL, Cochrane, PEDro, and MedLine, were searched, with the following terms: 'metronome gait', 'rhythmic auditory gait', 'cueing beat gait', 'cued gait', and 'timing auditory gait'. Figure 3 illustrates the selection process. Searches were conducted, with the help of an experienced librarian, between April 4 and April 10, 2013.

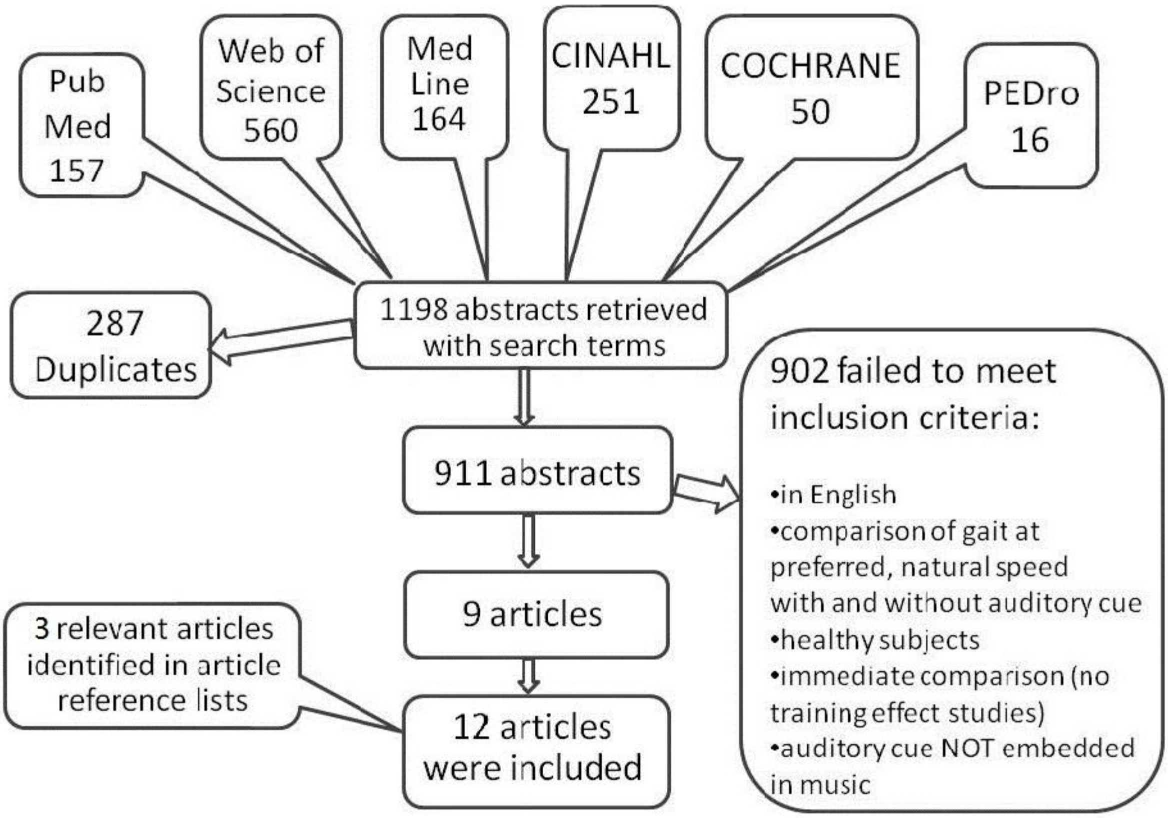


Figure 3 Results of literature search

The primary requirement for an article was simply that it compared the two conditions: human subjects first walking naturally without any constraint or cue, and then walking to an auditory beat which matched their cadence as determined by the first condition. Two studies without explicit instructions to synchronize were also included, as will be discussed later. A number of cued gait studies were excluded because the step speed used was either held constant for all subjects, or deliberately set to a velocity higher or lower than each individual's preferred speed. Similarly, a number of studies used cued-gait paradigms which manipulated the metronome timing instead of holding it constant. Their research focus varied from recovery response after rhythm perturbation (Roerdink et al. 2009) to training effects in both healthy and pathological populations (Hill et al. 2011, Johansson et al. 2012). Some studies switched from a cue triggered by a metronome to a cue triggered by previous steps in a feedback loop (Baram & Miller 2007).

Since we are specifically interested in quantifying gait differences related to the cued and uncued conditions at a constant tempo, these studies which varied the beat were excluded. Those which only reported learning effects were also excluded. Additionally, works had to be written in English, and subjects had to be healthy, since we were seeking to establish the effects of attending to a beat while walking on a population that does not have impaired attention or other pre-existing conditions. In this state, the automaticity and efficiency of gait would putatively be optimized, and the attentional requirements would be minimized. Most of the excluded articles involved subjects who were impaired in some way, whether by disease (such as Parkinson's or Alzheimer's) or trauma (such as stroke or amputation). Articles for which the rhythmic cues were embedded in music, either played live or digitally manipulated to provide the appropriate tempo for each subject, were also excluded, as were papers that provided the cueing via another sensory modality (e.g., touch, vision).

Results

From the more than 1,200 titles that were retrieved, nine fulfilled the inclusion criteria. An additional three studies were identified from the reference lists. Study dates ranged from 1996 to 2013. The studies used several measurement techniques, including pressure switches under the foot/feet, pressure mats, treadmills (with/without force sensors), video cameras, reflective markers and 3D camera systems, and accelerometers (attached to the heels, mid-thigh, sternum, and/or lower back). Seven articles reported overground walking and the remainder used treadmills, which are known to affect gait parameters. Tables 1 and 2 provide basic information about the selected articles: number of subjects, age, trial description, instrumentation, and research focus. For readability, overground (O) studies are described in Table 1 and treadmill (T) studies in Table 2. A formal meta-analysis of the results was not performed due to the many methodological differences between studies.

As with any compiled review, some of the included works have particularities which should be noted. Two papers (Hove et al. 2012 and Kaipust et al. 2012) differed from the others in that the subjects were not explicitly instructed to pay any attention to the beat they heard. In both works, the timing of the beat with respect to the gait cycle was both random and unreported. In fact, it should be noted that in the study by Hove et al. the beat started 25 seconds after the subjects started walking, so it is unlikely that beats and heel strikes were (at least initially) synchronized. These were nonetheless included because some effects of cueing were evident. Five of the studies actually focused on investigating Parkinson's disease or another pathology; we extracted the information provided from their healthy controls. One paper (Peper et al. 2012) provided different tones to each ear for the synchronization of the ipsilateral foot, while the rest used the same tone for both ears. The studies' subjects were either young (in their twenties) or older (over 60) or both (with two subject populations). The exception was the data shared by the Terrier & Déraz (2012) and Terrier (2012) articles, obtained from subjects with an average age of 36 years.

Authors[1]	Number of Subjects (Age in years, mean±std dev)	Description of Overground Trials	Instrumentation	Subjects Instructed to Synchronize?	Focus
Hausdorff et al. (1996)	10 (21.7, range 18-29)	225m or 400m oval, 1 hr uncued, 1/2 hr cued	Pressure sensors in 1 shoe	Yes	"1) to determine whether long-range correlations in gait extend over very long time scales, i.e., thousands of strides; 2) to define the conditions under which such correlations may exist; and 3) to evaluate potential mechanisms underlying this fractal property of gait."
Hausdorff et al. (2007)	26 (64.6±6.8)	One trial, 100 m (4x 180° turns)	Pressure sensors in right shoe	Yes	"to test the hypothesis that RAS (rhythmic auditory stimulations) reduces stride-to-stride variability in patients with PD (Parkinson's Disease)."
Hove et al. (2012)	18 (24.7±2.7)	One trial, 3 min (3x 90° turns)	Foot pressure sensors in both shoes	No	"to compare the effects of walking with fixed-tempo RAS and interactive rhythmic auditory stimulation... that can track and interact with a person's gait."
Rochester et al. (2005)	10 (63.5±7.0)	In subj's home. Complex fetch & carry task. 2nd of 2 trials used (avg 6.6 m)	Vitaport Activity Monitor (5 accelerometers)	Yes	"to evaluate (1) the influence of rhythmic cues on gait interference during a functional activity and (2) the relationship of clinical symptoms to gait interference."
Sejdić et al. (2012)	15 (23.9±4.7)	One trial, 15 min, 85 m (rectangular, w 90° turns)	Force-sensitive resistor in right shoe, accelerometer over L3	Yes	"to examine the effect of overground walking to the beat of an auditory, visual and tactile cue on the fractal dynamics and stability of human gait."
Willems et al. (2006)	10 (63.6±5.0)	1 trial, 8m	8 cameras (VICON), markers on legs & feet	Yes	"To study the effect of rhythmic auditory cues on gait in Parkinson's disease subjects with and without freezing and in controls."
Wittwer et al. (2013b)	19 (79.0±7.8)	3 baseline trials, 8 cued, 2 of each were practice (fastest and slowest were excluded), 8.3m	GaitRite mat	Yes	"to investigate the effects of music and metronome cues on spatio-temporal gait measures of healthy older people with normal cognition"

[1]Tables are organized alphabetically by first author.

Table 1 Article characteristics for overground studies

Many of these works focused on very different research questions than the one we sought to answer. As a result, they often did not report comparative values from the cued and uncued trials at natural speed. However, sometimes the statistical significance was reported, which was accepted as given. Thus in the following tables, some results are reported without the actual values of some parameters, including the statistical significance level. Further, different units and nomenclature were frequently used for equivalent measures. We describe the timing of the steps or strides, where given, as step rate (steps / min), or stride rate (strides / min), respectively. Thus the latter would describe the number of full gait cycles, comprising two steps, completed per minute.

Authors	Number of Subjects (Age in years, mean±std dev)	Description of Treadmill Trials	Instrumentation Used	Subjects Instructed to Synchronize?	Research Focus
Kaipust et al. (2012)	27 (25.7±3.0), 27 (71.4±4.4)	One trial, 6 min	6 3D cameras, markers on legs	No	"to investigate how listening to different auditory stimuli affects gait."
Peper et al. (2012)	12 (mean 24.9, range 22-28); 12 (mean 60.5, range 55-69)	Two trials, 25 sec	Treadmill w embedded force platform	Yes	"(to compare) the attentional demands of walking to visual stepping stones to those of walking to acoustic cues"
Roerdink et al. (2009)	9 (mean 60 yrs, range 42-71)	Trials, 70 strides (15 for video)	3D marker system, markers and accelerometers on heels, video	Yes	"to examine the stability and adaptability of auditory-motor synchronization in acoustically paced treadmill walking in stroke patients."
Terrier & Dériaz (2012)	20 (36±11)	One trial, 5 min, 100 strides	Instrumented treadmill	Yes	"to analyze the effect of the combination of treadmill walking (imposed speed) and auditory cueing (imposed cadence) on gait dynamics"
Terrier (2012)	same data as above				"to analyze whether the combined effect of treadmill and rhythmic auditory cueing (RAC) modified not only statistical persistence, but also fluctuation magnitude (standard deviation, SD), and stationarity of (stride length, stride speed, stride time, and stride width)"

[1]Tables are organized alphabetically by first author.

Table 2 Article characteristics for treadmill studies

Variables

Spatiotemporal Variables

The reported variables comprised gait speed, step and stride rate, step and stride length, step width, swing time, and double support time. The results for each variable follow, presented in a table and briefly discussed. Some variables were evaluated in both overground (O) and treadmill (T) studies, so a column is included indicating which paradigm was used. Where not explicitly stated in the table, the studies were conducted overground, usually along a track or corridor.

Gait Speed

Five papers reported subjects' walking speed. Of these, one did not report all of the values (Hausdorff et al.,1996). The slowest pace (0.95 ±0.10 m/s, uncued) is seen in Rochester et al.'s 2005 study with older subjects. This study was unique in its attempt to capture more naturalistic data, with the subjects performing a series of complex tasks in their own homes, from which the researchers extracted the simple cued and uncued gait portions for analysis. The fastest speed, averaged for cued and uncued gait, was obtained from Sejdić et al.'s 2012 study of young adults (approximately 1.5 m/s). Interestingly, the older adults in Wittwer et al.'s 2013b study were remarkably spry with an average gait speed of 1.24 m/s. No significant effect of cueing on walking speed was reported in any study. See Table 3 below.

Authors	Gait Speed in m/s Uncued	Cued	# Subjects (Age)	Significance of Cueing Effect
Hausdorff et al. (1996)	not given	not given	10 (21.7, 18-29)	ns
Hausdorff et al. (2007)	1.24 ±0.14	1.24 ±0.17	26 (64.6±6.8)	ns
Rochester et al. (2005)	0.95 ±0.10	0.96 ±0.15	10 (63.5±7.0)	ns
Sejdić et al. (2012)	≈ 1.5[1]		15 (23.9±4.7)	ns
Willems et al. (2006)	1.20 ±0.03	1.22±0.04	10 (63.6±5.0)	ns
Wittwer et al. (2013b)	1.25±0.15	1.27±0.17	19 (79.0±7.8)	ns

[1]Read from graph (averaged across cued and uncued trials)

Table 3 Gait speed

Step Rate

Three papers measured step rate, with two (Wittwer et al. 2013b and Willems et al.) reporting a significant increase in the cued condition, as shown in Table 4 below. This means that these subjects stepped slightly faster than the metronome beat set to their preferred speed. Rochester et al. also reported a non-significant increase. The subjects were all older. Wittwer et al. (2013b) also considered cadence variability (Coefficient of Variation for uncued 3.29±0.82% and cued 3.21±0.70%), which shows a slight, insignificant reduction in response to cueing.

Authors	Step Rate (steps/min) Uncued	Cued	# Subjects (Age)	Significance of Cueing Effect
Rochester et al. (2005)	98.4±10.8	100.8±11.4	10 (63.5±7.0)	ns
Willems et al. (2006)	114.90±1.91	118.10±1.96	10 (63.6±5.0)	p<0.01
Wittwer et al. (2013b)	115.4±9.1	116.5±9.2	19 (79.0±7.8)	p=0.001[1]

[1]See Table 1.a for methodology which decreased intra-subject differences, increasing statistical sensitivity to inter-subject differences

Table 4 Step rate

Stride Rate

Five papers reported stride rate; a significant change due to cueing was found only in Wittwer et al. (2013b), who reported increased stride rate (see Table 5). This variable is likely to be less sensitive to testing effects than step rate, since measures are taken every two steps. Of the four papers indicating stride rate variability, two found decreased variability in cued gait (Hausdorff et al., 1996 and Sejdić et al., 2012), while the 2007 study by Hausdorff et al. reported the opposite result, increased stride rate variability. This study made use of older subjects, while the other three comprised younger subjects. Hove et al. (2012) found no change, but as noted they did not instruct subjects to synchronize to the beat.

Authors	Mean, Coeff Var	Stride Rate (strides / min)		# Subjects (Age)	Significance of Cueing Effect
		Uncued	Cued		
Hausdorff et al. (1996)	Mean	Values not given		10 (21.7, 18-29)	ns
"	CV (%)	Values not given; Uncued>Cued		"	Significant; p value not given
Hausdorff et al. (2007)	Mean	55.6±4.7	55.1±5.1	26 (64.6±6.8)	ns
"	CV (%)	1.8±0.6	2.2±0.8	"	p=0.01
Hove et al. (2012)[1]	Mean	53.1±3.5	52.9±3.4	18 (24.7±2.7)	ns
"	CV (%)	2.1±0.6	2.1±0.7	"	ns
Sejdić et al. (2012)	Mean	≈ 57[2]		15 (23.9±4.7)	ns
"	CV (%)	Values not given; Uncued>Cued		"	p<0.01
Wittwer et al. (2013b)	Mean	57.3±4.7	57.9±4.8	19 (79.0±7.8)	p<0.0005[3]

[1]Subjects were NOT instructed to synchronize to the auditory cue

[2]Averaged across cued and uncued trials

[3]See Table 1.a for methodology which decreased intra-subject differences, increasing statistical sensitivity to inter-subject differences

Table 5 Stride rate

Step & Stride Length

Of the seven articles reporting step or stride length, four were overground. Since a stride comprises two steps (one complete gait cycle), stride length is likely to be sensitive to right/left asymmetries, but is otherwise equivalent to twice the step length. Only Wittwer et al. (2013b) found an effect: stride length was greater in the cued condition. No change in stride length variability was detected by the two studies that reported this value (ibid., Terrier 2012). See Table 6 below.

Authors	Mean / Coeff Var	Step / Stride Length (m) Uncued	Cued	# Subjects (Age)	Treadmill / Overground	Significance of Cueing Effect
Step Length						
Terrier (2012)[1]	CV (%)	1.8±0.8	1.5±0.4	20 (36±11)	T	ns
Rochester et al. (2005)	Mean	0.56±0.05	0.57±0.08	10 (63.5±7.0)	O	ns
Stride Length						
Terrier & Dériaz (2012)[1]	Mean	0.63±0.06[2]			T	ns
Kaipust el al. (2012)[3]	Mean	values not given		27 (25.7±3.0), 27 (71.4±4.4)	T	ns
Hausdorff et al. (2007)	Mean	1.35±0.19	1.37±0.23	26 (64.6±6.8)	O	ns
Willems et al. (2006)	Mean	1.26±0.03	1.24±0.04	10 (63.6±5.0)	O	ns
Wittwer et al. (2013b)	Mean	1.30±0.11	1.33±0.12	19 (79.0±7.8)	O	p<0.05
"	CV (%)	2.2±0.9	2.6±0.9	"	O	ns

[1]Same data

[2]Averaged across cued and uncued trials

[3]Subjects were NOT instructed to synchronize to the auditory cue

Table 6 Step & Stride length

Step Width

Four of the five studies which considered step width were treadmill studies. Two of these (Peper et al. 2012 and Roerdink et al. 2009) were the only ones to report significant differences due to cueing; both reported increased step width when subjects walked to the beat. The third, by Terrier (2012), showed a similar, albeit non-significant, increase. Peper et al. also found decreased step width variability (as standard deviation: uncued, 2.4±0.6 cm and cued, 1.8±0.5 cm, p<0.001). The overground study reported no cueing effect. The actual values cannot be compared across studies when different methods are used to measure step width (refer to Tables 1.a and 1.b for methodological details). See Table 7 below.

Authors	Step Width (cm) Uncued	Cued	# Subjects (Age)	Treadmill / Overground	Significance of Cueing Effect
Step Width					
Peper et al. (2012)	11.3±2.6	12.6±3.4	12 (24.9, 22-28), 12 (60.5, 55-69)	T	p<0.001
Roerdink et al. (2009)	16.4	17.0	9 (60, 42-71)	T	p<0.05
Terrier (2012)	13.7±3.4	14.2±3.5	20 (36±11)	T	ns
Kaipust et al. (2012)[1]	not given		27 (25.7±3.0), 27 (71.4±4.4)	T	ns
Wittwer et al. (2013b)	9.1±2.9	9.1±2.9	19 (79.0±7.8)	O	ns

[1]Subjects were NOT instructed to synchronize to the auditory cue

Table 7 Step width

Swing Time and Double Support Time

Three articles reported gait cycle measures. Swing time is the part of the full gait cycle spent with only one foot on the ground, while the other swings forward. Double support time occurs when both feet are in contact with the ground. Both of these phases occur twice per cycle. Both measures are reported here as percentages of one complete gait cycle. Only Wittwer et al. (2013b), who reported both, detected a cueing effect; the latter is decreased with cueing. Results are shown in Table 8.

Authors	Mean / Coeff Var	Swing / Double Support Time		# Subjects (Age)	Significance of Cueing Effect
		Uncued	Cued		
Swing Time (% Gait Cycle)					
Hausdorff et al. (2007)	Mean	36.3±1.1	36.1±1.1	26 (64.6±6.8)	ns
"	CV	2.9±1.3	2.8±1.2	"	ns
Wittwer et al. (2013b)[1]	Mean	35.6±2.2	39.4±2.2	19 (79.0±7.8)	ns
"	CV	4.34±0.89	4.21±0.99	"	ns
Double Support Time (% Gait Cycle)					
Willems et al. (2006)	Mean	23.50±0.72	22.39±0.59	10 (63.6±5.0)	ns
Wittwer et al. (2013b)	Mean	25.19±3.3	24.21±3.6	19 (79.0±7.8)	$p<0.05$

[1]Calculated from Swing Time and Stride Time

Table 8 Swing & Double support time

Time Series Analysis

Six articles presented time series analyses as a way of measuring the long-term correlations of a series of gait parameters. Of these, five used Detrended Fluctuation Analysis (DFA). Linearity correlation coefficient, autocorrelation time, Lyapunov exponents, and non-stationarity index were also calculated. (See Appendix for more information.)

DFA- Detrended Fluctuation Analysis

The α exponent was calculated for the following time series: stride interval, stride length, stride speed, and step width. Where there were significant cueing effects, the α exponent, or self-similarity parameter, was always reduced (Table 9). Five studies, two of which were on treadmills, reported the α exponent for stride interval. Only the young adult group in the 2012 study by Kaipust et al. demonstrated no effect of the metronome. Within the scope of their work, this suggests a difference due to age. In fact, Hausdorff et al. (1997) reported that older adults manifested a lower α exponent for stride interval than younger adults. The α exponent for stride length was similarly decreased in the two studies reporting it, with the exception, again, of Kaipust et al.'s younger subject group. The stride speed measure was unaffected in Terrier & Dériaz (2012), the only study to provide it. The step width α exponent was indicated only by Kaipust et al. As with stride interval and length, the α exponent was lower for their older subjects, and unchanged for their younger subjects.

Authors	DFA α		Treadmill / Overground	Significance of Cueing Effect
	Uncued	Cued		
Stride Interval				
Kaipust et al. 2012[1] (Old)	0.846±0.23	0.721±0.32	T	p=0.0001
" (Young)	0.600±0.20	0.535±0.21	T	ns
Terrier & Dériaz 2012	0.80±0.12	0.28±0.11	T	Significant[3]
Hausdorff et al.1996	0.90±0.04	0.42 [2]	O	Significant; p value not given
Hove et al. 2012[1]	1.03±0.11	≈ 0.9[2]	O	p=0.011
Sejdić et al. 2012	Uncued > Cued; no values given		O	p<0.01
Stride Length				
Kaipust et al. 2012[1] (Old)	0.758±0.27	0.741±0.28	T	p=0.044
" (Young)	0.775±0.19	0.699±0.28	T	ns
Terrier & Dériaz 2012	0.72±0.11	0.36±0.08	T	Significant[3]
Stride Speed				
Terrier & Dériaz 2012	0.31±0.12	0.30±0.06	T	ns
Step Width				
Kaipust et al. 2012[1] (Old)	0.740±0.23	0.655±0.23	T	p=0.003
" (Young)	0.757±0.23	0.688±0.20	T	ns

[1]Subjects were NOT instructed to synchronize to the auditory cue
[2]Read from graph
[3]Based on Effect size > 0.8, according to Hedges g, variant of Cohen's d

Table 9 Detrended fluctuation analysis measures

Other Analyses (see Table 10)

Correlation between log F(n) and log(n) (Hausdorff et al. 1996)

The correlation coefficient quantifies the linearity of the relationship between log(F(n)) and log(n), a characteristic not accounted for in the calculation of the self-similarity exponent α. Linearity of this relationship for the stride interval time series significantly decreases with auditory cueing, providing further evidence of decreased self-similarity of stride interval values over time.

Autocorrelation Time (Hausdorff et al. 1996)

This measure reports how many strides are required to for the autocorrelation to decay to 1/*e* (0.3678) of its initial value. Authors found faster decay (by an order of magnitude) in the stride interval time series for the cued compared to the uncued condition.

Lyapunov Exponent (LE) (Sejdić et al. 2012)

The LE is a measure of the stability of a dynamic system, in this case the gait cycle. The smaller the value, the more locally stable the time series. Two LEs were calculated, a short-term (λST) for the slope from the zeroth to first strides, and a long-term (λLT) for the slope from the fourth to the tenth stride. For all three axes (mediolateral, anterioposterior, and vertical), λST was unaffected by cueing while λLT decreased. These results indicate that auditory cueing did not affect the stability of contiguous strides, but it did decrease longer-term stability.

Non-Stationarity Index (NSI) (Terrier 2012)

This index is a means of quantifying the time-dependent fluctuations in a time series. First, the time series is normalized, and the averages of 20 ten-step sets are computed. The NSI is the standard deviation of these 20 values. The NSIs for step width and step speed showed no cueing effect, while step length and step time NSIs decreased, indicating that auditory cueing decreased the non-stationarity, or fluctuation, of these time series.

Authors	Analysis and Measures	Results: Uncued	Results: Cued	Significance of Cueing Effect
Hausdorff et al. 1996	**Stride interval time series**			
"	Correlation Coeff betw log F(n) and log(n)	0.995±0.003	0.956±0.031	p<0.005
"	Autocorrelation Time- time for F(n) to decay to 0.3678[1] times original value	73±70 strides (range 14-315)	3±1 strides (range 1-4)	Significant; p value not given
Sejdić et al. 2012	**Average Lyapunov exponents of stride interval time series- ML, VT, AP axes**			
"	λLT (long term)	Uncued > Cued; no values given		p<0.01
"	λST (short term)	Uncued ≈ Cued; no values given		ns
Terrier 2012	**Non-stationarity index (NSI)**			
"	Step length	0.11±0.03	0.07±0.02	Significant[2]
"	Step time	0.12±0.03	0.07±0.02	Significant[2]
"	Step width	0.14±0.02	0.14±0.03	ns
"	Step speed (Step length/Step time)	0.05±0.01	0.05±0.02	ns

[1] 1/*e*

[2] Based on Effect size > 0.8, according to Hedges g, variant of Cohen's d

Table 10 Other time series analyses

Discussion

After considering the effect of cueing on gait at the natural speed for healthy young and older adults, we can be reasonably certain that it influences some gait parameters in healthy subjects.

Spatiotemporal Measurements

Gait speed was unchanged by cueing in all six studies. In two out of three overground studies, step rate was increased (with a similar trend in the third). All three used older subjects. Additionally, stride rate was increased in Wittwer et al. (2013b), one of two with older subjects. It is not surprising that older subjects would be more affected by the additional attentional demands of the metronome task. It is surprising, however, that they would step more quickly than the beat, since increased task difficulty, dual-task paradigms, and reduced attentional resources generally give rise to slower task execution, not faster. The fact that they step faster than the auditory cue suggests that something other than increased cognitive challenge of the dual task is responsible.

A possible explanation for the increased step rate is the increased excitability of subcortical motor neurons by means of audio-spinal facilitation in response to steady auditory tones, as reported by Rossignol and Jones (1976). The tendency to walk with a faster stepping rate than the beat is most likely an unconscious, subcortical phenomenon, a priming effect on CPGs due to the predictable rhythmicity of the beat. Perhaps younger subjects are more capable of resisting this stimulating effect and synchronizing to the beat through an effort of conscious attention. However, in some circumstances they too are susceptible, according to research into music-embedded rhythmic synchronization. An increase in step speed has been reported for auditory cues embedded in music for young subjects (Styns et al., 2007). Leman et al. (2013) found that the step speed of their young-to-middle-aged subjects was increased or decreased, relative to the preferred cadence duplicated in the music's tempo, depending on the type of music. It seems that metronome cueing has a stimulating effect on stepping rate, at least in older subjects.

Four papers measured stride rate variability. Only Hove et al. (2012) found no difference between the cued and uncued conditions. Recall that their work did not instruct conscious synchronizing and thus would be expected to show at most a smaller effect of cueing, since subjects were presumably focusing less attention on modulating their gait in time to the beat. Both of the two studies with young subjects who were instructed to synchronize to the metronome found reduced stride rate variability. This result echoes Thaut et al.'s 1992 findings that walking to a musical beat increased stride symmetry and decreased the variability of muscle contraction amplitudes. Further, as explained by Roerdink et al. (2013), movement trajectory variability decreases at 'anchor points' in rhythmic movements, particularly when their occurrence coincides with an auditory cue. In gait, the heel strike is the most salient anchor point, since it is clearly felt at every step. Synchronizing the heel strike with the metronome beat provides a strong anchor point. For young subjects, at least, we see evidence of an anchoring effect in reduced stride rate variability in cued gait.

Additionally, previous work has found that treadmill walking also exhibits reduced stride rate variability, even in the absence of an auditory cue (Dingwell et al. 2001, Frenkel-Toledo 2005). None of the treadmill studies in this review reported this measure. Some feature common to treadmill and metronome gait may well be responsible. For example, the treadmill can also be considered as a pacemaker since it essentially fixes the average walking speed. Still, it is not fully clear what this feature might be and whether it is related to an anchoring effect.

In contrast with these findings, Hausdorff et al. 2007 reported increased stride rate variability with cueing. Their study was the only one of the four reporting this measure which tested older subjects. The reason for this result is unclear. Perhaps reduction in attentional or decision-making capacity, associated even with healthy aging, is responsible. Although anchoring is an unconscious process, there is no evidence that it is related to the automatic processes that contribute to the regulation of gait. It may be that there is a conflict between these different processes, resolved at some higher cognitive level. The attention required to smoothly resolve these different timing impulses may be beyond the ability of some older subjects, who thus become less consistent and more variable in their movements. Increased stride variability has been reported in Alzheimer's patients in response to both musical and metronome cueing (Wittwer et al. 2013a). Further research is needed to explore the influence of anchoring on gait in more detail, in order to understand the underlying rhythmic and timing mechanisms involved and investigate the possibility that physical limitations might also be a factor.

Only one of the six studies[1] reporting step or stride length reported an effect of cueing on either of these measures. The authors, Wittwer et al. (2013b), attributed the increase in stride length to a general stimulating effect of the metronome beat, similar to that experienced with music. The relationship between step rate and stride length is generally considered to be strongly linear and age-invariant (Zijlstra et al. 2008, Egerton et al. 2011) at different walking speeds. However, the latter study found that constraining either the stride length or the step rate weakened this relationship.

Two out of two articles reported no cueing effect on stride length variability. However, Terrier & Déraz's 2012 study was on a treadmill, so any possible effect would probably be much less evident in any case. Additionally, stride length variability is not as sensitive as step length variability (particularly in the case of a consistent left/right asymmetry), which no article reported. Thus, the possibility that there is an effect of cueing on step or stride length variability cannot be ruled out in the context of this review. In fact, it may be that step length variability decreases as a result of the

[1] Representing seven articles, since Terrier 2012 and Terrier & Dériaz 2012 analyzed the same data.

same anchoring effect that decreases the step rate variability, but that the effect is not very strong. Generally, stride measures are not as sensitive as step measures (Galna, Lord & Rochester 2013).

Increased step width in the cued condition was only observed in two of three treadmill studies (Peper et al. 2012 and Roerdink et al. 2009), both of relatively short duration: two trials of 25 seconds and 70 strides, respectively. The third treadmill study (Terrier 2012) reported a non-significant increase. Taken together, our findings support Roerdink et al. (2009), who suggest that synchronizing to a metronome beat and/or walking on a treadmill cause an increase in step width because these conditions require more conscious attention. Generally, increased step width is associated with a more conservative gait strategy, due for example to a fear of falling (Donoghue et al. 2012) or a higher likelihood of falls (Nordin et al. 2010), as well as dual task paradigms which challenge attentional capacity. It seems likely that the increased step width is the combined result of the treadmill paradigm and the synchronization task. Clearly, under these two conditions more attention would be required than during normal, unconstrained gait, and this fact alone may account for the increase in step width. We would expect older subjects to manifest these differences more strongly; unfortunately, from the available studies, we could not assess the role of age. The measure of step width variability was decreased with cueing in the only study to report it (Peper et al. 2012). This result suggests an anchoring effect similar to that seen for step/stride rate. However, Grabiner & Troy (2005) also reported reduced step width variability in young subjects performing a second cognitive task while walking without a metronome. It would seem that attributing decreased variability to a steady beat's anchoring effect is overly simplistic.

The double support phase of the gait cycle is the most stable phase, because it is easier to maintain balance when both feet are on the ground. Thus double support comprises a smaller percentage of a stride in cases where stability is less of an issue, and comprises a greater part of the gait cycle when subjects feel less confident, such as when they are frail or the ground is uneven. Conversely, swing time represents a period of relative instability and higher risk. Wittwer et al.'s 2013b finding of reduced double support time with cueing would suggest that subjects feel more stable when synchronizing to the metronome beat, which appears at odds with the increased step width results suggesting a perceived loss of stability. However, it is only one of two studies reporting this measure, and the other (Hausdorff et al. 1996) found no difference between cued and uncued conditions. Similarly, neither study found a difference for swing time. It is possible that the stimulating effect of the auditory cueing affects the rhythmic circuitry in such a way that less time is spent in the double support phase. More research is needed to support (or reject) this conjecture, particularly since the cautious wider step width is at odds with the increased confidence implied by the decreased double support time.

It must be pointed out that some of the significant results were by no means highly prevalent. We may be considering patterns which would not stand up to more intensive scrutiny (in the form of repeated studies with more subjects, for example). Alternatively, these findings might be more pronounced with more subjects who are older, or with a more challenging paradigm (such as an additional cognitive task).

Three studies (Hove et al. 2012, Rochester et al. 2005, and Kaipust et al. 2012) reported no significant changes in any of their spatiotemporal parameters in response to cueing. Because Rochester et al. were primarily investigating cueing effects on the elderly for more complex, real-life tasks, the portion of the trials available for our purposes was quite short and varied by subject (depending on the layout of the home), averaging 6.6 meters of walking; moreover, there were only ten subjects. Hove et al. had one three-minute trial, with younger subjects. Kaipust et al. used two age groups of 27 subjects each and trials of moderate length (six minutes). As previously noted, these latter two did not specifically instruct synchronization with the beat. Since increased trial length and specific attempts at synchrony would be more likely to demonstrate genuine effects of cueing, we do not need to consider these studies' (lack of) results anomalous.

For the spatiotemporal measures reported by these twelve articles, we see some evidence of a stimulating effect of the metronome beat in older subjects, demonstrated by increased step/stride speed, and perhaps also by increased stride length and decreased double support time. There may also be an anchoring effect in younger subjects, indicated by reduced variability of stride time and step width. Both of these influences on movement are well documented, although research examining their interaction, particularly with respect to gait, does not seem to exist. They both appear to be automatic responses but they are clearly very different. Further research could elucidate their relation to CPGs, and how they may vary in relative strength according to age. Additionally, increased step width is observed when subjects walk to a metronome on a treadmill. Both tasks require more attention than unconstrained, aboveground gait; the combined attentional demand alone may explain the adoption of a wider, more cautious gait.

Time Series Measurements

Detrended Fluctuation Analysis

This process quantifies the long-range correlations in a time series of values. The time series is integrated and the fluctuation of this accumulated sum is defined as F(n), where n is the window size or number of observations (i.e. strides). If the series is self-similar, $F(n) \sim n^{\alpha}$, which is to say F(n) increases proportionally with n; the double-log graph will be linear, with a slope of α. This value is interpreted as follows: when $\alpha < 0.5$ the statistical pattern is anti-persistent, meaning it is less self-similar than if it were random; when $\alpha \approx 0.5$ the values in the time series are uncorrelated, like white noise; when $0.5 < \alpha < 1.0$ there are persistent long-range correlations, meaning that subsequent values are partially dependent on previous ones in a scale-independent way; when α = 1.0, this is known as pink noise and is observed in dynamic systems which are not externally controlled; and finally when α ≈ 1.5, this is called brown or Brownian noise (the integration of white noise) and as the name suggests is more random. The range of 0.5 < α < 1.0 has been seen in a variety of dynamic physiological systems, such as heartbeats and finger tapping intervals, and is associated with the interaction between components of complex, self-organized systems. For this reason, when applied to gait it is often seen as evidence of some sort of higher level cortical control, such as central pattern generators (Goldberger et al. 2002). Indeed, a decrease in the α exponent has been taken to indicate a disruption of this control, for example as a result of disease (Peng et al. 1995); it has also been seen for some kinematic gait measures in treadmill gait studies (Dingwell & Cusumano 2010).

DFA was the most common method for analyzing the dynamics of metronome gait. For all reported DFA measures except gait speed (reported by Terrier & Dériaz, 2012), the uncued value for the α exponent was in the range consistent with long-range scale-invariant correlations. Auditory cueing decreased the α exponent for gait speed in one of two studies, for stride speed in four of four studies, for stride length in two of two studies, and for step width in the only study to report this value, but only in the older subject group (Kaipust et al. 2012). Although the values did not always descend below 0.5, which would indicate anti-persistence, their decrease is understood to indicate a loss of persistence in the time series. The anti-persistence of the gait speed time series for uncued gait was explained by Terrier & Dériaz (2012) as a non-optimal control process, due to the constraint of the treadmill moving at a fixed pace. If, as they suggest, “the controlled gait variable tends to ‘oscillate’ around the target value” (ibid., p. 1595), anti-persistence is the logical outcome for the gait speed time series. Unlike the other time series measures, gait speed in treadmill studies is already constrained even without an auditory cue. In fact, this finding reinforces the idea that the α exponent decreases in response to an externally imposed target value, be it gait speed fixed by a treadmill or step rate fixed by an auditory cue.

Furthermore, for all groups for which DFA was reported, only Kaipust et al.’s young subjects had no significant reductions for the α exponent-- and they had no changes to any spatiotemporal measures, either, as previously noted. It seems that DFA is sensitive to cueing effects. Both Hove et al.’s subjects and those in Kaipust et al.’s older group reported significant reductions in α for stride speed with cueing. Recall that these two studies did not instruct subjects to synchronize to the metronome beat, and neither study reported any significant change in the kinematic values.

Since α appears to be either unchanged or decreased in the cued condition, there is evidence that “long-range correlations break down in metronomic walking” (Hausdorff et al., 1996, p.1454), suggesting that some gait control mechanism (or rather its disruption) is responsible for the results reported. This may be due to a stimulating effect, an anchoring effect, attentional challenge, or some combination.

Following these findings, others have reported the continued existence of long-range correlations in cued gait using different measures, such as the relation between the stride interval and time difference between the beat and the footstep, the asynchrony interval (Delignières & Torre 1996). Since we are interested in assessing the effect of cueing on gait mechanisms specifically, rather than on timing mechanisms generally, we consider this worthy consideration beyond the scope of our review article.

Lyapunov Exponents (LE)

To calculate the LEs for the stride interval time series, Sejdić et al. (2012) followed the method of Dingwell & Cusumano (2000). They first established the ideal time delay from the autocorrelation function, and the appropriate embedding dimension by means of a 'global false nearest neighbor' analysis. With the construction of dimensional state vectors, they calculated the Euclidean distance between neighboring trajectories. The slope of the average logarithmic divergence of these trajectories dictated the Lyapunov exponent.

Sejdić et al. found that the long-term Lyapunov exponent (λLT) was decreased by cueing, but the short-term exponent (λST) was unchanged, meaning that while the auditory cue didn't affect the stability of the subsequent stride, it did increase the stability of subsequent strides over time. In their interpretation, synchronizing steps to a beat causes them to be more controlled, corresponding to a decrease in λLT and stride time variability, and the long-range correlations associated with the automaticity of natural gait are also decreased.

Other dynamic measures (autocorrelation, non-stationarity indices)

As for the other time series measures, Hausdorff's 1996 article presented additional quantitative information about the double-log DFA graph beyond calculating the α exponent. Both the correlation coefficient of the resulting line and the autocorrelation time were reduced in the cued condition, so we need not rely on α exponent alone to appreciate changes in long-range correlations.

In Terrier's treadmill study, the non-stationarity indices (NSIs) of step length and step time indicated decreased fluctuation due to cueing, while those of step width and step speed did not. His interpretation is that the two former values are elevated in uncued treadmill walking, because in order to match the treadmill's velocity the step length and step time must be constantly manipulated in an interdependent way. In the cued condition, however, step time must be matched to the beat, so they both become more controlled. The values fluctuate less and their NSIs decrease. Gait in both the cued and uncued conditions is constrained by the treadmill, which explains why they both also have a low α exponent. On the contrary, step speed NSI was low in both conditions; this is a calculated value (step length/step time), and the ratio may simply have remained fairly constant. Step width NSI remained high in both conditions. This may in some way be due to an effect of walking on a treadmill.

Review Summary

The results in this review may be attributed to the interaction of a series of discrete effects caused by the steady auditory cue. Specifically, we have seen evidence for stimulation, anchoring, and increased attentional demands (see Figure 4). Future studies that examine the role of age may be able to tease apart these confounding (and somewhat contradictory) influences on the regulation of gait. Paradigms with additional attentional demands may show that, when young subjects' attentional resources are sufficiently strained, their results become similar to those of older subjects; instead of reduced variability due to greater conscious control, we might see increases. The dynamic time series measures confirmed the disruptive influence of synchronizing to a beat on gait.

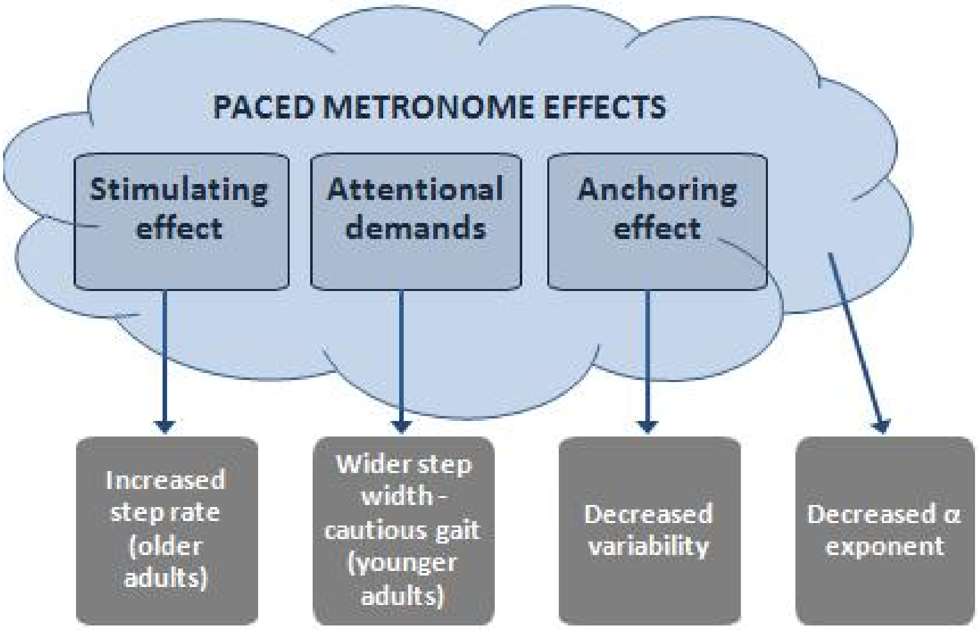


Figure 4 Effects of metronome pacing on gait

Further research might explore these possibilities to determine whether younger subjects also increase their step time in response to the beat. If it is due in some way to decreased attentional resources, which occurs even in healthy aging, we would expect no such effect in younger subjects. If it is a timekeeping mechanism that is affected, then younger subjects would also speed up their stepping, although the possibility that with sufficient cognitive resources they could successfully compensate should be considered, perhaps by providing further levels of attentional demands (via an additional simultaneous task, for example). On the other hand, a general stimulatory effect, such as is demonstrated with musical cues (Styns, Menon & Levitin, Wittwer et al. 2013b), might manifest in the younger subjects as well. Kinetic measures would also be useful in determining the mechanisms responsible and exactly how it is disrupted. No studies were found which presented such measures.

On the whole, the present review offers an intriguing but incomplete picture which might yield further insights into gait mechanisms with the use of more refined techniques exploring metronome timed gait in healthy subjects. The better our understanding of these mechanisms, the more specifically we can tailor rehabilitation programs to address specific challenges and deficits.

Chapter Three

Anti-Phase Gait Experiments

The contents of Experiment One have been accepted for publication: Mayberry KJ, Chiari L, "Does syncopated gait benefit from central pattern generators?", J Sci Research & Reports, (2014, in process). The contents of Experiment Two are in the process of being prepared for publication: Mayberry KJ, Mellone S, Chiari L, "Walking in Syncopation to the Beat" (in preparation).

The paradigm of anti-phase gait was developed to investigate how much this complex movement is similar to simpler movements, such as finger-tapping, which have been previously explored. Gait is obviously much more complicated, but unlike finger-tapping makes use of central pattern generators (CPGs). The intention is to explore the similarity of anti-phase gait and anti-phase tapping, and also to determine whether there is evidence that CPGs facilitate anti-phase gait, by determining whether it is performed more successfully at each subject's preferred walking speed than at either faster or slower speeds.

Two experiments were conducted. The first was a pilot project with a convenience sample of young university students as subjects. The second included older subjects in addition to additional younger subjects. Figure 1 demonstrates the experimental protocol and the major functional outcomes: timing of the acceleration signal, heel strike and metronome beat.

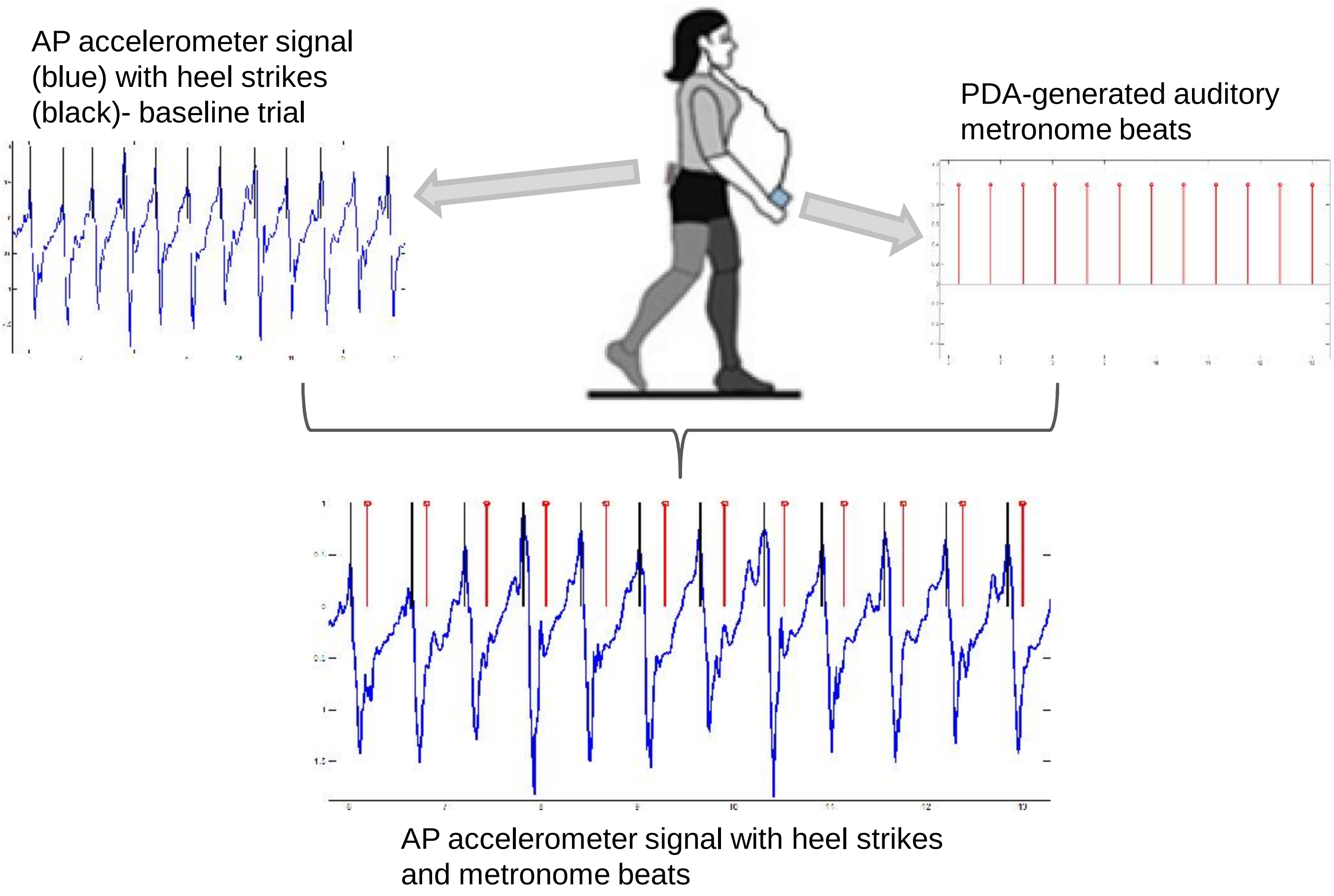


Figure 5 Experimental Protocol

Experiment One

Subjects

Ten university students were recruited to participate in this pilot project (see Table 11). All subjects were healthy and without any reported history of gait or neurological problems. All gave their informed consent.

Pilot group	Height (cm)	Mass (kg)	Age (yrs)	Cadence (Hz)	Sex
1	166	49	24	2	F
2	178	70	25	1.7	M
3	170	58	25	2	F
4	173	90	22	1.7	M
5	185	85	32	1.7	M
6	187	90	22	1.9	M
7	160	63	28	1.8	F
8	169	71	22	1.9	F
9	168	64	27	1.9	M
10	185	79	27	1.9	M
Mean	174.1	71.9	25.4	1.9	4F, 6M
Std Dev	9.2	13.9	3.2	0.1	

Table 11 Subject demographics, Expt One

Trials

There were 20 trials of one minute each for both groups (see Table 12). Trials 1 and 2 were baseline (BASE) trials with no metronome beat. The subject's preferred cadence was calculated from these two initial trials, a process which generally ensured a five to ten minute rest for the subjects. Preferred speed trials were conducted at 100% of this tempo, slow trials at 85%, and fast trials at 115%. Trials 3 and 4 were distractor (D) trials, in which the metronome beats were irregular; subjects were instructed to ignore them. Trials 5-10 were in-phase (IN), with two each at preferred, slow and fast speeds. Subjects were instructed to keep time with the beat, so that foot contact and the beat occurred simultaneously, while walking as normally as possible. A third IN trial at 100% was inserted next, followed by a third BASE trial. The next six trials, 13-18, were anti-phase (ANTI), with two each at 100%, 85%, and 115% of preferred speed, similar to the IN trials. For these ANTI trials, subjects were instructed to try to step midway between two beats. Finally, a fourth IN trial at 100% and a fourth BASE trial were performed. In total, there were four BASE trials without a metronome: two at the beginning, and the 12th and the 20th. As described, there were also four IN trials at preferred speed spaced similarly throughout the session; all other conditions consisted of two sequential trials.

TRIAL #	TYPE	METRONOME
1&2	BASELINE	none
3&4	DISTRACTOR	irregular
5&6	IN-PHASE 100%	preferred
7&8	IN-PHASE 85%	slow cadence
9&10	IN-PHASE 115%	fast cadence
11	IN-PHASE 100%	preferred
12	BASELINE	none
13&14	ANTI-PHASE 100%	preferred
15&16	ANTI-PHASE 85%	slow cadence
17&18	ANTI-PHASE 115%	fast cadence
19	IN-PHASE 100%	preferred
20	BASELINE	none

Table 12 Trial descriptions

Specific instructions for every trial were given immediately beforehand, along with further explanation as needed. Furthermore, trial order was fixed, as shown, for all subjects, for the most part increasing in difficulty throughout the session.This sequence greatly helped subjects continue. (In initial testing, subjects often stopped during the anti-phase trials.) The advantage of complete trials was considered to outweigh the disadvantage of a possible learning or repetition effect. Subjects were encouraged to request a break at any time between trials, although none did so. Trials were carried out on quiet side streets or pedestrian pathways.

Materials and Methods

Hardware

We used a portable accelerometer (McRoberts DynaPort MiniMod Hybrid Triaxial accelerometer and gyroscope- see Figure 6), worn at midback. A handheld Hewlett-Packard iPAQ 214 EnterprisePDA (see Figure 7) transmitted the acoustic metronome beats via ear buds, and synchronized the acceleration signal with the timing of the metronome beats. Figure 8 illustrates the setup.

Figure 6 McRoberts accelerometer & gyroscope

Figure 7 HP PDA (metronome)

Figure 8 Author demonstrating a trial

Variables

- **Cadence, CAD** (normalized units)- step frequency (normalized to 1.0 with respect to the nominal cadence of each trial) and its coefficient of variation, **CADCOV**.

- **Jerk Index, JI** (m2/s6)- derived from the anterior-posterior acceleration signal, adapted from the following formula (from Hogan, Sternad 2009): *JI* = $\frac{1}{t_{i+1}-t_i}\int_{t_i}^{t_{i+1}} \dot{a}(t)^2\,dt$, where t_i = the time index of heel strike i; a = acceleration , and $\dot{a}$ = time derivative of acceleration.

- **Harmonic Ratio, HR**- derived from power spectrum of the anterior-posterior acceleration signal, calculated as the sum of the first ten even harmonics divided by the sum of the first ten odd harmonics, using stride frequency as the fundamental frequency component (from Menz et al. 2003).

- **Drift**- a binary value (Yes/No), reflecting whether the subject kept pace with the metronome.

  Drift =Y if: $|beat_i - step_i|$ > nominal step time interval; i = index for beat and step series pairs.

- **Phase Shift, PS** (degrees)- the phase difference, or the interval between heel strike and beat, as a proportion of one full step cycle (where 360 degrees represents the time from one step, or heel strike, to the next). This value is only meaningful for trials where Drift = No.

Software Analysis

The acceleration signals, sampled at 100 Hz, were downloaded onto a PC and processed using MATLAB (MathWorks, Natick, MA, v.7.9). They were pre-processed with a fourth-order, zero-lag Butterworth filter with a cutoff frequency of 20 Hz. An algorithm derived from Zijlstra (2004) identified heel strike events from the anterior-posterior (AP) component. A custom program synchronized the acceleration signal with the timing of the metronome beats. The AP acceleraton signal for every trial was visually inspected, to eliminate the anticipatory postural adjustment (and occasional anomalous mistep) that occured at gait initiation and ensure that the algorithm correctly identified the heel strikes. Typically, four to ten 'steps' were deleted from the start of each trial, and zero or one from the end. Trials in which the algorithm misidentified heel strikes within the middle 40 seconds were not used. Trials were from 35 to 56 seconds long. Trials of 20 strides are considered sufficient for assessing parameters such as cadence, while variability is accurately assessed with longer trials (Hausdorff et al. 1997, Hollman et al. 2010, Roerdink et al. 2011). Most importantly, though, our trials were fairly similar in length throughout the study. Ten seconds of AP acceleration from a typical in-phase trial are shown in Figure 9, and a typical anti-phase trial is shown in Figure 10. The solid vertical lines identify the heel strikes, and the dotted lines identify the auditory metronome beats. Gray vertical arrows demonstrate the phase shift.

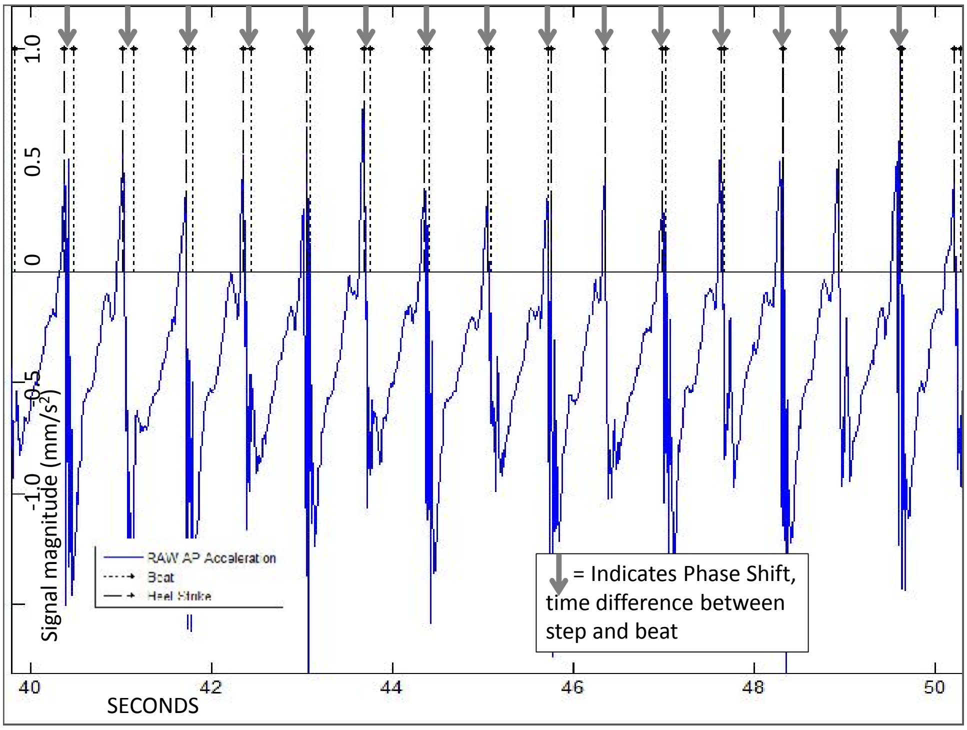


Figure 9 A/P Accelerometer signal from in-phase trial

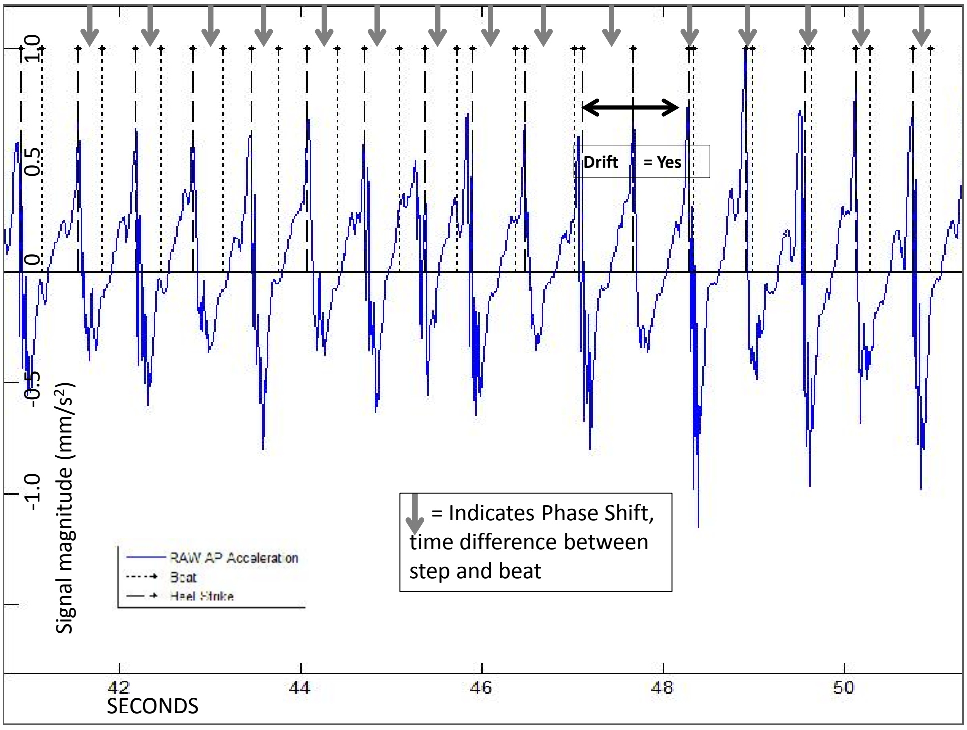


Figure 10 A/P Accelerometer signal from anti-phase trial

Statistics

Using NCSS software (Kayesville, Utah, v. 7.1) repeated measures ANOVAs were performed, with the within-subject factors of condition (BASE, D, IN, ANTI), metronome speed (preferred, fast, slow), and repetition (1, 2, 3, 4). If the difference was significant ($p<0.05$), multiple post hoc comparisons were performed using the Tukey-Kramer test. A Chi-Square analysis using Fisher's exact test was used to evaluate significance for the categorical Drift variable. Since PS is a rhythmically repeating measure, circular statistics (Watson-Williams F Test) provided the analysis for significant difference between conditions.

Results

There was no effect of repetition. Similarly, there was no difference between the DIST and BASE tasks for any measure, so the former were excluded from further analysis.

Across conditions

CADCV was lower in BASE trials than IN or ANTI, which did not differ (BASE: 5.08±0.65%; IN: 12.62±0.75%; ANTI: 13.84±0.97%; $P<0.001$). Similarly, JI was lower in BASE than the two paced conditions (BASE: 1524±233 m^2/s^6; IN: 1881±345 m^2/s^6; ANTI: 2901±348 m^2/s^6; $P=0.01$). IN and ANTI did not differ, but the *P* value for the pairwise comparison was almost significant at .06. The measures CAD (BASE: 1.00±0.01; IN: 0.99±0.01; ANTI 0.98±0.01; $P=.31$) and HR (BASE: 2.10±0.10; IN: 1.86±0.08; ANTI: 1.83±0.11; $P=.15$) were unaffected by condition.

For trials in which subjects matched the metronome speed (that is, Drift = No), PS was calculated. Drift occurred more frequently during ANTI than IN ($X^2(1,124)=31.4944$, $P<.001$). The average relative timing of in-phase heelstrikes was 350.3±44.8°, corresponding to a negative phase shift of -9.7°. Anti-phase PS was 173.4±65.7°, consistent with the ideal of 180°. These values were significantly different ($P<.001$; see Figure 11).

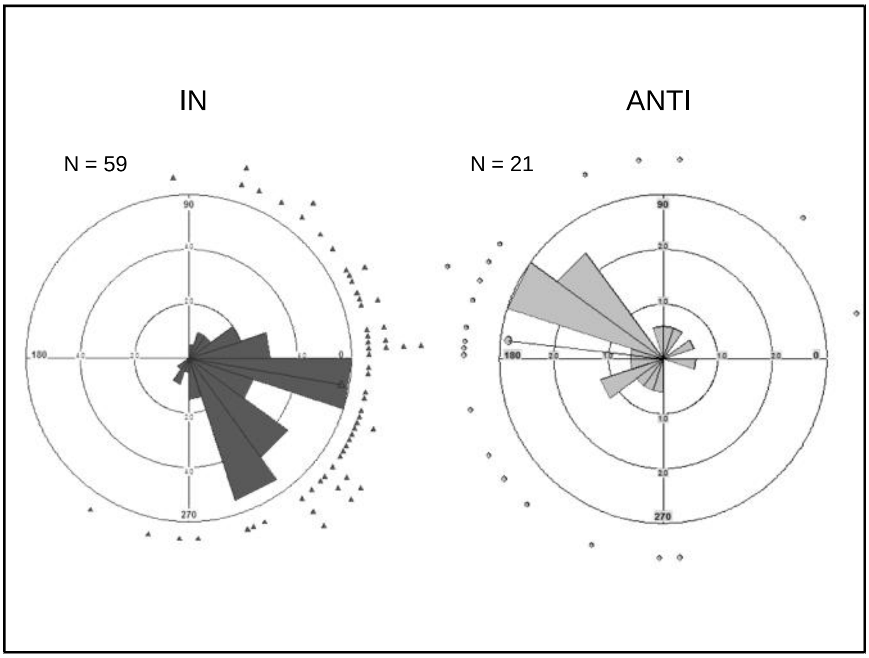


Figure 11 Phase Shift rose plots for IN & ANTI conditions

Across speeds (see Table 13)

For IN trials, CADCV was different for all three speeds: slow > fast > preferred, while JI increased with speed. Neither CAD nor HR was affected by speed. For ANTI trials, JI was the only measure that changed with speed: fast was greater than slow, but preferred did not differ from either. CAD, CADCV, and HR did not reflect differences in speed.

	IN				ANTI			
	slow	preferred	fast	*P*	slow	preferred	fast	*P*
CAD	1.00±0.01	0.99±0.01	0.99±0.01	.64	1.01±0.02	0.99±0.01	0.96±0.02	.08
CADCV	12.32±1.16[a]	7.54±0.49[a]	10.85±1.20[a]	<.001	12.75±1.04	13.84±0.98	13.26±1.07	.75
HR	1.93±0.11	1.98±0.05	2.10±0.12	.56	1.93±0.11	1.83±0.10	1.91±0.11	.69
JI	926±424[a]	1604±179[a]	5313±438[a]	<.001	1784±665[b]	2901±450	4946±687	.01

[a] Different from other speeds in that condition; [b] Different from fast in that condition

Table 13 Results across speeds for IN & ANTI conditions

Discussion

First of all, the Drift values indicate that anti-phase gait is more difficult than in-phase gait; the PS values indicate that it is possible.

Both JI and CADCV were sensitive to pacing, with higher values in the paced conditions IN and ANTI than in BASE. As mentioned, this result is consistent with the findings of Balasubramaniam, Wing & Daffertshofer (2004): jerk is higher for paced than unpaced finger-tapping, since pacing

requires more deliberate movement control to monitor timing and correct errors. However, they found that tapping frequency varied more in anti-phase than in-phase, while in our study gait frequency was no more variable in ANTI than IN. Thus it would seem that anti-phase gait, unlike anti-phase tapping, is no more variable than the equivalent in-phase movement. Others have reported that movement frequency is less variable when the movement is performed in time with a steady beat compared to no beat, due to the temporal anchoring effect of the beat, both for finger-tapping (Sasaki et al. 2011) and gait (Roerdink et al. 2011). As noted, CADCV in our study increased with pacing; this contrasting result is not without precedent, as it was also observed by Hausdorff et al. (2007).
It is not clear why metronome pacing has different effects on gait variability in different studies; perhaps the complex interaction of automatic processes and cognitive demands that constitute gait control are sensitive to a miscellany of environmental factors. In fact, it is worth noting that our study was conducted outdoors under naturalistic conditions, with a great deal of visual complexity. This setting may have increased attentional demands sufficiently that gait was perturbed, even when the beat provided an opportunity to ‘anchor’ the footstep.

During IN trials, gait was least variable at preferred speed, a finding compatible with a facilitating role of CPGs. ANTI trials, however, did not show this effect. The measure JI’s increase with speed is due to the physical characteristics of jerk. None of our measures demonstrated that anti-phase gait is less perturbed at preferred speed.

Conclusions

We conclude that the variables we selected provide no evidence of the facilitative effect of CPGs on gait at preferred speed in our subject population, when it is performed in anti-phase to an auditory metronome cue. In this respect, gait is like finger-tapping. Further investigation is warranted before concluding that CPGs do not influence anti-phase gait, however. At ten subjects, our sample size may lack sufficient statistical power. Perhaps what was gained in verisimilitude was lost in sensitivity, as the naturalistic setting may have proved too distracting to allow a subtle control effect of CPGs to reveal itself. It is possible that other measures or analyses such as detrended fluctuation analysis (DFA) may be more applicable. Gait research has been making use of dynamic systems analysis, and a growing body of work suggests that it is sensitive to CPG influence (Hausdorff et al. 1996, Terrier & Dériaz 2012).

Experiment Two

Subjects

Seven additional younger subjects participated, for a total of seventeen; sixteen older subjects were recruited. All subjects gave their informed consent. See Table 14 for details.

Younger group	Height (cm)	Mass (kg)	Age (yrs)	Cadence (Hz)	Sex
1	166	49	24	2	F
2	178	70	25	1.7	M
3	170	58	25	2	F
4	185	85	32	1.7	M
5	187	90	22	1.9	M
6	160	63	28	1.8	F
7	169	71	22	1.9	F
8	168	64	27	1.9	M
9	185	79	27	1.9	M
10	175	69	24	1.8	M
11	170	63	21	2	F
12	184	68	21	1.8	M
13	176	77	23	1.8	M
14	165	55	24	1.8	F
15	172	63	27	1.8	M
16	182	62	28	1.9	M
17	176	62	20	1.9	F
Mean	174.5	68.8	24.6	1.9	7F, 10M
Std Dev	7.8	11.5	3.1	0.1	

Older group	Height (cm)	Mass (kg)	Age (yrs)	Cadence (Hz)	Sex
1	170	82	65	1.8	M
2	175	90	75	1.8	M
3	170	72	68	1.8	M
4	177	77	77	1.8	M
5	170	68	66	1.8	M
6	166	65	69	1.9	M
7	161	83	66	1.8	F
8	164	61	70	1.9	M
9	169	57	63	1.8	M
10	176	85	64	1.9	M
11	166	82	65	1.9	M
12	168	65	73	1.9	M
13	160	62	61	2	M
14	170	71	61	1.9	F
15	160	53	71	1.6	M
17	153	52	59	2	F
Mean	166.4	69.9	67.2	1.9	4F, 13M
Std Dev	7.1	11.6	5	0.1	

Table 14 Subject demographics for Expt Two

Materials and Methods

Materials and methods were the same as in Experiment One.

Results

Results by Condition (Table 15)

CAD decreased with respect to the nominal trial cadence in ANTI compared to BASE for both groups. For older subjects IN and ANTI did not differ, while for young subjects BASE > IN > ANTI. CADCV increased with pacing (IN & ANTI) for younger subjects, with no difference between IN and ANTI. Older subjects, on the other hand, demonstrated a higher CADCV for ANTI compared to IN and BASE which were the same. HR was unchanged across conditions. JI was higher for ANTI than B and IN, which did not differ, for younger subjects only; this measure did not change for older subjects across conditions.

Young				
	BASE	IN	ANTI	p
CAD	1.01±0.01*	0.99±0.01*	0.97±0.01*	<0.001
CADCV	4.00±0.39*	11.06±0.43	12.81±0.63	<0.00001
JI	1507.8±185.2	1799.9±204.1	2652.0±299.5*	0.006
HR	2.09±0.05	1.98±0.06	1.92±0.08	0.14
Old				
CAD	1.01±0.01	1.00±0.01	0.97±0.01*	0.004
CADCV	5.00±0.58	4.86±0.58	7.52±0.79*	0.012
JI	1439.9±200.9	1752.0±200.0	1977.5±275.1	0.26
HR	2.22±0.05	2.17±0.05	2.03±0.07	0.093
* different from other conditions				

Table 15 Results by condition

Results by Speed (Table 16)

For IN trials, CAD was sensitive to speed for the older subjects only: they walked slower than the nominal cadence for the fast trials, and faster for the slow trials. CADCV and HR were unchanged for either group. JI increased with speed for both groups.

		IN				**ANTI**			
Young		slow	pref	fast	p	slow	pref	fast	p
	CAD	0.99±0.004	0.99±0.003	0.99±0.005	0.79	1.00±0.02*	0.97±0.01	0.95±0.01	0.02
	CADCV	11.32±0.62	11.06±0.35	10.81±0.49	0.81	12.60±0.87	12.81±0.74	12.02±0.70	0.73
	JI	930.8±510.9*	1799.9±289.6*	4480.4±402.5*	<0.0001	1599.4±591.5**	2652.0±505.7	3767.8±591.5	0.02
	HR	2.04±0.10	1.98±0.05	2.09±0.08	0.52	1.92±0.09	1.92±0.08	1.94±0.07	0.99
Old									
	CAD	1.02±0.01*	1.00±0.01*	0.98±0.01*	<0.001	1.07±0.02*	0.97±0.02	0.95±0.02	<0.0001
	CADCV	4.69±1.04	4.86±0.74	7.32±1.03	0.11	6.27±0.84	7.52±0.82	6.61±0.84	0.55
	JI	829.1±282.2*	1752.0±199.5*	3064.2±277.6*	<0.0001	1655.3±495.8	1977.5±488.0	2834.3±495.8	0.23
	HR	2.20±0.07	2.17±0.05	2.01±0.07	0.11	2.08±0.07	2.03±0.07	2.13±0.07	0.62
* different from other speeds in that condition; ** different from fast speed									

Table 16 Results by speed

For ANTI trials, both groups walked faster in the slow trials than in either preferred or fast trials (which did not differ from each other). However, as for the IN condition, in slow trials the older subjects walked faster than the beat (1.07±0.02), while the younger subjects matched the beat (1.00±0.02). CADCV and HR were unchanged for either group. JI was sensitive to speed for the younger subjects only, as slow > fast.

Drift (Table 17)

	Yes	No	p
Young			
IN	13	112	<0.0001
ANTI	66	32	
Old			
IN	40	78	<0.0001
ANTI	69	24	

Table 17 Drift

All subjects had more trouble walking at the same frequency as the beat (more trials were categorized as Drift = Yes) during ANTI trials than IN (Younger: X^2 (1,223) = 81.8289, p<0.0001; Older: X^2 (1,212) = 34.41346, p<0.0001). Older subjects were worse than younger during IN trials (X^2 (1,246) = 19.863, p<0.0001), but suprisingly were no worse during ANTI (X^2 (1,189) = 0.686, p=0.408). Drift was no different across speeds for either group for both conditions.

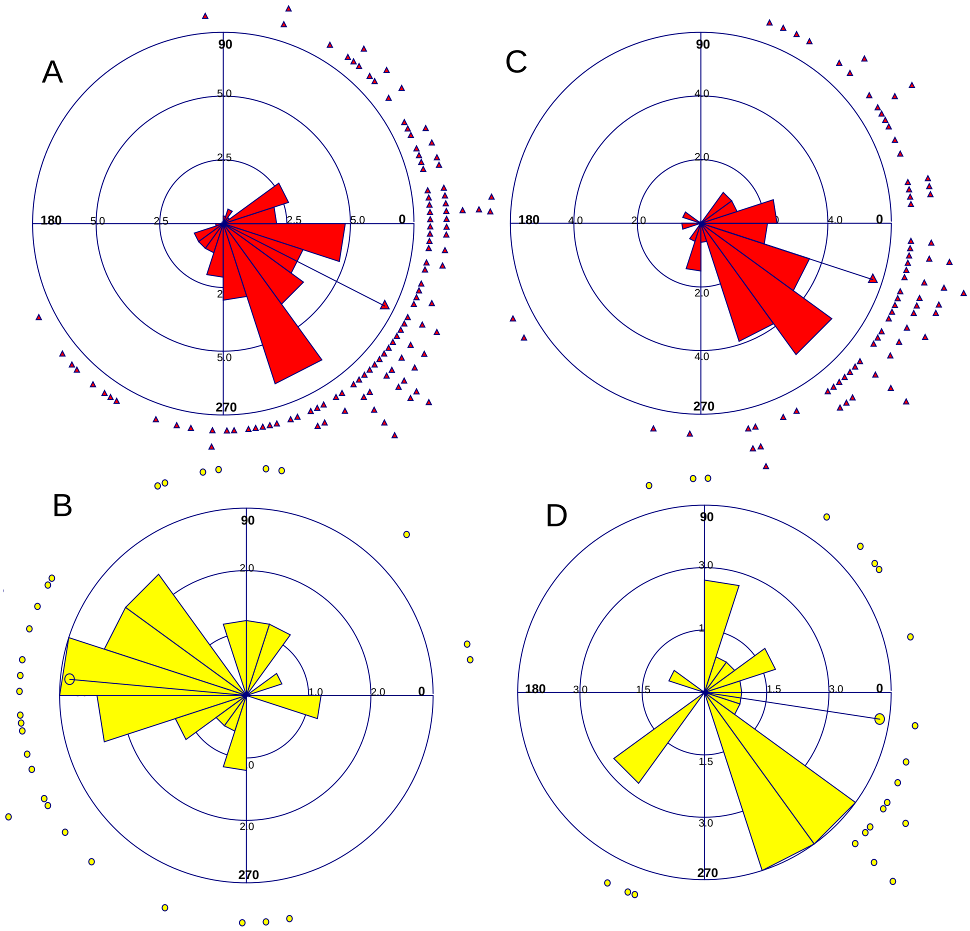
Phase Shift (Table 18, Figure 12)

Because so many subjects had difficulty staying in time with the beat, Drift occurred frequently. Thus we had a limited number of trials suitable for defining an average PS value across a trial, most notably in the anti-phase condition. We have provided the phase shift results in both table and in graph form, in order to best illustrate the circular distributions. For young subjects, PS for IN and ANTI were different at 333.1±51.2° and 174.8±68.1°, respectively (p<0.0001). Strikingly, older subjects' PS results were no different for IN and ANTI at 341.9±47.6° and 351.4±73.2°, respectively (p=0.52). For IN trials, these circular values are equivalent to values of -26.9° (younger group) and -18.1° (older group), indicating negative phase shift (the heel strike preceded the auditory beat). Madison and Merker (2004) and Balasubramaniam et al. (2004) reported negative phase shifts of -28 and -30 ms, respectively, in a 500 ms interval (-20.2° to -21.6° if the interval is defined as a complete 360° phase). However, the small sample sizes for ANTI trials and the large differences between kappa values for both pairs of results means they should be viewed primarily as descriptive.

Young					
		PS (°)	v*	sample	kappa**
	IN	333.1	51.2	112	1.8466
	ANTI	174.8	68.1	32	1.1390
	p	p<0.0001			
Old					
	IN	341.9	47.6	78	2.0674
	ANTI	351.4	73.2	24	0.9888
	p	0.52			
	*v is the circular analog of the linear standard deviation				
**The Watson-Williams F-test assumes that all kappas are equal and that their average is > 1					

Table 18 Phase Shift

During fast trials the beat occurred first, for both groups. The PS values were different for fast compared to slow and pref speeds for younger subjects, while PS values were different for all three speeds for older subjects (Younger: 306.3±43.8°, 323.0±43.8°, and 22.9±32.9°; Older: 305.8±47.6, 333.0 ±34.0, and 29.0±27.9°, for slow, pref and fast speeds respectively).



A. Younger subjects, IN condition (N=114)
B. Younger subjects, ANTI condition (N=30)
C. Older subjects, IN condition (N=79)
D. Older subjects, ANTI condition (N=24)

Figure 12 Phase Shift rose plots

Discussion

Selecting the appropriate methodology in gait research is a challenge in which priorities must be weighed and compromises made. We chose to use a wearable sensor to investigate anti-phase gait in a naturalistic setting, in order to study gait in healthy subjects in as realistic an environment as possible. Replicating what most of us do naturally every day is an advantage for our study results' convenience and realism (and thus its possible relevance for future work). Alternatives include using indoor spaces, such as corridors-- which limit the length of the possible walking time, oval tracks-- which due to curves may affect gait, or treadmills. While the latter don't constrain trial length, they introduce the possibility of affecting gait parameters themselves. The extent to which treadmills alter gait is not without its controversies, but one clear difference from aboveground walking is visual flow, which is known to affect gait (Mohler 2007, Lee & Hidler 2008). We preferred to avoid this possibly confounding factor in this preliminary study, but a comparison between anti-phase gait in aboveground and treadmill walking deserves further investigation.

An additional design decision deserves mention. Our older subjects had higher BMIs, on average, than the younger group. As a result, the 2 groups are not equivalent with respect to BMI, and we included subjects with BMIs as high as 30, although over 25 is considered overweight. Since studies have shown gait differences associated with higher BMI, there is a possibility that this accounts for some of the group differences. However, we consider this unlikely because, except for a loss of power which gave us fewer significant findings, the results didn't change when we excluded subjects with BMIs outside the normal range of 18.5 to 25. In fact, it may be worth investigating in future research how gait is changed in overweight and obese subjects, with respect to challenging paradigms such as anti-phase gait.

We measured cadence and cadence variability with the wearable accelerometer in order to quantify the influence of metronome pacing, both in-phase and anti-phase, on gait. To more fully investigate the changes in gait caused by following the auditory cue, we also calculated the Jerk Index and the Harmonic Ratio from the anterior-posterior acceleration signal. These measures describe the smoothness and consistency of movement.

Regarding cadence frequency, I did not observe the stimulating effect reported by some researchers (Willems et al. 2006 & Wittwer et al. 2013, as described in the previous review section), in which subjects' cadence increased with respect to a beat set at their preferred tempo during in-phase gait. Instead, there was actually a decrease in relative cadence in the in-phase trials, for young subjects only. Recall that the stimulating effect was seen predominantly in the studies with older subjects. It is unclear why, rather than a speeding-up in older subjects, our study revealed a slowing-down in younger subjects. One difference between our study and those which reported the stimulating effect is the fact that ours was conducted outdoors rather than in a controlled, indoor environment. Perhaps the additional sensory input presented an attentional challenge that the two groups resolved in different ways: younger subjects, by allocating more attention to the external environment and slowing down; older subjects, by fixating more on the task. However, this interpretation is speculative. It is reasonable to expect that our healthy older subjects had fewer attentional resources in excess. It is unclear why the two groups responded differently.

Further experiments, with more subjects, might shed some light. Specifically, testing a variety of age groups could help clarify whether there are in fact two responses, which depend on age, or whether this result is an artefact of insufficient statistical power.

Considering cadence across speeds, we see that only older subjects varied in the in-phase condition. They were faster in the slow trials, and slower in the fast trials. During anti-phase trials, both groups were faster in slow trials compared to the other speeds (which didn't differ). However, young subjects successfully matched the pace in slow anti-phase trials, while older subjects were relatively faster. Older subjects thus demonstrated the same pattern for both in-phase and anti-phase trials, tending towards their natural cadence. This behavior may be an indication of the strength of CPGs, together with insufficient attentional resources to resist the body's natural pace. Thus younger subjects, more able to match the metronome frequency even at non-preferred speeds, only exhibited this tendency in the more challenging syncopated condition.

A reduction in cadence variability was expected for young subjects during IN trials compared to unpaced trials, due to the anchoring effect. However, the opposite was seen: cadence variability for young subjects increased for paced (IN and ANTI) compared to unpaced condition. For older subjects, it only increased during ANTI.

Increased variability is not surprising during anti-phase gait, because it is challenging and requires more attention. In fact, this increase has been attributed to the anchoring effect in other syncopated movements (such as the wrist; see Roerdink 2008), since subjects must perform constant error correction to overcome the tendency to synchronize beat and heel strike. In other words, resisting the anchoring effect increases variability. However, it remains unexplained why the young subjects increased their cadence variability during in-phase trials, especially given that older subjects did not. Previous research has revealed a similar phenomenon: Hausdorff et al. (2007) found that healthy subjects demonstrated increased stride rate variability in paced gait. These were older subjects (mean age 64.6 yrs). Generally, we would expect older subjects to have more variable gait, particularly as conditions become more demanding, such as in paced gait.

The study of parameter variability has benefitted from the application of dynamic systems analysis. We understand that considering aspects of physiology and biomechanics as flexible systems provides a powerful paradigm for modeling their complexity. We can appreciate that too much, or too little, variability are both counterproductive to the loosely controlled equilibrium which living organisms must maintain. That said, we must also appreciate that variability is a non-precise measurement. Thus-- to return to the paradigm of paced gait-- it may be possible to discover an infinite number of ways in which variability can be manipulated during gait. In particular, reducing gait variability, in healthy subjects, would be an interesting challenge, and would certainly prove immeasurably useful for furthering our understanding of gait control.

In our testing environment, harmonic ratio was not a sensitive indicator of the differences between synchronized and syncopated gait. This may reflect the fact that, even if subjects did not always walk 'normally', the perturbations were generally right-left symmetrical and consistent over the time course of the trial.

We expected JI to increase for in-phase compared to baseline, since successfully synchronizing a movement to a beat requires manipulating the movement's speed (and acceleration) to maintain synchrony (Balasubramaniam et al., 2004). However, for both groups JI was unchanged for IN trials. We expected a further increase in JI for the ANTI condition as a result of the struggle to resist anchoring to the beat. This increase was seen for young subjects only. Perhaps the consistent jerk values in synchronized gait reflect the fact that, unlike finger tapping, gait consists of a complex series of coordinated movements-- and there is no single limb responsible for the target movement. Recall that the accelerometer is placed at mid-back, which means it is recording jerk of the trunk, which would certainly be attenuated with respect to jerk of a specific limb. Additionally, changes to jerk in gait may be affected somewhat by the coordination constraints of gait, whereas in finger tapping the movement and the measurement are more directly linked.

For IN trials, JI increased as speed increased for both groups. This is an artefact of the increased speed (and acceleration) itself. We would expect the same increase with speed for ANTI trials, but JI increased with speed only in younger subjects, and the difference was less marked. In older subjects, although the values increased similarly, the differences were not significant.
Thus we see that the younger subjects became jerkier during syncopated gait, but the older ones did not. Moreover, the natural increase of JI with speed was less evident in anti-phase gait, particularly for older subjects. Together these results suggest that older subjects reacted to anti-phase gait in a different way than the younger ones.

The variable HR was unaffected by condition or speed. Although commonly referred to in much of the literature as a measure of smoothness or stability, it is more accurately a measure of symmetry (Bellanca 2013). Relatively constant harmonic ratios confirm that step-to-step symmetry does not change in healthy subjects even when they struggle with the challenging anti-phase paradigm. This can be considered a useful finding. Perhaps HR would be sensitive to subclinical (or preclinical) disability on one side of the body only (as might be manifested in transient ischemic attacks, for example). Further work might reveal its relevance as a clinical diagnostic tool.

In a similar vein, comparing the number of trials that 'drifted' informs us that although older subjects were less successful at keeping time in synchronized trials than young subjects, they did equally well in syncopated trials. On a more subjective level, there are two relevant points of information: younger subjects visibly struggled during the anti-phase task more than the older ones, and generally older subjects were more confident about their performance after the experimental session. These facts all add up to a more successful execution of anti-phase gait by the older subjects, in the sense of keeping time with the beat.

The final variable, phase shift, provides actual values for the step relationship to the beat, quantifying how well participants maintained the desired timing (syncopated or synchronized). It seems clear that for both groups the fast trials were simply too fast to maintain the correct relationship with the beat, since the phase shift became positive.

Unlike the older group, younger subjects were capable of making a distinction between in-phase and anti-phase, and their cadence variability increased for the in-phase condition. It may be that these two findings are linked, but it isn't clear how. The idea that excessive variability is counter-productive may be less relevant for younger subjects, who are more capable generally of responding successfully to instabilities and sudden changes while walking. At some unconscious level, therefore, it is conceivable that the younger subjects focused more on the task of synchronizing to the beat, and less on maintaining strongly controlled gait, with the result that they essentially allowed themselves to walk with more variability. Although I find this idea appealing, it is speculative. It also leaves unresolved the issue that they were, in fact, less successful at synchronizing since their step frequency was more varied. Interestingly, the visible physical awkwardness displayed by the younger subjects while walking anti-phase (much more than the older ones) was not captured by any of our measures.

Older subjects-- when they kept the appropriate timing-- walked in phase with the beat. During the anti-phase trials, they struggled more than they had struggled during in-phase, as evidenced by cadence variability and jerk, but only succeeded in maintaining the tempo by synchronizing to the beat. They apparently could not resist the anchoring effect of the auditory cue. However, the observed confidence levels post-test indicate that these subjects were unaware that they had reverted to synchronization.

Conclusions

Summary

The review of in-phase gait led us to expect to see evidence of two specific phenomena: anchoring and stimulation. Anchoring, as reduced variability of movement endpoint, was not observed. The difficulty maintaining syncopation that both groups experienced could be considered in terms of the challenge of resisting the anchoring effect. A stimulation effect was not seen, except in terms of older subjects tending towards their preferred speed in slower trials. Increased variability seems to generally indicate a challenge to less consciously controlled gait. We would expect that the capacity to smoothly adjust movements in response to timing requirements diminishes with age, as extra attentional resources tend to. If the older subjects weren't aware of their failure to maintain syncopation, perhaps their perception of their synchronizing performance was similarly limited: they did their best, but in some way failed to utilize or experience the same corrective feedback information which the younger ones received.

Younger subjects were more obviously perturbed during anti-phase gait, but actually managed to do it, unlike the others. Considering this fact along with their increased variability during in-phase gait, and a possible unifying explanation presents itself. It may be that the two groups differed in degreeof attentional engagement: that indeed they perceived the tasks, and their abilities, differently. This would mean that the younger group was working harder, with a finer awareness of the tasks and a commensurate greater amount of effort. Exactly what this means, and how it would be explored, is tantalizing to consider.

As for evidence of CPGs, we had also speculated that anti-phase gait at preferred speed would be smoother and more successful than at slower or faster speeds. Since CPGs are believed to play a role in many locomotive behaviors, from gait transitions to obstacle avoidance and even backwards walking (Thorstensson 1986; Lacquaniti et al. 2012), we predicted that they would facilitate anti-phase gait at preferred speed. We did not see any differences in the results of the preferred speed trials, such as reduced cadence variability or jerk, or increased harmonic rato, which support this prediction. However, the modest result of gait speed, which reverted closer to preferred speed in the non-preferred speed trials, suggests an influence of CPGs on gait speed. Recall that this was seen more strongly in older subjects, suggesting that this tendency to walk at preferred speed is countermanded by a process with an attentional component. That is, more attentional focus was required than the older subjects had available, either to follow the metronome instead of walking at their preferred, more habitual speed, or alternatively, to actually realize that they were deviating from the metronome speed in favor of their preferred speed.

Limitations

There are several issues which made this project less successful than it might have been. It is important to acknowledge these limitations as lessons learned. Unfortunately the operating system of the PDA would sometimes prioritize its own operations over the accurate timing of the beats, causing first a delayed beat, creating a longer time interval, followed by an anticipatory beat which created a shorter interval. Thus the timing returned to the original, but the subject experienced two anomalous beats.

This issues was not resolvable with the hardware available, although there is evidence that the discrepancies were sometimes large enough to be detectable. Even below the threshold of conscious detection, Repp's 2000 work has shown that even very small timing perturbations are perceived at a subconscious level. As Dr. Repp pointed out (personal communication, 2011), if these discrepancies occur 'randomly' in the subject trials, their net effect would be to increase the variability of the responses. In the anti-phase trials, already difficult, the number of trials in which subjects could not maintain the correct tempo certainly increased.

Another issue was the imprecise recording of preferred cadence from the baseline trials, which became clear when the data was analyzed. This error was due to my inexperience. Having been accustomed to seeing cadence referred to as Hz to one decimal place, I did the same, without taking into account that rounding off was unnecessary and, in fact, greatly limited the precision of the data. The error introduced here means that although the first two baseline trials provide the cadence, when the frequency of these trials is evaluated it is not necessarily equal to precisely one, even though all values are normalized with respect to these very values.

Although the literature review was presented first in this thesis fo the sake of clarity, it was in fact conducted after the research on anti-phase gait. One important finding of the review is the potential usefulness of DFA analysis as a sensitive measure of gait perturbation. Four subject groups in three studies (Hove et al. 2012, Sejdić et al. 2012 and Kaipust et al. 2012) reported no significant changes to spatiotemporal parameters, but the α exponent was decreased in three of them. No differences were revealed for any measures for the fourth group (younger subjects from Kaipust et al. 2012). All other studies reported cueing effects for both spatiotemporal and time series measures. Thus DFA was the most sensitive measure used for detecting the effects of walking to a metronome. However, we did not perform time series analysis because we had not previously been aware of its potential in this area. Future research might well incorporate time series analysis as a parameter in more demanding gait paradigms, to further understand and quantify the

complexities of motor control.
A final limitation was due to our choice of naturalistic setting. Use of a public street certainly provided more distractions than a tranquil lab setting. Furthermore, the extent of these distractions was not held constant over all trials or all subjects. Different times of day meant a large variation in traffic, both pedestrian and vehicular, along with differences of lighting, temperature, and even terrain. Obvious interruptions led to trials being repeated, but with hindsight the attention of the participants was frequently taxed.

Future implications

To explore this possibility of degrees of attentional engagement, and attentional capacity during gait, I would first propose recruiting more subjects, younger, older and a middle demographic. Thus (assuming our results are robust and repeatable) we could learn more about how these changes occur at different ages. And what changes should be identified? At what level of processing might age-related differences become apparent in healthy subjects? From bottom to top, peripheral proprioceptive signals might be weaker; they might be transmitted or received less efficiently, or less effectively processed at the cognitive level. At this highest level, they may be integrated less well. Or outbound signals in this feedback process may function more poorly. And of course, at any point in this theoretical, dynamic locomotor process, which at the subcortical level may comprise solely CPGs, attentional demands may have a detrimental influence, in the sense that other events or processes may reduce the amount of attention necessary. Adding the quantification of dynamic processes during or gait tasks, by means of time series analysis such as DFA, might prove useful going forward.
These speculations present the possibility of continuing with a paradigm that could elucidate aspects of locomotion, and help us understand more about the role CPGs play, and how their automaticity can be exploited to help the frail elderly or those with movement pathologies.

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