

**MUSIC TRAINING AND FUNCTIONAL GAIT PERFORMANCE IN
PARKINSON'S DISEASE**

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Dedication

This thesis is dedicated to Mick.

Abstract

Music is a powerful stimulus for movement. This thesis examined the effects of music on walking performance. First, the effect of music salience (familiarity and enjoyment) and tempo on walking performance was examined amongst healthy young adults. Subsequently, the safety and efficacy of incorporating salient music into a comprehensive walking program was investigated amongst people with mild to moderate Parkinson's disease (PD). Music was found to be effective in influencing walking performance; furthermore the magnitude of change was influenced by the salience of music to the listener. Walking performance and motor symptom severity were significantly improved amongst people living with PD following a 13-week music-accompanied walking program. These findings imply that music may be a safe, effective, and enjoyable alternative to the traditional auditory cues currently used in gait rehabilitation programs. These results also have implications for intervention participation and adherence and as a consequence patient mobility and quality of life.

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Table of Contents

	Page
List of Tables	x
List of Figures	xi
List of Abbreviations	xii
Chapter 1: General Introduction	1
1.1. Parkinson's Disease	2
1.1.1 A brief history	2
1.1.2 Clinical symptoms	5
1.1.3 Dopamine and dopaminergic pathways	8
1.1.4 The basal ganglia	9
1.1.5 Aetiology	16
1.1.6 Treatment	18
1.2. Gait	21
1.2.1 Parkinsonian gait	24
1.2.2 Gait and cognition	26
1.2.3 Dual-task costs	28
1.2.4 Strategies to reduce dual-task gait deficits	30
1.2.5 Obstacle Negotiation.	33
1.3. The Power of Music	39
1.3.1 Perceptual characteristics of music	39
1.3.2 Therapeutic potential of music	43
1.3.3 Speculated mechanisms of auditory-motor coupling	45
1.4. Summary	47
Chapter 2: Objective of Thesis	49
2.1. Theory	49
2.2. Objective	49
2.3. Experiments	49
2.3.1 Experiment 1: Music salience influences the gait performance of young adults	49
2.3.2 Experiment 2: Walking with music is a safe and viable tool for gait training in PD: The effect of a 13-week feasibility study on single- and dual-task walking.	50
2.3.3 Experiment 3: Training-related changes to obstacle crossing gait performance amongst people with PD	50

Chapter 3: Music salience influences the gait performance of young adults	52
3.1 Abstract	52
3.2 Introduction	53
3.3 Methods	56
3.3.1 Subjects	56
3.3.2 Protocol	58
Study 1: Music	58
Study 2: Cue frequency	58
3.3.3 Cues	61
Study 1: Music	63
Study 2: Cue frequency	63
3.3.4 Apparatus	63
3.3.5 Data Processing	63
3.3.6 Statistical Analysis	64
Study 1: Music	64
Study 2: Cue frequency	64
3.4 Results	65
3.4.1. Study 1: Music	65
3.4.2. Study 2: Cue frequency	68
3.5 Discussion	71
3.6 Conclusions	73
Chapter 4: Walking with music is a safe and viable tool for gait training in Parkinson's disease: The effect of a 13-week feasibility study on single- and dual-task walking	74
4.1 Abstract	74
4.2 Introduction	75
4.3 Methods	77
4.3.1 Subjects	77
4.3.2 Ethics statement	78
4.3.3 Intervention	78
4.3.4 Pre- and post-intervention assessment	78
4.3.5 Music	81
4.3.6 Apparatus	81
4.3.7 Outcome measures	82
4.3.8 Data processing	83
4.3.9 Statistical analysis	83
4.4 Results	84
4.4.1 The effect of task on gait parameters	87
4.4.2 The effect of intervention on outcome measures	91

4.4.3 Feasibility of intervention	92
4.5 Discussion	93
4.5.1 Limitations	95
Chapter 5: Training-related changes to obstacle crossing gait performance amongst people with Parkinson’s disease	98
5.1 Abstract	98
5.2 Introduction	99
5.3 Methods	100
5.3.1 Subjects	101
5.3.2 Procedures	101
5.3.3 Apparatus	104
5.3.4 Intervention	104
5.3.5 Music	105
5.3.6 Outcome measures	105
5.3.7 Data processing	107
5.3.8 Data analysis	107
5.4 Results	108
5.5 Discussion	113
Chapter 6: General Discussion	117
6.1 Music Salience Influences Gait Performance	119
6.2 Salient Music is a Safe and Efficacious Tool for Gait Training in PD	123
6.3 Music-accompanied Gait Training Influences Complex Gait Activities in PD	127
6.4 Implications of Results	130
6.5 Therapeutic Implications	133
6.6 Future Research	135
6.7 Limitations	137
6.8 Conclusion	139
Bibliography	142

List of Tables

		Page
Table 3.1	Subject demographics	57
Table 3.2	Example of cue tempi	62
Table 3.3	Summary of tempo data and enjoyment scores	69
Table 4.1	Subject demographics and clinical characteristics at baseline	86
Table 4.2	Summary of descriptive statistics and change scores for CTRL group	88
Table 4.3	Summary of descriptive statistics and change scores for MUSIC group	89
Table 5.1	Subject characteristics at baseline	109

List of Figures

		Page
Figure 1.1	Illustration of posture of typical and atypical PD patient	4
Figure 1.2	Illustration indicating location of the basal ganglia	7
Figure 1.3a	Schematic of direct and indirect pathways through the normal basal ganglia-thalamocortical circuit	12
Figure 1.3b	Schematic of direct and indirect pathways through the parkinsonian basal ganglia-thalamocortical circuit	13
Figure 1.4	Schematic of events and phases of a single gait cycle	23
Figure 1.5	Schematic of the spatial measures and phases of obstacle negotiation	36
Figure 1.6	A schematic representation of the organisation of the musical brain	42
Figure 3.1	Experimental design	60
Figure 3.2	Effect of cue modality on spatiotemporal parameters of gait	67
Figure 3.3	Effect of cue frequency on spatiotemporal parameters of gait	70
Figure 4.1	Experimental design	80
Figure 4.2	Study flow chart	85
Figure 4.3	Effect of intervention on gait parameters in single- and dual-task conditions	90
Figure 5.1	Experimental design for pre- and post-intervention gait assessments	103
Figure 5.2	Example of steps for obstacle negotiation trials	106
Figure 5.3	Effect of intervention on spatiotemporal parameters of the approach, crossing and recover steps of obstacle negotiation	112

List of Abbreviations

ABC	Activities-specific Balance Confidence scale
ACh	Acetylcholine
AP	Anterior-posterior
BPM	Beats per minute
COM	Centre of mass
CS	Crossing step
CTRL	Control group
DA	Dopamine
DBS	Deep brain stimulation
DLS	Double limb support
Enk	Enkephalin
F	Female
FL	Frontal lobe
GABA	Gamma-aminobutyric acid
GABS	Gait and Balance Scale
Glu	Glutamate
GPe	Globus pallidus external
GPi	Globus pallidus internal
HG	Heschl's gyrus
H&Y	Hoehn and Yahr
INS	Insula
LAS	Lead approach step
LS	Limbic system
M	Male
MAO	Monoamine oxidase
MC	Motor cortex
MET	Metronome
MLR	Mesencephalic locomotor region

MMSE	Mini-Mental Status Examination
MTG	Middle temporal gyrus
MUS	Music
MUSIC	Experimental group
NC	No cue
NSM	Non-salient music
OBS	Obstacle
PAC	Primary auditory cortex
PD	Parkinson's disease
PDQ-39	Parkinson's Disease Questionnaire-39
PL	Parietal lobe
PMC	Primary motor cortex
PPN	Pedunculopontine nucleus
PT	Planum temporal
RAS	Rhythmic auditory stimulation
RM-ANOVA	Repeated-Measures Analysis of Variance
RS	Recovery step
SLICE	Stepwise limit cycle entrainment
SM	Salient music
SMA	Supplementary motor area
SNe	Substantia nigra pars compacta
SNr	Substantia nigra pars reticulata
SP	Substance P
SPSS	Statistical Package for the Social Sciences
STG	Superior temporal gyrus
STN	Subthalamic nucleus
T	Time
Ta	Task
TAS	Trail approach step

TP	Temporal pole
UPDRS	Unified Parkinson's Disease Rating Scale
VA	Ventral anterior thalamus
VLa	Ventral lateral thalamus
VTA	Ventral tegmental area

Every disease is a musical problem; every cure is a musical solution.
Georg Philipp Friedrich von Hardenberg (Novalis).

Chapter 1: General Introduction

Parkinson's disease (PD) is a neurodegenerative disease that affects more than one million individuals in North America, a number that is expected to double over the next two decades as the population ages (Dorsey et al., 2007). The disease is characterised by tremor, muscle stiffness, slowness of movement and difficulties with balance and walking. The gait disturbances associated with the disease are commonly identified as one of the most debilitating aspects of PD and are associated with an increased risk of falls (Grimbergen, Munneke, & Bloem, 2004; Stolze et al., 2004), loss of functional independence (Grimbergen et al., 2004; Shulman et al., 2008), decreased quality of life (Asimakopoulos et al., 2008; Fitzsimmons & Bunting, 1993; Soh, Morris, & McGinley, 2011) and an increased need for institutional care (Hely et al., 1999; Temlett & Thompson, 2006). Furthermore, gait impairments typically remain resistant to medication therapies (Blin, Ferrandez, Pailhous, & Serratrice, 1991; Rascol et al., 2003), which has led to the development of rehabilitation interventions directed towards the management of gait disorders in PD. Whilst gait rehabilitation programs that incorporate rhythmic auditory cues, such as a metronome tone or rhythmically accentuated music have been shown to be effective in improving gait performance amongst people with PD (Bryant, Rintala, Lai, & Protas, 2009; Lim et al., 2005; Nieuwboer et al., 2007; Rochester et al., 2010) the benefits are typically short-lived, necessitating long-term engagement in the program. Yet, despite the recognised benefits of exercising exercise participation and adherence remains low amongst those with PD potentially limiting the benefits of 'traditional' rehabilitation interventions. Interestingly, promising research has shown that the inclusion of

appropriately selected music in an exercise program can encourage exercise participation and adherence (Bauldoff, Hoffman, Zullo, & Scieurba, 2002; Johnson, Otto, & Clair, 2001; Karageorghis & Terry, 1997). Given the inherent rhythmicity of music in addition to the emotional and motivational qualities of rhythm and music, it is feasible that salient (familiar and enjoyable) contemporary music may be an attractive alternative to traditional auditory cues for inclusion in long-term gait rehabilitation interventions. The purpose of this thesis was to initially investigate the effect of music on walking performance, with a second aim of examining the potential of using salient contemporary music as a gait training tool amongst people with mild to moderate severity PD.

The aim of this introduction is to outline the focus of this thesis. The literature review which follows is organised into three main sections. The first section presents brief background information on PD, including its history, associated symptoms and aetiology, and current treatment options for people with PD. The following section will provide an overview of parkinsonian gait, the role of cognition in gait, and current strategies used by people with PD to alleviate gait deficits. The final section of the literature review will describe the perceptual qualities of music, the therapeutic potential of music, and speculated mechanisms through which rhythm and music may influence human movement.

1.1. Parkinson's Disease

1.1.1. A brief history. Parkinson's disease is a chronic, progressive neurodegenerative disease that was first precisely described by James Parkinson in his 1817 monograph *An Essay on the Shaking Palsy* in which the British doctor, geologist, and palaeontologist reported on his observations of six individuals with PD

(Parkinson, 1817). Parkinson (1817) identified and described the progressive nature and symptoms of the disease. Over 50 years following *An Essay* French neurologist Jean-Martin Charcot refined the clinical description of the disease, differentiating the cardinal feature of bradykinesia from weakness and recognising that people with PD need not display tremor. Furthermore, Charcot was successful in differentiating PD from other tremor dominant diseases. He observed that the patients who displayed a resting tremor also had rigidity, bradykinesia, and a distinctive hunched posture (Figure 1.1; Goetz, 2011). In recognition of these distinctions and James Parkinson's contributions to the description of the disease, Charcot coined the term "maladie de Parkinson" or "Parkinson's disease" to replace the previous labels of *paralysis agitans* or *shaking palsy*. It took until the early twentieth century for the Russian neuropathologist Konstantin Tretiakoff to link the degeneration of pigmented cells in the substantia nigra to the development of PD, work that was subsequently confirmed by Rolf Hassler in the 1930's (Lees, Selikhova, Andrade, & Duyckaerts, 2008). During the 1950's a major piece of the puzzle was uncovered when Swedish Nobel laureate, Arvid Carlsson identified the neurotransmitter dopamine (DA) and its associated role in PD (Fahn, 2008). These foundational works have not only provided a description of the clinical characterisation of the disease, but have provided the groundwork for the development of the pharmaceutical interventions that are still used to this day in the symptomatic management of PD.



Figure 1.1 An illustration from Charcot's original lesson (June 12, 1888) contrasting a typical PD patient and the flexed posture (left) and an atypical variant of PD (right)

(Goetz, 2011).

1.1.2. Clinical symptoms. Parkinson's disease is reported to be the second most common neurodegenerative disorder after Alzheimer's disease; afflicting millions of people worldwide including an estimated 100,000 individuals in Canada (Parkinson Society Canada, n.d.). Over the next two decades as the population ages and the first 'baby boomers' become seniors the prevalence of neurodegenerative diseases such as PD is expected to more than double (Dorsey et al., 2007).

The diagnosis of PD is predominantly based upon clinical and neurological examination of the patient as opposed to imaging or diagnostic tests. The cardinal motor symptoms of PD are rest tremor, rigidity, and bradykinesia (slowness of movement) or akinesia (absence of movement). Postural instability is typically identified as the fourth classical motor symptom; however, this feature may not develop until later stages of the disease. Clinical diagnosis of PD requires that two out of the three cardinal motor symptoms are present, that there is unilateral or asymmetrical onset of motor symptoms, and a strong, sustained response to anti-parkinsonian drug (levodopa) administration (Gelb, Oliver, & Gilman, 1999; Rao, Hofmann, & Shakil, 2006).

Tremor is the most frequent and apparent motor symptom of PD, occurring in approximately 70% of people with the disease (Hoehn & Yahr, 1967; Jankovic, 2008). Tremor involves a rhythmic movement of the limbs, jaw, lips, face and/or trunk. In PD the tremor typically presents at rest, although action and/or postural tremor may develop with disease progression (Koller, Vetere-Overfield, & Barter, 1989; Lance, Schwab, & Peterson, 1963).

Rigidity describes the stiffness and resistance to passive movement that is often experienced in limb and axial musculature of people living with PD (Jankovic,

2008). Axial rigidity has been identified as a contributing factor to the stooped posture that is characteristic of PD (Figure 1.1).

The third cardinal motor symptom, bradykinesia, is one of the defining features of PD. The signs of bradykinesia can be subtle in the early stages of PD, being expressed in problems such as hypophonia (weak voice), hypomimia (reduced facial expression), micrographia (small, cramped handwriting), dysphagia (difficulty swallowing), and reduced arm swing. In advanced stages of the disease bradykinesia may be manifested in freezing of gait (inability to initiate or maintain locomotion or perform a turn), a symptom that is closely intertwined with the high incidence of falls experienced in people with PD (Bloem, Hausdorff, Visser, & Giladi, 2004). Postural instability typically develops several years following the onset of initial symptoms (Jankovic, 2008) and is exhibited in the impairment of postural reflexes potentially leading to falls and gait difficulties in advanced stages of the disease.

Whilst PD is primarily characterised as a motor disorder, people with PD will also experience a spectrum of autonomic, cognitive, affective and sensory impairments resulting from the involvement of multiple functional and neurotransmitter systems in the pathology of the disease. The characteristic motor symptoms of PD are considered to result from the dopaminergic deafferentation of the basal ganglia, a collection of subcortical nuclei that reside in the basal forebrain (Figure 1.2).

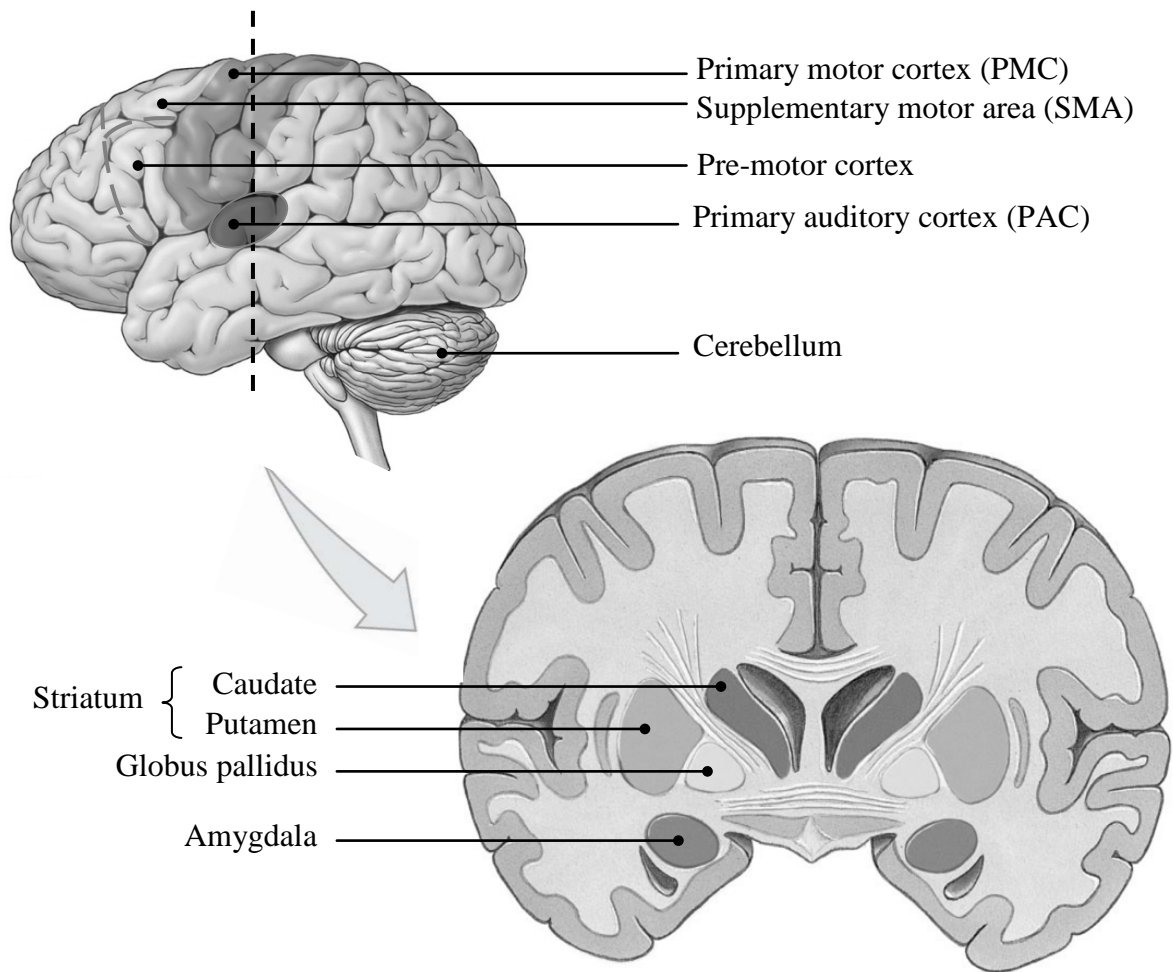


Figure 1.2 Illustration detailing the location of the basal ganglia, cerebellum, primary motor cortex (PMC), supplementary motor area (SMA), pre-motor cortex and primary auditory cortex (PAC) (adapted from Martini, Nath, & Bartholomew, 2011).

1.1.3. Dopamine and dopaminergic pathways. Dopamine, a monoamine neurotransmitter contributes to many diverse and critical nervous system functions in the human body via regulation of neurotransmission that is facilitated by glutamate and gamma-aminobutyric acid (GABA). Central nervous system functions of DA include the modulation of voluntary movement, affect, reward, attention, sleep, and learning whilst in the periphery DA plays a role in numerous physiological functions such as hormone regulation and sympathetic regulation (Beaulieu & Gainetdinov, 2011; Carlsson, 2001; Iverson & Iversen, 2007).

Dopaminergic neurons comprise less than one percent of the brain's neuronal population yet the distribution of dopaminergic neurons in the brain is widespread with the majority of DA neurons originating from two main sources; the ventral tegmental area (VTA) and the substantia nigra pars compacta (SNc). Four major dopaminergic pathways have been identified in the brain; the nigrostriatal, mesolimbic, mesocortical and tuberoinfundibular pathways. The nigrostriatal pathway connects the substantia nigra with the striatum in the basal ganglia motor loop, this pathway is implicated in motor control and will be described in more detail in the subsequent section (section 1.1.4) as the loss of DA secreting neurons in the SNc has been identified as one of the major pathological features of PD. The dopaminergic pathway projecting from the VTA in the midbrain is known as the mesolimbic pathway. The mesolimbic pathway connects to the limbic system via the nucleus accumbens in the striatum, with extensive dopaminergic projections to the amygdala, hippocampus and septum in addition to the medial prefrontal cortex. The mesolimbic pathway is widely considered to be important for both memory and motivating behaviours and is also thought to contribute to the fine-tuning of motor functions. The mesocortical pathway is closely associated with the mesolimbic pathway and also

originates in the VTA and projects to the prefrontal, cingulate and perirhinal cortex. The mesocortical pathway is thought to be critical to normal cognitive function as well as emotional and motivational responses. Due to the overlap in anatomy and function of the mesolimbic and mesocortical pathways the pathways are often communally identified as the mesocorticolimbic system. The final major dopaminergic pathway that has been identified is the tuberoinfundibular pathway which travels from the arcuate nucleus in the hypothalamus to the pituitary gland, where it regulates the secretion of hormones such as prolactin (Iversen, Iversen, Dunnett, Bjorklund, 2010).

1.1.4. The basal ganglia. The basal ganglia comprises a group of four functionally related and interconnected nuclei that play a key role in the control of normal voluntary movement, as well as skeletomotor, oculomotor, cognitive and potentially emotional functions (Kopell, Rezai, Chang, & Vitek, 2006; Yelnik, 2002). The capacity of the basal ganglia to influence such a range of behaviours results from their role in a number of functionally and anatomically distinct basal ganglia-thalamocortical circuits. The most relevant of these pathways to the discussion of PD in this thesis will be the motor circuit, although it is recognised that the heterogeneous symptomatic profile of PD does support the suggestion that multiple additional basal ganglia-thalamocortical pathways (i.e. cognitive and limbic; Lewis & Barker, 2009) may be affected in PD.

The four principle nuclei of the basal ganglia are the striatum, globus pallidus, subthalamic nucleus (STN), and substantia nigra (consisting of the pars reticulata, SNr and the pars compacta). The striatum comprises two anatomical subdivisions; dorsal striatum (the caudate nucleus and putamen) and ventral striatum (nucleus accumbens and olfactory tubercle). The striatum forms the main input structure in the basal

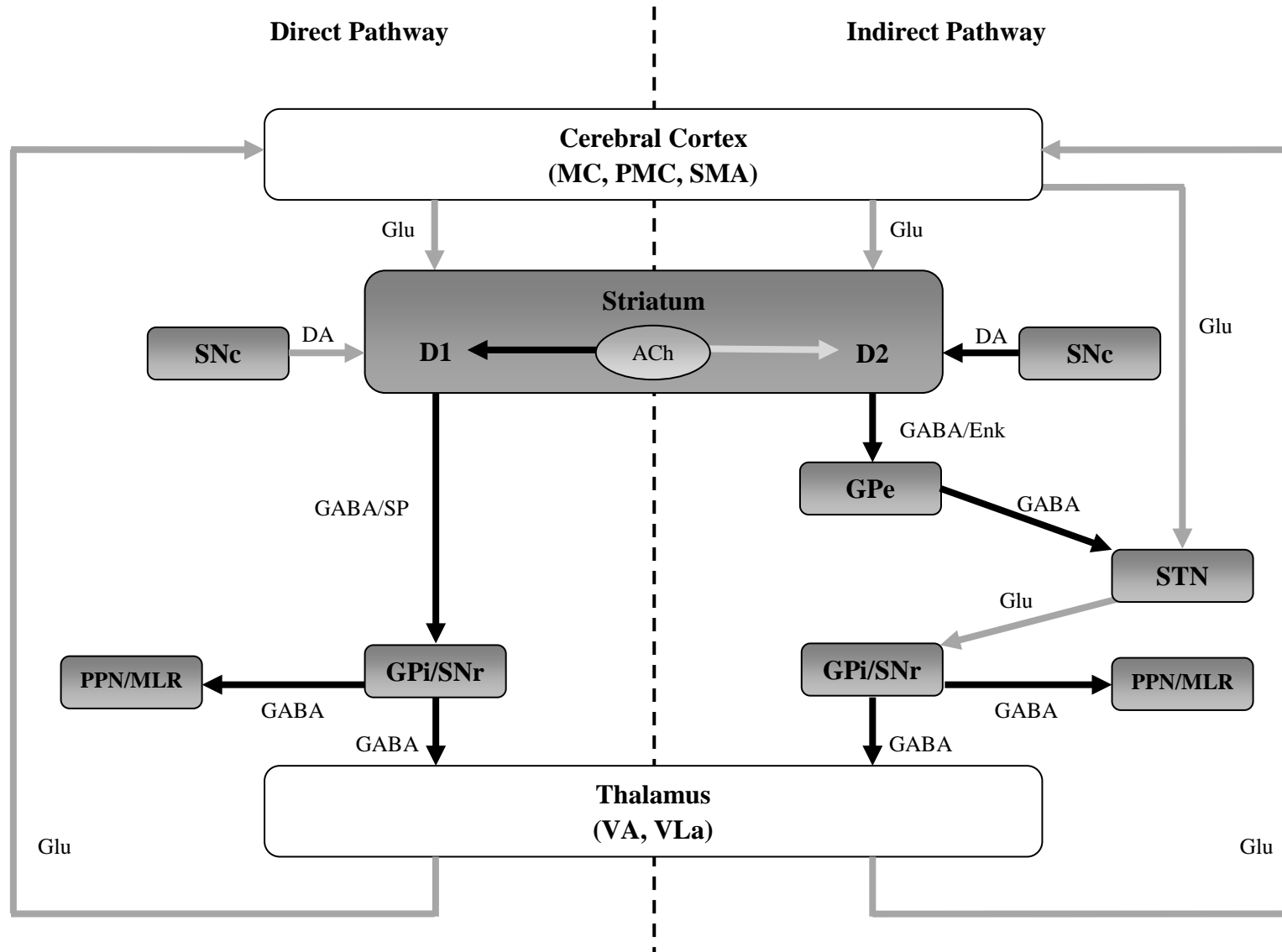
ganglia, receiving projections from diverse regions of the cortex, as well as the thalamus, and SNc. Striatal efferents project to both segments of the globus pallidus (internal, GPi and external, GPe) and to the SNr. The GPi and SNr are morphologically very similar and are considered the major output structures of the basal ganglia, projecting back to the cortex (via the ventral anterior (VA) and ventral lateral (VL) nuclei of the thalamus), with a smaller projection to the pedunculopontine nucleus (PPN) and mesencephalic locomotor region (MLR). The pars compacta region of the substantia nigra contains pigmented dopaminergic cells that project to the striatum (Rothwell, 2011; Yelnik, 2002).

As previously stated, one of the many roles of the basal ganglia is considered to be the facilitation of purposeful and appropriate movements and the inhibition of unwanted and inappropriate movements (Alexander, 1994). This duality is achieved through the intrinsic connectivity of the basal ganglia. Initially, glutamatergic corticostriatal projections cause excitation of striatal medium spiny neurons. The striatum subsequently controls the activity of the output nuclei of the basal ganglia via two separate and opposing neuroanatomical pathways - the direct and indirect pathways. The pathways originate at two distinct subpopulations of striatal neurons that function to modulate the thalamic output to the motor cortex. The direct pathway is composed of inhibitory (GABAergic) striatopallidal and striatonigral projections which use substance P (SP) as a co-transmitter. The projections from the GPi and SNr are also GABAergic and therefore inhibitory, producing disinhibition of thalamic neurons, thereby increasing thalamocortical activity and facilitating voluntary movement (Alexander, 1994). In contrast, the indirect pathway is comprised of inhibitory GABAergic projections from the striatum to the GPe (co-transmitter is enkephalin, Enk), and then the STN, which becomes disinhibited and increases

activity. The increase in excitatory (glutamatergic) discharge from the STN excites cells in the GPi and SNr, ultimately increasing inhibitory outflow from the GPi and SNr onto the thalamus. Output to the motor cortex is therefore decreased resulting in a reduction in voluntary movement (Figure 1.3a) (Alexander, 1994).

In a normal functioning system, the direct and indirect pathways are modulated by dopaminergic and cholinergic inputs. Diffuse dopaminergic inputs to the striatum are provided by the SNc. Dopamine provides an excitatory effect to the striatal neurons (D1 type dopaminergic receptors) of the direct pathway and an inhibitory influence to the striatal neurons (D2 type dopaminergic receptors) of the indirect pathway. Despite the difference in actions at the synapse, the dopaminergic input to the direct and indirect pathways ultimately facilitates movement through the disinhibition of thalamocortical neurons (Figure 1.3a). The population of cholinergic interneurons in the striatum synapse on the GABAergic striatopallidal neurons. The cholinergic inputs to the striatal neurons have the opposite effect on motor activity to those of DA, with the cholinergic interneurons inhibiting the striatal cells that form direct pathway and exciting the striatal cells that form the indirect pathway. Therefore the overall effect of the striatal cholinergic interneurons is to inhibit movement through the inhibition of thalamocortical neurons (Figure 1.3a).

(a)



(b)

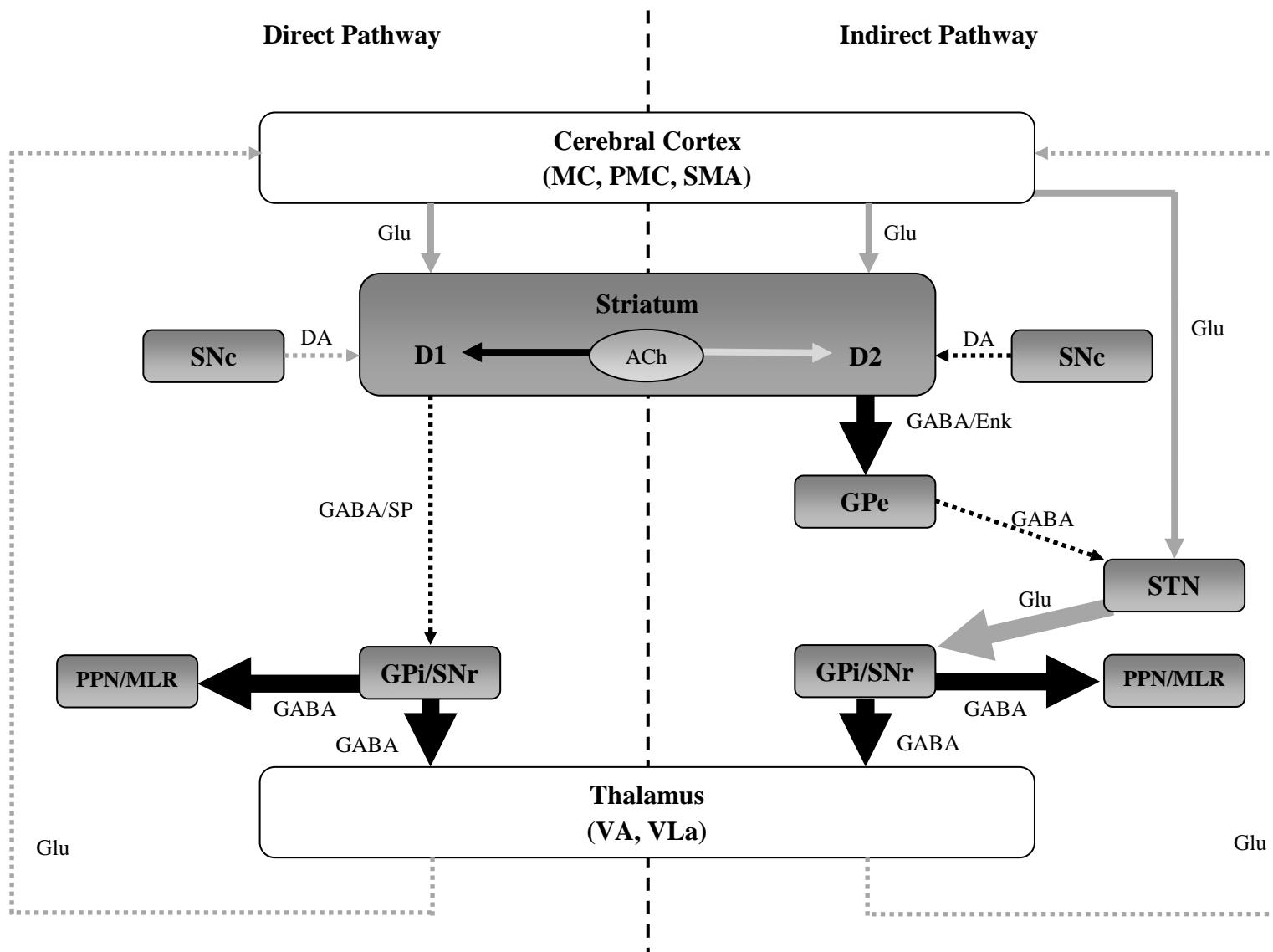


Figure 1.3 Schematic representation of the direct and indirect pathways through the (a) normal and (b) parkinsonian basal ganglia-thalamocortical circuit. Excitatory connections are shown by grey arrows; inhibitory connections are shown by black arrows. In (b) solid thick arrows indicate increased activity; dashed thin arrows indicate decreased activity. ACh = acetylcholine; DA = dopamine; Enk = Enkephalin; GABA = gamma-aminobutyric acid; Glu = glutamate; GPi = globus pallidus internal; GPe = globus pallidus external; MC = motor cortex; MLR = mesencephalic locomotor region ; PMC = primary motor cortex; PPN = pedunculopontine nucleus; SMA = supplementary motor area; SNc = substantia nigra pars compacta; SNr = substantia nigra pars reticulata; SP = Substance P; STN = subthalamic nucleus; VA = ventral anterior thalamus; VL_a = ventral lateral thalamus.

PD is the most common and well-studied disease of the basal ganglia. PD results from the progressive degeneration of dopaminergic neurons in the SNc and other brainstem regions, ultimately resulting in striatal DA deficiency and a resultant imbalance in both the direct and indirect pathways. The direct pathway loses the excitatory effect of the DA to the striatal neurons, decreasing the activity of the pathway with a decrease in inhibitory outflow from the striatum to the output nuclei and a resultant increase in inhibitory outflow to the thalamic nuclei, ultimately reducing motor activity (Figure 1.3b). Furthermore, the reduction in dopaminergic facilitation to the direct pathway is compounded by unopposed inhibition of striatal cells by the cholinergic interneurons. Conversely, activity in the indirect pathway is increased. The inhibitory effect of DA on the striatal neurons of the indirect pathway is reduced leading to an increase in inhibitory discharge to the GPe which in turn produces disinhibition of STN neurons. The subsequent increase in excitatory discharge from the STN again activates the GPi and SNr leading to an increase in inhibitory outflow to the thalamus. In addition, the loss of dopaminergic inhibition to the indirect pathway is exacerbated by the unimpeded excitatory actions of the striatal cholinergic interneurons that drive the indirect pathway. Therefore, the loss of striatal DA ultimately results in an overall abnormal increase in firing activity of the output nuclei, leading to increased inhibition of thalamocortical and brainstem (PPN and MLR) systems (Figure 1.3b; DeLong & Wichmann, 2007; Wichmann & DeLong, 2003) and inhibition of voluntary movement, clinically expressed as bradykinesia and akinesia.

Motor symptoms are typically not detected until striatal DA depletion exceeds 50 percent (Fearnley & Lees, 1991; Gaig & Tolosa, 2009). Initially DA loss is thought to be fairly limited to the posterior putamen, a region of the striatum that is considered

to be involved in sensorimotor processing. It is this DA loss in the posterior putamen that is considered to result in the appearance of early motor symptoms. With disease progression DA loss becomes more widespread affecting other regions of the basal ganglia as well as additional structures such as the cortex, thalamus and hypothalamus (Rothwell, 2011). Nigrostriatal pathway degeneration in PD has also associated with the accumulation of the protein alpha-synuclein in the hypothalamus, motor nuclei of the cranial nerves and the autonomic nervous system (Olanow & Tatton, 1999). The development of non-motor signs and symptoms with disease progression are theorised to result from the spread of neuronal degeneration to nondopaminergic systems (Rothwell, 2011).

1.1.5. Aetiology. Idiopathic PD is thought to be multi-factorial in origin. The pathogenetic mechanisms that contribute to nigrostriatal cell death in PD have yet to be fully elucidated but are considered to include oxidative stress, abnormal protein processing, mitochondrial stress, apoptosis, and inflammation (Huang, de la Fuente-Fernandez, & Stoessl, 2003; Schapira, 2006). These mechanisms are presumed to be triggered by a combination of genetic, environmental and endogenous factors and their influence on the developing and aging brain (Feldman & Ratner, 1999; Gorell, Peterson, Rybicki, & Johnson, 2004; Seidler et al., 1996).

The discovery of familial forms of parkinsonism has advanced our understanding of the pathogenesis of PD considerably. Parkinson's disease has now been credibly linked to 28 distinct chromosomal regions, with six of these regions (alpha-synuclein, parkin, UCHL1, DJ1, PINK1, and LRRK2) having been demonstrated to conclusively cause monogenic PD (Klein & Westenberger, 2012). These genetic mutations are thought to account for only a small portion (~10 percent) of all cases of PD (Thomas & Beal, 2007), however, even in idiopathic cases of PD

(i.e. cause of disease is unknown) a family history of the disease is associated with an increased risk of developing PD (Lazzarini et al., 1994). It is possible however, that this theorised link with family history may be indicative of a shared living environment as opposed to shared genetics (Calne et al., 1987).

Indeed, the potential role of environmental factors in the aetiology of PD has been suggested in a number of epidemiological studies. Potential environmental risk factors for PD are thought to include prolonged environmental or occupational exposure to specific metals (i.e. copper, lead, mercury, manganese; Coon et al., 2006; Gorell, Rybicki, Cole Johnson, & Peterson, 1999), pesticides (Ascherio et al., 2006; Gorell, Johnson, Rybicki, Peterson, & Richardson, 1998; Menegon, Board, Blackburn, Mellick, & Le Couteur, 1998; Priyadarshi, Khuder, Schaub, & Shrivastava, 2000), solvents (Pezzoli et al., 1995), well-drinking water (Gorell, et al., 1998), rural living (Ferraz, Andrade, Tumas, Calia, & Borges, 1996; Gorell, et al., 1998), high fat (Logroscino et al., 1996) and high dairy diets (Wirdefeldt, Adami, Cole, Trichopoulos, & Mandel, 2011) and occupation (i.e. carpenters, cleaners, teachers, medical workers, forestry, logging, mining; Fall, Fredrikson, Axelson, & Granerus, 1999; Tsui, Calne, Wang, Schulzer, & Marion, 1999). As indicated previously environmental and genetic risk factors are not mutually exclusive, with an individual's genetic profile predisposing them to be more or less vulnerable to particular environmental toxins and exposures.

Advancing age is the single largest independent risk factor for the development and progression of PD (Mayeux, 2003). The incidence of PD rises sharply with increasing age, from 17.4 in 100, 000 person years in the sixth decade of life to 93.1 in 100, 000 person years in the eighth decade (Bower, Maraganore, McDonnell, & Rocca, 1999). The median age of onset is approximately 60 years of

age, however, it should be noted that PD is not limited to individuals approaching their senior years with 4 to 10% of cases of PD occurring before the age of 45 (Van Den Eeden et al., 2003).

Epidemiological studies have not only been critical to the identification of possible causative factors for PD, they have also been instrumental in indentifying a number of factors that potentially protect against the development of the disease. Indeed, the risk of developing PD has been inversely associated with caffeine consumption (Popat et al., 2011; Singh et al., 2010; Xu, Xu, Chen, & Schwarzschild, 2010), cigarette smoking (Fratiglioni & Wang, 2000; Riveles, Huang, & Quik, 2008; Singh, et al., 2010), and non-steroidal anti-inflammatory drug intake (Manthripragada et al., 2011; Rees et al., 2011). Increasingly, evidence is also suggesting that exercise may provide neuroprotection against symptom onset in PD (Ahlskog, 2011; Al-Jarrah & Jamous, 2011; Fisher et al., 2004; Hirsch & Farley, 2009; Lau, Patki, Das-Panja, Le, & Ahmad, 2011; Petzinger et al., 2010; Tajiri et al., 2010). The proposed mechanism for this benefit is that cell survival and new cell growth are stimulated by the up-regulating of neurotrophic factors and the increased cerebral oxygenation that result from exercising (Dishman et al., 2006). The identification of potential preventative factors has important implications for the future prevention and treatment of PD.

1.1.6. Treatment. Despite the recent identification of a number of potential neuroprotective factors for the development of PD, at this point in time there is no permanent cure to replenish the depleted dopaminergic neurons. The available treatments for PD do not change the course of the disease, but instead provide symptomatic relief, improving functional capacity and quality of life.

Dopamine replacement and enhancement therapies have been the ‘gold standard’ treatment for PD since their introduction in the early 1960’s. These pharmacotherapeutic treatments intend to replace or augment diminished striatal DA and potentially also work in other DA depleted regions of the brain. The DA precursor 3, 4-dihydroxy-L-phenylalanine (levodopa) was one of the first drugs to be introduced for the treatment of PD. Levodopa is metabolised into DA both peripherally and centrally, ultimately ameliorating tremor, rigidity and bradykinesia. It has been found however, that the peripheral conversion of levodopa causes cardiovascular risks in addition to adverse gastrointestinal and autonomic side effects (Fernandez, 2012). This predicament has been addressed by the development of combination therapies in which an enzyme inhibitor is combined with levodopa. The enzyme inhibitor is not able to cross the blood-brain barrier and is therefore able to block the peripheral conversion of levodopa to DA. Unfortunately, despite the manifest benefits of DA replacement therapies, as many as 50% of people with PD see diminished returns within approximately five years following initial treatment with the medication (Poewe, Lees, & Stern, 1986), with patients experiencing a number of often debilitating side effects, such as hallucinations, dyskinesias (involuntary movements), and rapid effect fluctuations when on the medication (Schrag & Quinn, 2000).

Dopamine (receptor) agonists are an important alternative or complement to levodopa. Whilst these pharmaceutical agents are not free from side effects, with many people experiencing dyskinesias, nausea, daytime sedation, and cognitive disturbances, they do appear to have a mild neuroprotective effect (Le & Jankovic, 2001; Schapira, 2002). Furthermore, the half-life of this class of compounds is longer than that of the levodopa and can be beneficial to supplement levodopa in later stages of the disease or to delay the introduction of levodopa (Lees, 2005; Tambasco et al.,

2012). Monoamine oxidase (MAO) inhibitors are also commonly prescribed to people living with PD. Monoamine oxidase inhibitors assist in maintaining DA levels by reducing DA metabolism in the brain (Guttman et al., 2003). Finally, anticholinergic drugs which reduce the levels of ACh in the striatum can be effectively administered to treat some aspects of PD.

Functional neurosurgery can prove beneficial in alleviating parkinsonian motor symptoms in appropriately selected patients who are refractory to medical management. Deep brain stimulation (DBS) is currently the most common form of surgery for symptomatic treatment of PD. High-frequency stimulation is typically applied to the STN or GPi depending on the symptom profile of the individual (Voon, Kubu, Krack, Houeto, & Troster, 2006; Yu & Neimat, 2008). Both STN and GPi DBS produce sustainable improvements in tremor, rigidity and bradykinesia in the off-medication state and furthermore, lead to a significant reduction in drug-induced dyskinesias (Follett et al., 2010; Hamani, Richter, Schwalb, & Lozano, 2005; Kleiner-Fisman et al., 2006; Kumar et al., 2000; Pahwa et al., 1997). Unfortunately, there is not an analogous improvement of postural instability or gait dysfunction following surgery. Postural instability and gait dysfunction are usually improved immediately following surgery, however, this improvement is not sustained at five year follow-up (St George, Nutt, Burchiel, & Horak, 2010). The PPN has been identified as a possible alternative DBS target that may address postural instability or gait dysfunction, but data to support the use of PPN DBS is currently limited (Benabid & Torres, 2012; Follett & Torres-Russotto, 2012). The mechanisms through which any motor symptoms are mitigated using DBS have yet to be fully elucidated.

Whilst the use of medication remains the typical approach to the symptomatic management of PD, a number of symptoms of PD are unresponsive or show limited

response to pharmacological therapies despite optimal dosing (Blin et al., 1991; Fahn, 2008). The administration of dopaminergic medications typically reduces tremor, rigidity and bradykinesia, however, the effects on postural instability and resultant gait dysfunction are variable (Olanow, Stern, & Sethi, 2009). The gait deficits associated with PD increase in severity with disease progression and are commonly identified as the most functionally debilitating symptom of the disease (Zijlstra, Rutgers, & Van Weerden, 1998). As such, the development of rehabilitation interventions that address dopa-resistant gait deficits are a healthcare priority for people living with PD.

Increasing evidence has identified exercise interventions and/or physical therapy as beneficial adjunct treatments to supplement standard medications. Indeed, the inclusion of exercise therapy as part of a comprehensive multidisciplinary treatment plan may improve motor performance and disability beyond improvements produced by pharmacological agents alone (de Goede, Keus, Kwakkel, & Wagenaar, 2001; Ellis et al., 2005). Moreover, animal studies have consistently shown that exercise can be effective in positively influencing brain plasticity and dopamine production (see Hirsch & Farley, 2009 for review).

1.2. Gait

Walking is a complex, learned activity which is fundamental to independence and quality of life. The term ‘gait’ refers to a particular manner of walking and is often used interchangeably with ‘walking’ to describe the series of rhythmical, alternating movements of different segments of the body which result in the forward propulsion of the centre of gravity. As the body moves forward, support is provided sequentially by one leg and then the other in a series of ‘controlled falls’. The gait

cycle describes the time between two consecutive events by the ipsilateral limb, for example, from one right foot initial contact to the successive right foot initial contact (Figure 1.4). Each gait cycle can be described to consist of a stance and a swing phase. The stance phase comprises approximately 60 percent of the gait cycle. It begins with initial contact of one foot and ends with terminal contact of the ipsilateral foot (typically 'toe-off'), which corresponds to the initiation of the swing phase of the cycle. The swing phase occupies the remaining 40 percent of the gait cycle and describes the period of the gait cycle in which the defining limb is not in contact with the ground. Two brief transitional periods of double limb support (DLS) occur during the stance phase of the gait cycle, when both lower extremities are in contact with the ground and the body's weight is transferred from one limb to the other. These periods of DLS occur between initial contact of one foot and toe-off of the contralateral foot and represent approximately 25 percent of the gait cycle in normal walking (Winter, 1995).

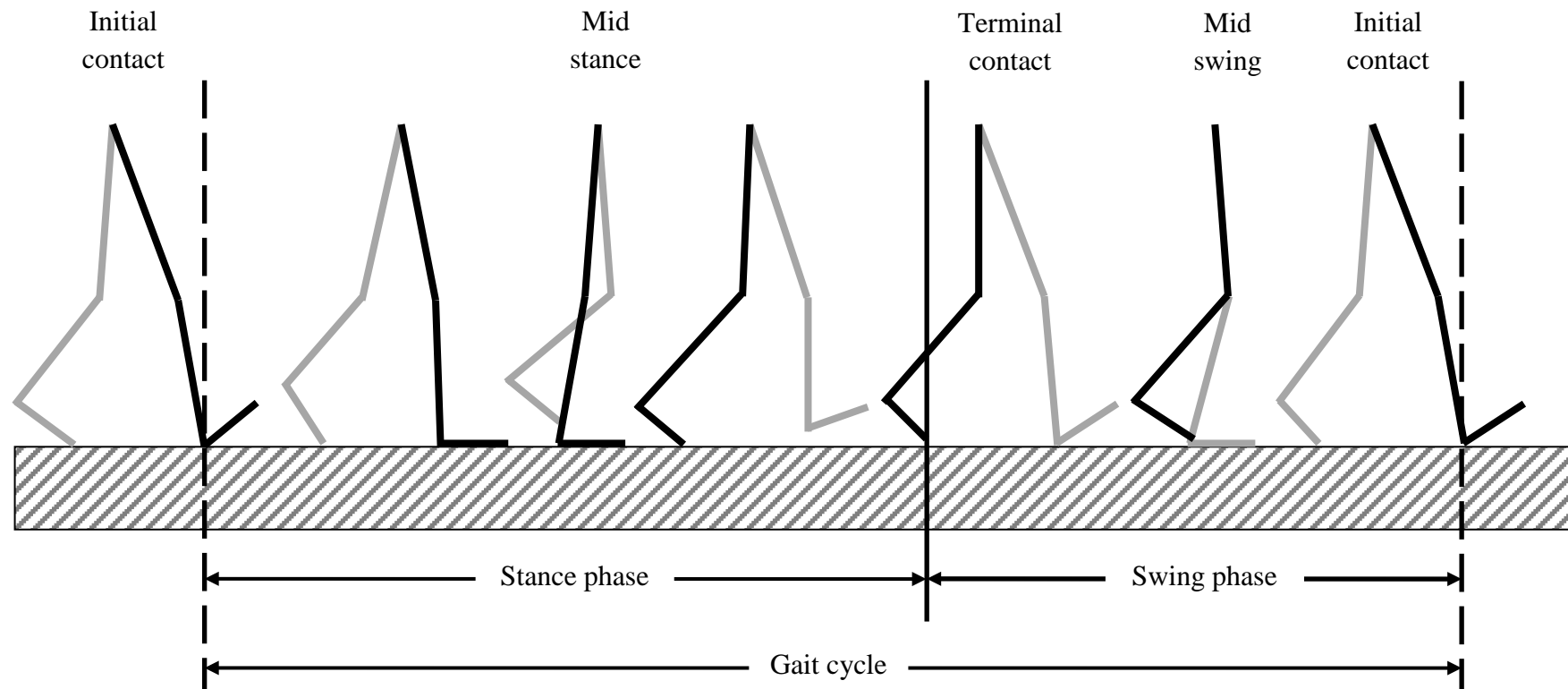


Figure 1.4 A schematic of the events and phases of a single gait cycle. Right leg is shown in black, left leg is shown in grey.

Mature gait patterns appear at approximately three years of age (Sutherland, Olshen, Cooper, & Woo, 1980), but our gait pattern continues to change over the course of the lifecycle and typical age-related changes to gait patterning have been described extensively in the literature (Baloh, Ying, & Jacobson, 2003; Maki, 1997; Marigold & Patla, 2008; Prince, Corriveau, Hebert, & Winter, 1997; Salzman, 2010; Woo, Ho, Lau, Chan, & Yuen, 1995). Older adults are reported to decrease hip and knee extension and reduce ankle dorsiflexion when compared to younger adults resulting in reduced walking speed, and step and stride length (Goldberg & Neptune, 2007; Ostrosky, VanSwearingen, Burdett, & Gee, 1994). The combined reduction in velocity and stride length leads to a maintenance of cadence (step rate) as we age. Additionally, DLS time and stance times are reported to be increased relative to the gait cycle amongst older adults (Woo, et al., 1995). These age-related adaptations to the gait pattern are thought to be the consequences of muscle weakness, impaired balance control and reduced proprioceptive sensitivity (Hurley, Rees, & Newham, 1998; Lord & Ward, 1994) associated with ageing.

1.2.1. Parkinsonian gait. Disordered gait is a common consequence of the postural instability, bradykinesia, and rigidity expressed by people living with PD. People with PD are commonly described as having a shuffling gait. They walk with a distinctive flexed posture with the trunk, head and neck inclined forward (Knutsson, 1972). Arm swing is typically reduced or absent (Carpinella et al., 2007; Morris, Huxham, McGinley, Dodd, & Iansek, 2001; van Emmerik & Wagenaar, 1996; Winogrodzka, Wagenaar, Booij, & Wolters, 2005), with the arms held flexed and the hands carried in front of the body (Knutsson, 1972). In the lower limbs reduced knee and ankle flexion are observed (Morris, Iansek, McGinley, Matyas, & Huxham, 2005; Morris et al., 2001). In addition, people with PD exhibit less marked heel strike

(Kimmeskamp & Hennig, 2001) and reduced foot clearance during the swing phase of the gait cycle. In combination these characteristics lead to decreased stride length and walking speed, an increased time spent in DLS (Morris et al., 2001; Morris, Iansek, Matyas, & Summers, 1996; Sofuwa et al., 2005) and greater variability (Baltadjieva, Giladi, Gruendlinger, Peretz, & Hausdorff, 2006; Blin, Ferrandez, & Serratrice, 1990; Hausdorff, Cudkowicz, Firtion, Wei, & Goldberger, 1998; Lord, Baker, Nieuwboer, Burn, & Rochester, 2011; Schaafsma et al., 2003) when compared to the healthy older adult population. Gait deficits increase in severity with disease progression and the emergence of gait festination and freezing is common (Morris, Iansek, & Galna, 2008) in advanced stages of the disease.

Technological advances are allowing us to progress our understanding of how the basal ganglia dysfunction associated with PD contributes to the gait disturbances experienced by this population. Evidence from neuroimaging studies indicates that during normal internally cued gait the supplementary motor area (SMA) plays a central role, with the basal ganglia-SMA pathway regulating the timing and scaling of the motor pattern (Alexander, DeLong, & Strick, 1986; Hanakawa, 2006; Hanakawa et al., 1999). It is theorised that the phasic output from the basal ganglia indirectly controls increases and decreases in cortical activity via the SMA (Brotchie, Iansek, & Horne, 1991), allowing appropriately timed movement initiation and termination. This postulation provides support for the speculated role of the basal ganglia as an endogenous timekeeper (Buhusi & Meck, 2005; Ivry, 1996; Meck, Penney, & Pouthas, 2008), which internally regulates the timing of well-practiced, rhythmical movements such as walking.

The dysfunctional gait experienced by people living with PD is thought to be a result of changes in the activity of the basal ganglia-thalamocortical loop which ultimately leads to deficits in the activity of motor-related cortical areas including the SMA, PMC, and anterior cingulate cortex when performing rhythmical activities (Brotchie et al., 1991; Hanakawa, Katsumi, et al., 1999). It is also theorised that the changes in the activity of the basal ganglia-thalamocortical loop in PD likely reduce the automaticity of locomotion with patients being required to direct greater attentional resources towards the task of walking (Morris, Iansek, Matyas, & Summers, 1994; Yogev-Seligmann et al., 2008).

1.2.2. Gait and cognition. Traditionally, gait has been considered to be a simple automated motor activity that was independent from cognitive function. Indeed, it has been demonstrated that locomotion can be produced through central pattern generators (spinal neuronal networks) with negligible higher-level cognitive contributions (Dietz, 2003; Grillner & Wallen, 1985; MacKay-Lyons, 2002). Recent research, however, suggests that this view is overly simplistic, and that locomotion particularly that which requires precise visuomotor coordination involves dynamic interactions between spinal circuits, subcortical, and cortical regions (Fukuyama et al., 1997; Jahn et al., 2008; Jahn et al., 2004; Malouin, Richards, Jackson, Dumas, & Doyon, 2003; Miyai et al., 2001; Wang, Wai, Kuo, Yeh, & Wang, 2008). Moreover, it has been found that cognitive, executive, and association brain regions are in fact activated when performing motor tasks that were previously identified as automated processes and that activity levels increase with increasing environmental demands and task complexity (Drew, Jiang, Kably, & Lavoie, 1996).

Walking in the real world rarely occurs as an isolated task. Indeed, maintenance of mobility and independence in everyday life often requires the ability to walk whilst carrying out a concurrent task (dual-tasking), such as maintaining a conversation, carrying shopping, or navigating an obstruction in the pathway. Dual-task paradigms are often used to indirectly measure the automaticity of gait control whilst performing a concurrent motor or cognitive task. Experiments involving dual- or multi-tasking rely on a number of hypotheses: 1) each individual has a finite attentional resource capacity; 2) attentional resources will be flexibly divided amongst concurrent tasks; and 3) if the attentional resource capacity of the individual is exceeded the performance of one or more tasks will be compromised (Abernethy, 1988; Kahneman, 1973). Therefore, the capacity to efficiently dual-task with minimal interference (i.e. deterioration in walking and/or secondary task performance) is indicative of the automaticity of gait, with minimal executive control or attention directed towards the task of walking (Poldrack et al., 2005; Wu, Kansaku, & Hallett, 2004).

Executive function is used as an umbrella term for a collection of higher cognitive processes and sub-processes involved in the planning, production and modulation of effective goal-directed actions, such as walking (Royall et al., 2002). Normal aging results in subtle declines in specific components of executive function, however, in people with PD it is suggested that usual age-related executive function deficits are exacerbated by pathology of the dopaminergic basal ganglia-thalamocortical pathways that project to the prefrontal cortex (an area associated with executive function; Royall et al., 2002; Zgaljardic, Borod, Foldi, & Mattis, 2003; Zgaljardic et al., 2006). Several studies have attempted to determine the interdependence between executive function and gait. It has been established that

executive function is increasingly important in complex gait scenarios, with executive function being associated with walking speed and gait variability in dual-task contexts (Holtzer, Verghese, Xue, & Lipton, 2006; Springer, Giladi, Peretz, Yogev, Simon, & Hausdorff, 2006). Furthermore, it appears that the relationship between gait and executive function is strengthened in populations with reduced movement automaticity, such as PD.

Attention is one component of executive function (Stuss & Levine, 2002; Woodruff-Pak & Papka, 1999) and has been described as the ‘information processing capacity of an individual’ (Woollacott & Shumway-Cook, 2002) and ‘the process of attending to a single, specific aspect of the environment at the expense of all others’. There is, however, no clear consensus on how attention should be defined. Divided attention refers to the capacity to attend to two or more task concurrently and it is this facet of attention that plays a critical role in our ability to walk whilst carrying out a second activity such as conversing with a companion, talking on a cellphone or carrying a cup of coffee to the next room.

1.2.3. Dual-task costs. The effects of dual-tasking on gait have been extensively studied in healthy young and older adults, and selected pathological populations (Al-Yahya et al., 2011; Beauchet et al., 2009; Bloem, Grimbergen, van Dijk, & Munneke, 2006; Huang & Mercer, 2001; Kelly, Eusterbrock, & Shumway-Cook, 2012; Lee, Sullivan, & Schneiders, 2012; Woollacott & Shumway-Cook, 2002; Yogev-Seligmann et al., 2008). Age-related motor performance deficits have been consistently reported in the literature, with older adults showing greater dual-task walking decrements than their younger counterparts (see Beurskens & Bock, 2012; Lord & Rochester, 2007 for review). Deterioration in dual-task gait performance

could be explained by reduced attentional resource capacity. Empirical evidence suggests that walking is a more attentionally demanding activity for older adults thereby requiring additional cognitive resources (Beurskens & Bock, 2012; Lord & Rochester, 2007). Given this, it is hypothesised that as we age, central control mechanisms, likely involving prefrontal cortical regions, basal ganglia and cerebellum systems become more important to movement control. Meanwhile, it is these same brain structures and cortical regions which are associated with executive function, attention and motor control that exhibit some of the largest structural changes across age groups (Burke & Barnes, 2006; Craik & Grady, 2002; Gunning-Dixon & Raz, 2003).

People living with PD experience exacerbated gait impairments in dual- and multi-task situations, with further decreases in walking speed, step length, and cadence and increases in variability and gait asymmetry (see Kelly et al., 2012 for review) when compared to single-task walking (walking only). Moreover, these decreases in dual-task gait performance exceed those reported amongst healthy age-matched populations. Beyond age-related changes that may contribute to dual-task walking deficits there are several specific mechanisms that potentially compound these deficits in people with PD. As previously stated, PD is characterised by decreased movement automaticity due to basal ganglia dysfunction. In the example of walking, the increased cortical involvement required for efficient movement control necessitates the direction of considerable attentional resources towards the primary task of walking; as a result the residual resource capacity available for the processing of simultaneous tasks will be considerably diminished. A second possibility which need not be mutually exclusive is that the degeneration of the dopaminergic neurons in PD also affects cognitive circuits that travel through the basal ganglia. This

speculated PD-specific mechanism likely contributes to the executive function and specifically attentional deficits that are commonly reported amongst people with PD (Zgaljardic et al., 2003; Zgaljardic et al., 2006). It is also probable that non-dopaminergic pathology contributes to motor (Devos, Defebvre, & Bordet, 2010) and cognitive deficits (Kehagia, Barker, & Robbins, 2010), and therefore dual-task walking deficits in PD.

1.2.4. Strategies to reduce dual-task gait deficits. Functional gait in the home and community requires the capability to multi-task. Impaired multi-tasking abilities have been associated with increased disability and dependence, an increased risk and incidence of falls (Allcock et al., 2009; Beauchet et al., 2009; Hausdorff et al., 2006) and a reduced quality of life. Therefore, to ensure the maintenance of functional mobility and patient independence it is important that strategies and interventions that target parkinsonian gait encompass dual-and multi-tasking walking deficits.

Dopaminergic therapies have been shown to be effective in improving specific aspects of single- and dual-task walking performance in people with PD; however, a number of gait parameters are dopa-resistant despite optimal medication levels (Blin et al., 1991; Fahn, 2008). Furthermore, with disease progression parkinsonian gait continues to deteriorate and becomes increasingly difficult to manage with medications, often necessitating the inclusion of compensatory rehabilitation strategies and interventions to augment pharmacological benefits to gait.

There is a growing body of evidence suggesting that ‘dual-task gait training’ may be an effective strategy to improve dual-task walking (Brauer & Morris, 2010; Canning, Ada, & Woodhouse, 2008; Schwenk, Zieschang, Oster, & Hauer, 2010;

Yang, Wang, Chen, & Kao, 2007; You et al., 2009). Dual-task training involves the repeated practice of walking whilst concurrently carrying out one or more additional motor or cognitive tasks. The majority of the evidence thus far has come from small pilot studies; however, significant and sustainable improvements in dual-task gait performance have consistently been reported amongst people with PD following dual-task gait training (Brauer & Morris, 2010; Canning et al., 2008; Yogev-Seligmann, Giladi, Brozgol, & Hausdorff, 2012). Furthermore, the improvements in dual-task gait performance can be generalised to novel (untrained) dual-task contexts following a period of training. To date, the findings regarding the necessary specificity of dual-task gait training and the associated retention effects in people with PD are equivocal and further research is necessary to determine the optimal training protocol.

An alternative strategy that is increasingly prescribed by clinicians and therapists to facilitate walking and mobility amongst people with PD is the provision of rhythmic sensory cues. External sensory cues are provided to direct the attention of the user towards specific aspects of their gait pattern, such as step amplitude or step frequency. For example, spatial cues are commonly provided as patterns or lines on the floor to normalise the patients step length. Visual stimulation has consistently been reported to improve stride length, walking speed and stride length variability (Lim et al., 2005). A second portable and practical means of cueing that has been studied extensively in the parkinsonian population in recent years is the use of auditory rhythmic cues. Auditory cues are intended to regulate the step rate (cadence) of the user and are typically delivered as a metronome tone or a musical rhythm. Immediate improvements in velocity, stride length, cadence and gait variability have been reported in single (Lim et al., 2005; Picelli et al., 2010) and dual-task (Rochester et al., 2005; Rochester et al., 2007) contexts in the presence of rhythmic auditory cues.

In addition, training paradigms incorporating rhythmic auditory cues have produced significant improvements in gait performance across cued (Rochester et al., 2010) and uncued conditions (Bryant et al., 2009; de Bruin et al., 2010; del Olmo & Cudeiro, 2005; Marchese, Diverio, Zucchi, Lentino, & Abbruzzese, 2000; Miller, Thaut, McIntosh, & Rice, 1996; Nieuwboer et al., 2007; Rochester et al., 2010; Thaut et al., 1996). Moreover, the reported improvements in spatiotemporal parameters of gait are typically retained for a period of weeks following cessation of training (Bryant et al., 2009; del Olmo & Cudeiro, 2005; Marchese et al., 2000; Miller et al., 1996; Nieuwboer et al., 2007; Rochester et al., 2010; Thaut et al., 1996). Despite the evident benefits of exercise programs incorporating rhythmic stimuli for people living with PD the sustainability of training benefits is dependent on continuing engagement in the exercise program. Exercise participation and adherence are reported to be low amongst people with PD (Ene, McRae, & Schenkman, 2011; Fertl, Doppelbauer, & Auff, 1993), an outcome that can be attributed to a lack of motivation, as well as disease-related motor symptoms and fatigue (Quinn et al., 2010; van Nimwegen et al., 2011). Interestingly, recent research in non-parkinsonian adults has indicated that supplementing an exercise program with appropriate music selections can prove motivational (Karageorghis & Terry, 1997; Karageorghis, Terry, & Lane, 1999), improve affective states (Bishop, Karageorghis, & Loizou, 2007; Crust & Clough, 2006; Karageorghis & Terry, 1997), attenuate perceptions of fatigue and discomfort (Crust, 2004; Karageorghis & Terry, 1997; Lim, Miller, & Fabian, 2011; Shaulov & Lufi, 2009; Yamashita, Iwai, Akimoto, Sugawara, & Kono, 2006), and encourage participation and adherence (Bauldoff et al., 2002; Johnson et al., 2001; Karageorghis & Terry, 1997).

1.2.5. Obstacle Negotiation. Independent and safe locomotion in the home and community requires the ability to continually adapt the motor pattern in response to the changing environment. Avoiding or negotiating obstacles in the path of travel (i.e. a sidewalk curb, a door threshold) is one example of adaptive locomotion that is necessary for the maintenance of functional mobility.

Obstacle crossing behaviours have been comprehensively described in healthy adults (Begg & Sparrow, 2000; Chou & Draganich, 1997; Galna, Peters, Murphy, & Morris, 2009; Harley, Wilkie, & Wann, 2009; Kovacs, 2005; Mohagheghi, Moraes, & Patla, 2004; Siu, Catena, Chou, van Donkelaar, & Woollacott, 2008; Siu, Lugade, Chou, van Donkelaar, & Woollacott, 2008). Despite the identification of some commonalities in obstacle negotiation strategies between young and older adults, changes to the integrity of the cognitive and sensorimotor systems with advancing age have been associated with a decline in specific aspects of obstacle crossing, such as toe clearance height during obstacle crossing and heel-obstacle distances (Kovacs, 2005; van Dieen, Pijnappels, & Bobbert, 2005). Moreover, age-related deterioration to obstacle crossing skills have been implicated in the high incidence of falls experienced by the older adult population. Indeed, it is reported that one third of community-dwelling adults over the age of 65 will fall each year (Blake et al., 1988; O'Loughlin, Robitaille, Boivin, & Suissa, 1993). Half of these falls will be a result of tripping (Campbell et al., 1990; Lord, Ward, Williams, & Anstey, 1993; Overstall, Exton-Smith, Imms, & Johnson, 1977) with the majority of the trips resulting from contacting an object in the travel path (Overstall et al., 1977; Tinetti & Williams, 1998).

When challenged with an obstacle at a fixed location in the path of travel older adults do not show a greater propensity for contacting the obstacle than younger adults (Galna et al., 2009; Kovacs, 2005), however, they do adopt what is considered to be a conservative crossing strategy to achieve this outcome. Specifically, older adults tend to approach and step over the obstacle slower and with shorter steps than young adults (Chapman & Hollands, 2007; Chen, Ashton-Miller, Alexander, & Schultz, 1991; Lowrey, Watson, & Vallis, 2007; McFadyen & Prince, 2002; McKenzie & Brown, 2004). In addition, the obstacle is typically located further forward in the shortened crossing step amongst older adults (Figure 1.5), resulting in a longer toe-obstacle distance (pre-obstacle distance; Figure 1.5a) and a shorter heel-obstacle distance (post-obstacle distance; Figure 1.5a) (Chen et al., 1991). When the obstacle is further forward in the obstacle crossing step the risk of tripping on the front of the obstacle with the lead foot is reduced as vertical foot clearance is increasing towards the end of the swing phase (Figure 1.5b). The decreased post-obstacle distance does however, increase the risk of stepping on the obstacle although it is considered that this may be preferable and easier to recover from than a trip (Chen et al., 1991). The decreased obstacle crossing velocity observed amongst older adults is also deemed to represent a conservative crossing strategy as it provides the individuals with sufficient time to modify their stepping pattern to safely accommodate the obstacle and lessen the risk of tripping. In time-sensitive conditions where there is limited time to plan and execute adjustments to foot placement in response to an obstacle that comes to attention rapidly older adults adopt similar strategies to navigate the obstacle however, they do contact the obstacle more frequently than their younger counterparts, increasing the likelihood of a fall incident

(Brown, Doan, McKenzie, & Cooper, 2006; Chen, Ashton-Miller, Alexander, & Schultz, 1994; Chen et al., 1996).

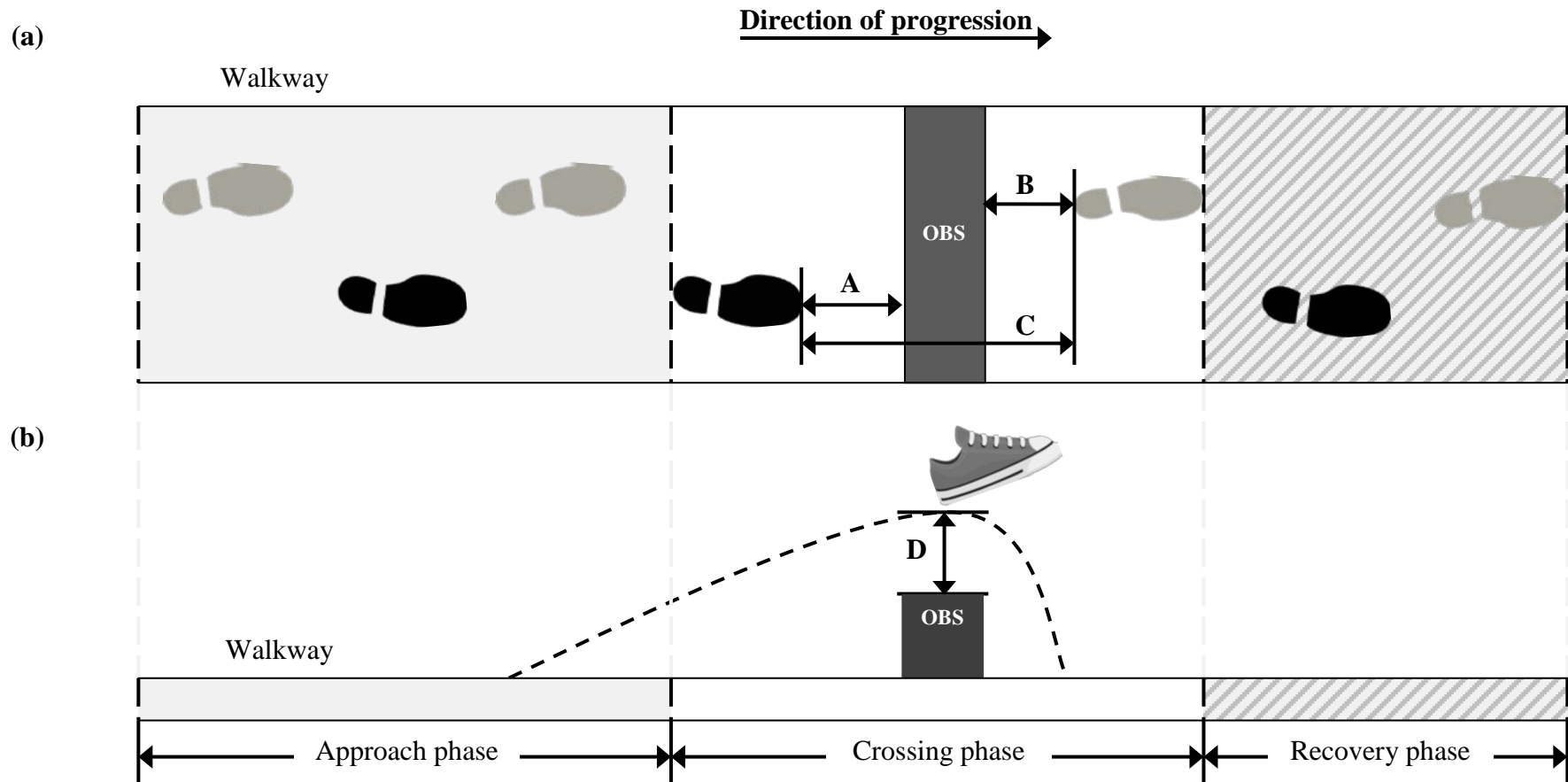


Figure 1.5 (a) Top-down view of spatial measures and phases of obstacle negotiation and (b) Sagittal view of approximate trajectory (dashed line) of lead foot when crossing the obstacle. Grey footprints indicate lead foot (first foot to cross obstacle); black footprints indicate trail foot (second foot to cross obstacle). Measures shown are (A) pre-obstacle distance; (B) post-obstacle distance; (C) crossing step length; and (D) vertical clearance height. OBS denotes obstacle.

The fall rate amongst people with PD exceeds that of the healthy older adult population, with two in every three people with PD reported to fall during the span of one year (Ashburn, Stack, Pickering, & Ward, 2001; Wood, Bilclough, Bowron, & Walker, 2002). Whilst a number of disease-specific intrinsic (patient-oriented) risk factors for falls have been identified (e.g. higher disease severity, dyskinesias, freezing of gait; Ashburn et al., 2001; Bloem et al., 2004; Stolze et al., 2004; Wood et al., 2002) the majority of extrinsic (environmental) risk factors are common to both the general older adult population and those with PD. Indeed, trip related falls are reported to account for a large portion of falls amongst people with PD (Bloem et al., 2004; Stolze et al., 2004; Wood et al., 2002). It is speculated that disease-related deficiencies in visual processing (Azulay, Mesure, Amblard, & Pouget, 2002; Azulay, Mesure, & Blin, 2006), proprioception (Boecker et al., 1999; Martens & Almeida, 2012; Mongeon, Blanchet, & Messier, 2009; O'Suilleabhain, Bullard, & Dewey, 2001; Zia, Cody, & O'Boyle, 2000) and sensorimotor integration (Almeida et al., 2005; Machado et al., 2010) compound the gait deficits experienced by people with PD in complex gait situations such as where an obstacle must be negotiated. Consistent with the bradykinesia that is a hallmark of PD during unobstructed walking (Blin, et al., 1990; Morris et al., 1994), people with PD demonstrate shorter and slower steps during the approach, crossing, and recovery phases of obstacle crossing (Figure 1.5a) when compared to non-parkinsonian older adults (Galna, Murphy, & Morris, 2010; Nocera, Horvat, & Ray, 2010; Stegemoller et al., 2012; Vitorio, Pieruccini-Faria, Stella, Gobbi, & Gobbi, 2010).

During the crossing phase of obstacle avoidance, deficits in step length regulation typically result in people with PD stepping closer to the back of the obstacle with their lead foot than older adult control subjects (Brown et al., 2010;

Galna et al., 2009; Vitorio et al., 2010; Figure 1.5). Similar to healthy older adults, it could be suggested that a shorter post-obstacle distance could predispose people with PD to stepping on or contacting the obstacle, however, few if any obstacle contacts were reported in the series of studies. This is again likely a reflection of the obstacle being in a fixed position and visible for multiple steps prior to crossing, thereby allowing individuals ample time to identify obstacle characteristics and adjust their gait patterning to safely step over the obstacle (Chen, et al., 1994).

Interestingly, and contrary to expectations of hypometric movements it has been consistently reported that people with PD demonstrate vertical foot clearances that are either comparable to (Brown et al., 2010; Galna et al., 2010; Vitorio et al., 2010) or exceed (Stegemoller et al., 2012) those demonstrated by healthy older adults. This obstacle crossing behaviour has previously been interpreted as a conscious safety strategy (Chen et al., 1991; Hahn & Chou, 2004) but in the case of people with PD it is also possible that this is an indication of an inability to regulate step height based on the identified sensory deficits experienced by this population (Almeida et al., 2005; Azulay et al., 2002; Azulay et al., 2006; Boecker et al., 1999; Machado et al., 2010; Martens & Almeida, 2012; Mongeon et al., 2009; O'Suilleabhain et al., 2001; Zia et al., 2000).

Despite the acceptance that independent and safe locomotion requires the capacity to adequately avoid obstacles in the travel path very few gait training interventions investigate the potential of the strategy to influence obstacle negotiation performance. A five-week exercise training program, which included exercises on an obstacle course, was shown to be effective in improving obstacle crossing success rates (Weerdesteyn et al., 2006) and obstacle negotiation parameters (Weerdesteyn et

al., 2008) amongst healthy older adults. In addition, Lamoureux and colleagues (Lamoureux, Sparrow, Murphy, & Newton, 2003) successfully implemented a strength training intervention amongst community-dwelling older adults that resulted in improvements to a number of parameters associated with safe obstacle negotiation. A single study (Mirelman et al., 2011) has reported improvements in gait speed and stride length during overground obstacle negotiation amongst people with PD after they had received six weeks of intensive and progressive treadmill training with virtual reality in which obstacle negotiation was practiced. Functional task measurements should be routinely included in the assessment of novel gait rehabilitation strategies that aim to reduce falls and improve walking performance in daily life.

1.3. The Power of Music

1.3.1. Perceptual characteristics of music. Music is an incredibly powerful stimulus. Indeed, music listening often encourages spontaneous movements, such as tapping our feet or nodding our head in time to the music (Large, 2000; Snyder & Krumhansl, 2001). Temporal structure in music is provided by the rhythm, tempo, and metre of the musical piece. Rhythm assumes an essential role in arranging temporal musical events into consistent and understandable patterns and as such is a critical component of the personality of the melody. Rhythm also guides the listener in making sense of temporal patterns by directing attention towards key musical events in the composition (Thaut, 2005). The ‘beat’ indicates the basic metrical unit of time, dividing the music with regular temporal reference points. The repetition rate of the beat within a given period of time is referred to as the tempo of the music (in Western music tempo is expressed in beats per minute). The beat of the music also creates

anticipation and predictability in rhythm perception, two properties that are crucial in the organisation of motor performance. Within a musical composition there will be repeated patterns of alternating strong and weak beats which will be organised together into regular groups to shape the percept of metre and whilst metre does help to organise the temporal structure of the music the most perceptually salient recurrent pulse is that to which we will synchronise our movements (Parncutt, 1994). Despite a reported deficit in beat perception (Grahn & Brett, 2009), people with PD retain the ability to entrain their movements to a complex auditory rhythm. It is postulated that people living with PD or other pathologies that result from basal ganglia dysfunction may use non-temporal cues within the music to assist them in detecting the beat (Warren, 2008).

Indeed, the perceptual characteristics of music are not limited to those that provide temporal structure to the musical piece. Attributes such as pitch, timbre, contour and loudness also contribute to the listeners' overall perception of and response to a piece of music. In addition, the meaning of the music for the listener may be defined by the familiarity of the piece, as well as whether the musical piece evokes any extra-musical associations (i.e. association of the music with a life event, location or person). Lastly, emotion is an important but subjective quality that is expressed in a musical piece and along with the previously mentioned properties can differentially impact the listener's enjoyment of the music, as well as their affective and physiological responses to the music (Berlyne, 1971).

Similar to other sounds, initial processing of music takes place in the primary auditory cortex (PAC) which resides in Heschl's gyrus (HG; Figure 1.6) which itself is located in the lateral sulcus. Distinct neural circuits process the individual

perceptual components of the music (i.e. rhythm, pitch, timbre) before transmitting the information to a network of auditory association areas that surround HG for subsequent stages of auditory processing (Figure 1.6) (Griffiths & Warren, 2002; Warren, 2008; Warren, Uppenkamp, Patterson, & Griffiths, 2003). Ultimately, music listening engages diverse regions of the brain, including all four lobes, and cortical and subcortical structures (Chen, Penhune, & Zatorre, 2008; Peretz & Zatorre, 2003; Platel et al., 1997).

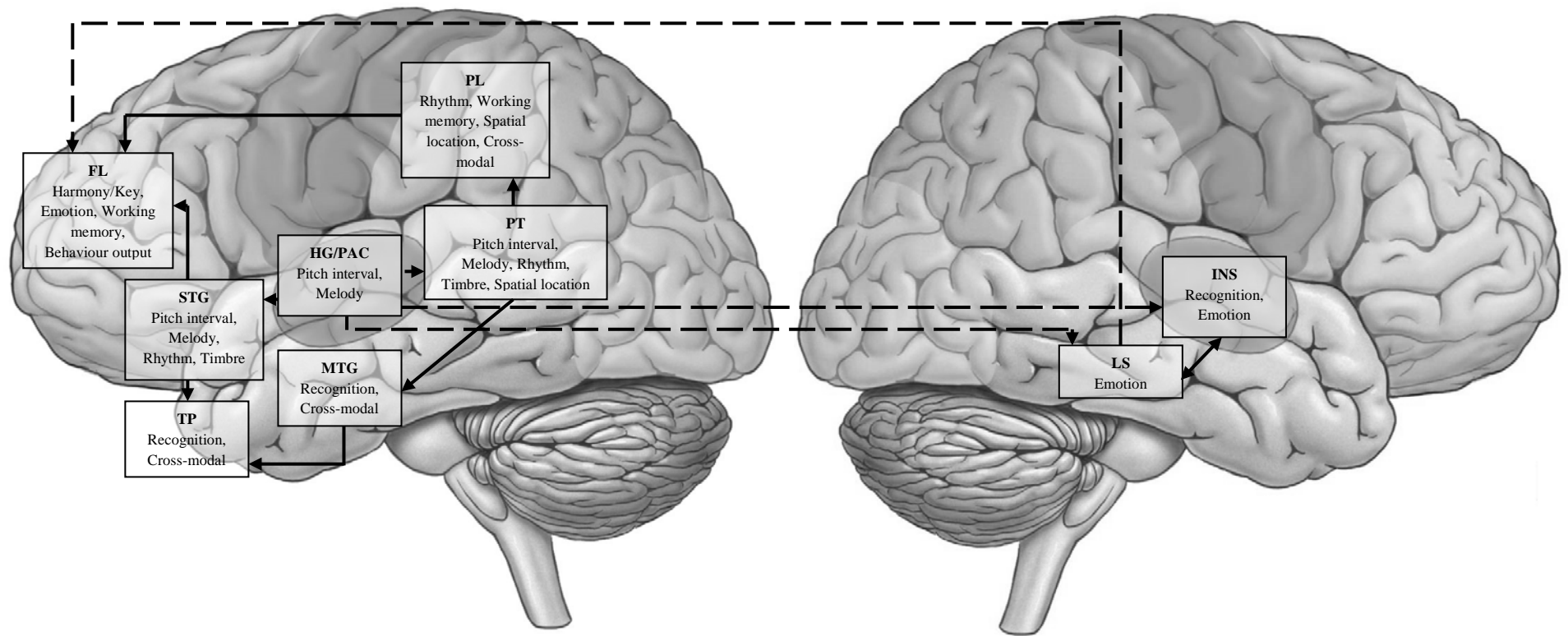


Figure 1.6 A schematic representation of the organisation of the musical brain. Important brain regions and functional associations between these regions are illustrated. Dashed lines and arrows indicate the flow of information between cortical regions. The hierarchical nature of music processing is illustrated, with increasing complex properties of music represented by areas further outside of the primary auditory cortex (PAC). FL = frontal lobe; HG = Heschl's gyrus (site of PAC); INS = insula (shown with overlying cortex); LS = limbic system (shown with overlying cortex); MTG = middle temporal gyrus; PL = parietal lobe; PT = planum temporal; STG = superior temporal gyrus; TP = temporal pole (adapted from Warren, 2008).

1.3.2. Therapeutic potential of music. Music is thought to have been in existence for over 50,000 years and has evolved to become a basic ingredient of human life. Indeed, music is pervasive in modern society, permeating many facets of our daily life, with music being played in countless social and commercial spaces, such as shops and shopping malls, eateries and bars, offices, banks and public gyms. Moreover, in contexts or environments where music is not provided for us many of us choose to create our own music listening experiences.

The therapeutic potential of music has been recognised for millennia, with music forming a key component of healing rituals in many cultures. Traditionally, the therapeutic application of music was limited to the promotion of well-being, the expression of feelings and social interactions with the focus placed on music's traditional social and emotion roles in society (Thaut, 2005). In the latter half of the 20th century however, the potential therapeutic benefits of music were increasingly recognised and as a result studied more systematically. Subsequent evidence-based research has shown that music can be effective in modulating pain, blood pressure, heart rate, respiratory rate (Chan, 2007; Kemper & Danhauer, 2005), anxiety (Nilsson, 2008, 2009), and depression (Hsu & Lai, 2004; Morgan & Jorm, 2008; Siedliecki & Good, 2006) in a variety of patient populations.

The recognition that rhythm and music can effectively stimulate and modulate non-musical behaviours has more recently led to the development of sensorimotor rehabilitation programs incorporating auditory rhythms as a means to organise motor function amongst pathological populations. Rhythmic auditory stimulation (RAS) is a specific neurologic technique that capitalises on the identified physiological effects of auditory rhythm on the motor system to facilitate the control of movement during intrinsically rhythmical movements, such as walking (Thaut, 2005). In RAS, auditory

cues in the form of a metronome tone or rhythmically accentuated music are provided to the patient at their natural movement frequency (i.e. preferred step rate). The auditory cues are proposed to act as a powerful external timekeeper to which endogenous movement frequencies can be entrained. The theorised role of auditory rhythm as a physiological attractor has been substantiated by the finding that there is almost instantaneous coupling between auditory rhythms and motor responses even when auditory rhythms are provided at levels that are imperceptible (Thaut & Kenyon, 2003).

In people with PD the external cue provided by RAS is thought to compensate for the deficient internal timing function of the basal ganglia, allowing the improvement and stabilisation of spatial and temporal parameters of the gait pattern. Indeed, a considerably body of research has demonstrated that RAS can be used as an effective immediate entrainment stimulus amongst people with PD (Lim et al., 2005; Picelli et al., 2010; Rochester et al., 2005; Rochester et al., 2007). Furthermore, when people with PD engage in a gait training program incorporating RAS they are able to achieve significant and sustainable improvements in gait patterning that carry-over to uncued gait (Bryant et al., 2009; del Olmo & Cudeiro, 2005; Lim et al., 2005; Nieuwboer et al., 2007; Rochester et al., 2010), suggestive of motor plasticity in networks controlling rhythmicity (Hausdorff et al., 2007).

The parameters of the auditory cues applied during RAS are critical to the efficacy of the technique. For example, it is important that the rhythmic timekeeper frequency is initially set at the current intrinsic frequency of the person's step rate (Thaut, 2005). This allows the stabilisation and optimisation of gait patterning at the individuals' natural frequency prior to treatment progression. Indeed, it has been demonstrated that the provision of an auditory rhythm that has not been controlled for

tempo (Brown, de Bruin, Doan, Suchowersky, & Hu, 2010; Brown, de Bruin, Doan, Suchowersky, & Hu, 2009) or has been provided at a rate that is too high or too low (del Olmo & Cudeiro, 2005; Howe, Lovgreen, Cody, Ashton, & Oldham, 2003) is detrimental to gait performance amongst people with PD, potentially increasing the cognitive demands associated with the strategy and compromising patient safety.

1.3.3. Speculated mechanisms of auditory-motor coupling. Music based rehabilitation has been guided by the finding that the majority of the brain regions and networks that are activated by listening to music are not exclusive to music listening, but also process language, auditory perception, elements of cognition, and/or motor control (Bengtsson et al., 2009; Janata, Tillmann, & Bharucha, 2002; Patel, 2003).

Entrainment is thought to result from direct and dynamic neuronal coupling between the auditory and motor systems. Studies in the 1960s and 70s provided early evidence for the existence of auditory-motor pathways (Paltsev & Elnor, 1967; Rossignol & Melville-Jones, 1976). These early works established that the entrainment of muscle activation patterns through rhythm perception takes place via reticulospinal pathways. Subsequent studies have substantiated these findings and demonstrated that rhythmic cues can modulate motor neuron activity and facilitate stable and efficient motor unit recruitment patterns, thereby improving movement timing (Miller et al., 1996; Thaut et al., 1996).

Advances in neuroimaging techniques in recent years have contributed greatly to our understanding of auditory-motor coupling. The majority of recent studies aiming to elucidate the neural correlates of auditory-motor synchronisation have focused on the simple task of finger tapping in response to a metronome beat sequence. Tapping in synchrony to an auditory rhythm has been shown to engage a

simple collection of auditory and sensorimotor regions of the brain, including the STG, PMC, SMA, pre-motor cortex, prefrontal cortex, cerebellum, basal ganglia and thalamus (Chen, Penhune, & Zatorre, 2008a, 2008b; Chen, Zatorre, & Penhune, 2006; Levitin & Menon, 2003; Lewis, Wing, Pope, Praamstra, & Miall, 2004; Rao et al., 1997). Interestingly, many of the same brain regions that are activated during rhythmically entrained movement are also activated and entrained by simply listening to an auditory rhythm, suggestive that there is not a dedicated neuroanatomical network that underlies entrainment mechanisms in the motor system but rather the involved neural circuitry is a combination of auditory and motor circuits. Amongst the regions activated during rhythmically entrained movement the pre-motor cortex has been identified as a region of particular relevance to auditory-motor interactions (Hoshi & Tanji, 2007; Zatorre, Chen, & Penhune, 2007). The pre-motor cortex is thought to be the only motor region of the brain that has direct anatomical connections to auditory areas as well as the PMC (Chen et al., 2008a, 2008b; Hoshi & Tanji, 2007; Zatorre et al., 2007), as such it is theorised to be the ‘gateway’ between the auditory and motor systems.

It has been demonstrated that in PD the provision of an appropriate external auditory cue allows the bypassing of the dysfunctional basal ganglia-SMA pathway (Samuel et al., 1997) and the facilitation of the walking program via the pre-motor cortex (Debaere, Wenderoth, Sunaert, Van Hecke, & Swinnen, 2003; Mushiaki, Inase, & Tanji, 1991; Vaillancourt, Mayka, & Corcos, 2006). Indeed, it is theorised that when task-appropriate external cues are provided to PD patients the pre-motor cortex may take over responsibility for movement scaling (Hanakawa, Fukuyama, Katsumi, Honda, & Shibasaki, 1999), disregarding the dysfunctional basal ganglia. It therefore appears that task-relevant cues may facilitate the use of previously

underused neural pathways. A comprehensive understanding of this phenomenon could facilitate improvements in targeted symptomatic treatments for pathological populations experiencing motor impairments, potentially utilising underused pathways to produce sustained improvements in motor performance.

1.4. Summary

The development of more effective pharmacological and surgical treatments for PD has led to significantly longer life expectancy for patients following diagnosis. Many of the symptoms of PD including debilitating gait impairments, however, are unresponsive or show limited response to medications and surgical therapies significantly impacting patient independence and quality of life. Rehabilitation interventions incorporating external auditory cues have been shown to be effective in improving parkinsonian gait, and are increasingly being accepted as a mainstream therapy. An important consideration when developing novel therapeutic approaches to assist in the management of gait impairments is that the patient needs to be motivated as they may be engaged in the therapy for a number of years. Given the documented potential of music to rhythmically entrain motor function as well as its capacity to modulate emotional and motivational states, it is feasible that music may be an attractive alternative to traditional auditory cues for inclusion in long-term gait rehabilitation programs. The efficacy of the intervention may be further enhanced when musical selections are meaningful and carry emotional valence to the patient.

The studies included in this thesis represent initial steps towards a long-term goal of developing a functionally and ecologically relevant, meaningful gait rehabilitation program for people with PD that maximises motor function whilst

encouraging participation and adherence, thereby enabling the patient to maintain their functional independence and preserve their quality of life.

Chapter 2: Objective of Thesis

2.1. Theory

Music has a potent ability to stimulate and modulate physical movement and emotions in healthy and pathological populations (de Dreu, van der Wilk, Poppe, Kwakkel, & van Wegen, 2012; Kim et al., 2011; Koelsch, 2009; Koelsch, 2010; Murrock & Higgins, 2009; Schneider, Askew, Abel, & Struder, 2010; van der Vlist, Bartneck, Maveler, 2011; Wittwer, Webster, & Hill, 2012). The temporal periodicity of music encourages auditory-motor entrainment, which is considered to result from direct neuronal coupling between the auditory and motor systems (Thaut et al., 1999). The listeners familiarity with and enjoyment of the music (herein referred to as salience) evokes a range of physiological responses including increased brain dopamine levels and associated positive affect (Ashby, Isen, & Turken, 1999).

2.2. Objective

The three studies conducted for this thesis represent initial steps towards a long-term objective of developing an individualised and sustainable gait rehabilitation program for people living with PD that is functionally and ecologically relevant. The first study investigated how specific acoustical parameters of music influence gait amongst healthy young adults. The second and third studies in this thesis examined the safety and efficacy of incorporating salient music into a comprehensive gait training program for people with PD.

2.3. Experiments

2.3.1. Experiment 1: Music salience influences the gait performance of young adults. This study examined the effects of contemporary commercially available music on the gait performance of younger adults. Gait was assessed whilst

subjects listened to different auditory cues. Music cues differed with respect to salience to the listener, as well as tempo.

- **Hypothesis 1a:** Appropriately selected commercially available music will influence gait patterning in healthy young adults.
- **Hypothesis 1b:** Music salience will influence the magnitude of change in gait performance amongst young adults.
- **Hypothesis 1c:** Music tempo will influence the magnitude of change in gait performance.

2.3.2. Experiment 2: Walking with music is a safe and viable tool for gait training in PD: The effect of a 13-week feasibility study on single- and dual-task walking. This study examined the feasibility and effectiveness of including cadence-matched salient music in a walking program for people with mild to moderate severity PD. Subjects in the experimental group walked with a personalised music playlist, three times a week for the 13-week intervention period. Falls were recorded during the intervention period and motor symptom severity and gait performance were assessed pre- and post-intervention.

- **Hypothesis 2a:** A music-accompanied walking program can be safely implemented in people with PD.
- **Hypothesis 2b:** Single- and dual-task gait performance will be improved amongst people with PD following a music-accompanied walking program.

2.3.3. Experiment 3: Training-related changes to obstacle crossing gait performance amongst people with PD. This study examined the effects of a music-accompanied gait training program on the performance of the complex gait activity of

obstacle crossing amongst people with PD. Spatiotemporal measures of obstacle crossing performance were examined pre- and post-intervention.

- **Hypothesis 3a:** Obstacle crossing performance will be improved amongst people with PD following a music-accompanied walking program.

Chapter 3: Music salience influences the gait performance of young adults

3.1 Abstract

Music is known to be a powerful stimulus often encouraging spontaneous movement such as head nodding or foot tapping in time to the beat. This study examined the effects of commercially available music on the walking of healthy young adults. Twenty-five subjects walked the length of an unobstructed 55m walkway whilst listening to music that differed with respect to its enjoyability and familiarity (salience) to the listener or its tempo. The effects of music on gait were assessed using standard spatiotemporal parameters. The findings of this series of studies suggest that listening to music whilst walking was an enjoyable activity that influenced gait characteristics amongst healthy young adults. Music salience was important to the physical response of the individual. Specifically, salient music selections increased measures of cadence, velocity, and stride length; in contrast gait was unaltered by the presence of non-salient music. Music tempo did not differentially affect gait performance in this population of subjects. These results have implications for practitioners considering using commercially available music as an alternative to the traditional rhythmic auditory cues used in rehabilitation programs.

3.2 Introduction

Music has long been considered to have therapeutic properties and has been used in healing practices for millennia. It was not until following the World Wars however, that music therapy received recognition as an allied health profession (Tyson, 1981). Traditionally, music has been applied passively through receptive listening or actively through improvisation to modify psychological, physiological and emotional states in patient groups (Cevasco, Kennedy, & Generally, 2005; Hicks-Moore, 2005; Hsu & Lai, 2004; Maratos, Gold, Wang, & Crawford, 2008; Morgan & Jorm, 2008; Pacchetti et al., 2000; Schneider, Schonle, Altenmuller, & Munte, 2007). More recently, the appreciation that auditory rhythm can effectively modulate non-musical behaviours has led to the development of rehabilitation programs that incorporate rhythmic accompaniment as a means to organise (or re-organise) movement amongst pathological populations (Bradt, Magee, Dileo, Wheeler, & McGilloway, 2010; Clair & O'Konski, 2006; Conklyn et al., 2010; Delval et al., 2008; Hausdorff et al., 2007; Hurt et al., 1998; McIntosh, Brown, Rice, & Thaut, 1997; Thaut et al., 2007; Thaut et al., 1997; Thaut et al., 1996; Thaut, Miltner, Lange, Hurt, & Hoemberg, 1999). Despite the recognition that individuals with motor dysfunction can receive benefit from exercise programs incorporating rhythmic stimuli (Bryant et al., 2009; de Bruin et al., 2010; del Olmo & Cudeiro, 2005; Marchese et al., 2000; Nieuwboer et al., 2007; Rochester et al., 2010; Thaut et al., 1996), the sustainability of training-related motor improvements is undoubtedly dependent on continued engagement in the rehabilitation program (Ellis et al., 2005). This possibility may be questionable though, especially given the low exercise participation and adherence that are commonly reported amongst people with movement pathologies (Ene et al., 2011; Fertl et al., 1993). Interestingly, recent research is increasingly indicating that

adding appropriate music selections to an exercise program can prove motivational and improve affective states (Bishop et al., 2007; Crust & Clough, 2006; Karageorghis & Terry, 1997; Karageorghis, Terry, & Lane, 1999). Furthermore, listening to music during moderate intensity exercise can attenuate perceptions of fatigue and discomfort (Crust, 2004; Karageorghis & Terry, 1997; Shaulov & Lufi, 2009; Yamashita et al., 2006) and increase exercise participation and adherence (Bauldoff et al., 2002; Johnson, et al., 2001; Karageorghis & Terry, 1997).

In view of the complimentary bodies of literature demonstrating the beneficial effects of rhythmically cued and music-accompanied exercise, we suggest that contemporary commercially available music may be an attractive alternative to typical stimulus modes, such as a metronome tone or cue-accentuated music selections that are currently implemented in cued gait rehabilitation programs. This possibility is grounded in the rich literature base showing the potential of contemporary music (Priest, Karageorghis, & Sharp, 2004) to influence movement performance, affect (Bishop et al., 2007; Crust & Clough, 2006; Karageorghis & Terry, 1997), and exercise adherence (Johnson et al., 2001; Karageorghis & Terry, 1997). Further, the relative ease and minimal outlay with which an individualised music playlist can be created and administered, through software applications such as iTunes[®], makes commercially available music an appealing proposition as a rhythmic cue. We have previously confirmed the feasibility of using this approach in a walking intervention for people with mild to moderate severity PD (de Bruin et al., 2010). Whilst our findings did suggest that commercially available music was an effective, enjoyable and safe gait training tool for use amongst those with PD, we recognise that the potential for music, particularly music that is familiar and enjoyable (herein defined as salient music) to differentially influence the psychophysical response of each listener

may limit the generalizability of our findings. Therefore, to overcome this potential limitation and to fully explore the breadth of application in using commercially available music as a temporal cue we conducted a series of studies to explore how specific acoustical parameters of music can influence gait.

Accordingly, there were three aims of this series of studies. The first was to confirm that commercially available music can be used to influence gait patterning. Based on the inherent rhythmicity of the music and the identified temporal interactions of the auditory and motor systems (Thaut, 2005), we hypothesised that commercially available music would influence gait patterning. In follow-up to this foundation, the second aim was to establish whether the salience of the music differentially modulated the effects observed. Specifically, does the effect of the music on gait patterning change if the music selections are familiar and enjoyable? The value of this question is in consideration of the fact that when selecting music for therapeutic purposes rhythm is typically the primary focus (Thaut, 2005), however, the patients' affective response to the music will conceivably influence their enjoyment of the cued intervention and accordingly has the potential to mediate physical performance and activity adherence (McAuley, Morris, et al., 2007; Motl et al., 2000). We therefore expected that music salience would affect the magnitude of observed change in gait performance, with salient music mediating the greatest change to gait patterning.

A crucial feature of standard gait treatment protocols that incorporate RAS is the ability to adjust the timekeeper frequency. Rhythmic auditory stimulation therapies typically utilise stepwise limit cycle (step rate) entrainment. Once the patients natural step rate has been effectively stabilised new step rates are entrained at a lower or higher cadence depending on the goals of the protocol. Accordingly, the

third aim in this series of studies was to determine whether we could replicate this protocol design using music cues of differing tempi. Given the widely reported phenomenon that gait patterning can be effectively modulated by the tempo of an auditory rhythm (Ford et al., 2007; Hurt et al., 1998; Kenyon & Thaut, 2000; Lim et al., 2005; Mauritz, 2002; Thaut et al., 2007; Thaut et al., 1997; Thaut, Miltner, et al., 1999; Willems et al., 2006), we hypothesised that temporal parameters of gait would be up-or down-regulated in accordance with the tempo of the music.

3.3 Methods

3.3.1 Subjects. Twenty-five young adults (18-25 years) were recruited from the University of Lethbridge undergraduate student population. All subjects were self-declared to be of good health, with no known neurological or orthopaedic conditions that could affect gait performance. The studies were approved by the University of Lethbridge Human Subject Research Committee. All subjects were informed of the nature of the study and provided informed written consent prior to the start of the study. Following enrolment into the study, subjects were randomly assigned to one of two study groups. Subject demographics are provided in Table 3.1.

Table 3.1 *Subject demographics*

Characteristic	Study 1	Study 2
No. of subjects	15	10
Sex (M/F)	5/10	4/6
Age (years)	21.3 (1.6)	21.3 (2.2)

Note. Values are mean (standard deviation) for continuous variables, and number for nominal variables. M: Male; F: Female.

3.3.2 Protocol. Subjects were asked to walk the length of an unobstructed 55 metre walkway, marked on the straight of an indoor running track (1st Choice Savings Centre, University of Lethbridge) in differing test conditions. Data were collected from the central 50 metres of the walkway so as to minimise the effects of acceleration and deceleration. Subjects were not provided with instructions regarding synchronisation with cues; they were simply instructed to “walk the length of the walkway at a comfortable pace”. One uncued practice trial was completed by each subject prior to data collection.

Study 1: Music. To establish the potential of using music to manipulate gait patterning and furthermore to investigate the influence of music salience on cue efficacy, test conditions were differentiated by cue modality; no cue (NC), metronome (MET), non-salient music (NSM) and salient music (SM). Criteria for cue selection are defined in section 3.3.3. Subjects performed a total of 16 walking trials; four baseline (NC) trials followed by three blocks of four trials each, one block of each cue modality (MET/NSM/SM). The order of blocks of cued trials was randomised between subjects. Subjects listened to the cue for approximately 30 seconds prior to the onset of each trial to ensure that they were walking to the harmonic section of the musical tracks.

Study 2: Cue frequency. Subsequently, we investigated the effect of cue frequency on gait performance. Given our interest in exploring music as a cue modality for people with PD, we explored this possibility with traditional (metronome) and music cues. Test conditions were differentiated by cue modality and frequency; no cue (NC), metronome at frequencies of 90, 100, and 110% of subjects preferred walking cadence (MET90, MET100, MET110 respectively), and salient music with tempi at frequencies of 90, 100, 110% of preferred walking cadence

(MUS90, MUS100, MUS110 respectively). Procedures for the determination of subjects' preferred walking cadence and required cue frequencies are described fully in section 3.3.3. Subjects completed blocks of three trials in each condition for a total of 21 trials (Figure 3.1). MET and MUS conditions were randomised within subjects. Subjects listened to the cue for approximately 30 seconds prior to the onset of each trial, in the case of the MUS condition this was to ensure that subjects were walking to the harmonic section of the music.

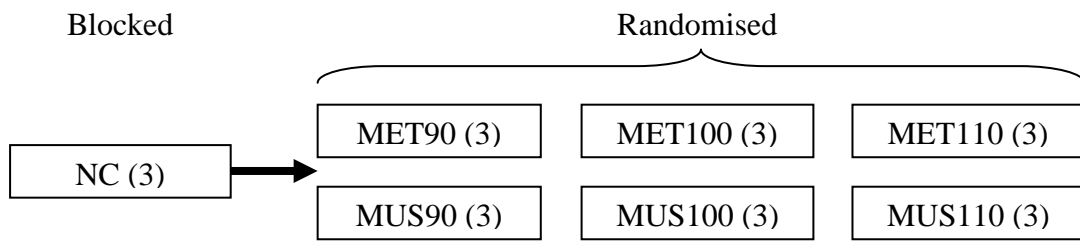


Figure 3.1 Experimental design for Study 2.

3.3.3 Cues. Each subjects' preferred walking cadence was determined across three 10 metre (Study 1) or 50 metre (Study 2) walking trials during a screening visit. During screening subjects were also asked to select their favourite music genre (Pop/Rock/Country/Rap/Classical/Other) and to provide their three preferred artists within that music genre, in order of preference, on a musical tastes questionnaire. Metronome tracks were created using Audacity 1.4.0 software (<http://audacity.sourceforge.net>). The tempo of each metronome track was matched exactly to tempo requirements (90, 100, or 110% of subject's preferred walking cadence; Table 3.2). The range of tempi for the SM and NSM tracks was matched to within ± 2.5 beats/minute (bpm) of the tempo requirements (90, 100, or 110% of subject's preferred cadence; Table 3.2). The tempo of each music track was determined independently by two raters using DJ sequencer software (Jackson 1.34; <http://vanaeken.com/>), agreement between raters was absolute. Salient music was selected for each subject by matching indicated genre and artist preferences. Playlists were loaded to an iPod Nano® (Apple Inc., Cupertino, CA, USA). Following each trial subjects were asked to rate their enjoyment of each music and metronome track on a scale from 0 to 10, where 0 would represent 'no enjoyment', and 10 would represent 'very enjoyable'.

Table 3.2 *Example of cue tempi used in Study 2 based on subjects' preferred walking cadence*

	Cue condition	Tempo of provided track (bpm)
Subjects preferred walking cadence = 100 steps/minute	MET90	90
	MET100	100
	MET110	110
	MUS90	87.5 - 92.5
	MUS100	97.5 - 102.5
	MUS110	107.5 - 112.5

Study 1: Music. An individualised playlist was created for each subject comprising of a MET track, two SM tracks and two NSM tracks. The tempo of the each track was matched to the subjects' calculated preferred cadence (100%; MET100/MUS100; Table 3.2). Non-salient music tracks were selected from a single genre and artist not representative of music typical to contemporary Western society.

Study 2: Cue frequency. Each subject's playlist included three MET tracks and three SM tracks. The tempi of the MET tracks were matched to 90, 10, and 110% of the subject's preferred cadence (MET90/MET100/MET110; Table 3.2). Three different SM tracks were selected for each playlist, one track with a published tempo at each of 90, 100, and 110% of the subject's preferred cadence (MUS90/MUS100/MUS110; Table 3.2).

3.3.4 Apparatus. Cues were played through earphones at a self-selected volume from an iPod Nano® attached to the waistband of the subject's pants. Footswitches attached to a patient unit secured at the subjects' waists were used to collect temporal gait data. The footswitches were placed in the subjects' right shoes beneath both the head of the first metatarsal and the calcaneus. A timing light system (in-house) consisting of an infrared light emitter and sensor attached to the subjects' belt and reflectors at either end of the (50m) walkway allowed the collection of timing data. When subjects passed the reflector at the beginning and end of the walkway the light source was reflected, providing the signal to commence or terminate timing. Analog data were collected using Labview® software (100Hz; Version 5.0, National Instruments, Austin, TX, USA).

3.3.5 Data Processing. Custom written algorithms were created in Matlab® (Version R2007a; The Mathworks, Natick, MA, USA) to process the footswitch data

and calculate spatiotemporal parameters of gait. Gait parameters consisted of: (1) gait velocity (m/s), (2) stride length (m), (3) cadence (steps/min), and (4) stride time variability (coefficient of variation = 100 [standard deviation/mean]; %). Mean values were calculated across gait cycles and within each cue condition.

3.3.6 Statistical Analysis. Statistical analyses were completed using SPSS Statistics 17.0 for Windows (SPSS Inc., Chicago, IL). Statistical significance was set at $\alpha = 0.05$ unless stated. Effect size (ES) was reported as partial η^2 values.

Study 1: Music. Tempo data and enjoyment scores for each cue modality were summarized descriptively and compared between modalities using one-way (Cue [MET/NSM/SM]) Repeated-Measures Analyses of Variance (RM ANOVA). To assess the effect of cue modality on parameters of gait separate one-way (Cue [(NC/MET/NSM/SM)]) RM ANOVAs were performed for each parameter. When statistical significance was determined Bonferroni corrected pairwise comparisons were performed between the uncued (NC) and cued (MET/NSM/SM) conditions ($p \leq .017$), as well as between cued conditions (MET/NSM/SM; $p \leq .017$).

Study 2: Cue frequency. The tempi and enjoyment scores were summarized descriptively and compared between cue modalities (MET/MUS) using pairwise comparisons at each presentation frequency (90/100/110). To establish the effect of differing tempi on kinematic parameters of gait, separate one-way (Tempo [NC/90/100/110]) RM ANOVAs were calculated for each parameter and cue modality (MET/MUS). Bonferroni corrected pairwise comparisons were performed between the baseline condition (NC) and each cue frequency (90/100/110) for the relevant cue modality (MET/MUS; $p \leq .017$) when statistical significance was

established. Comparisons were also performed between different cue frequencies (90/100/110) for each cue modality (MET/MUS; $p \leq .017$).

3.4 Results

3.4.1 Study 1: Music. The mean tempo of tracks selected for each cue modality did not differ significantly between cues ($p > .05$; MET=117.7bpm; NSM=117.8bpm; SM=117.4bpm). Enjoyment scores were significantly different between cue modalities ($F[2, 28] = 65.542, p < .001, ES = .824$), with subjects indicating that they enjoyed the music conditions significantly more than the metronome condition (NSM, $t[14] = 5.524, p < .001$; SM, $t[14] = 10.126, p < .001$). Moreover, subjects indicated greater enjoyment during the SM condition than the NSM condition ($t[14] = 7.448, p < .001$).

Cue modality significantly affected spatiotemporal parameters of gait as confirmed by a main effect of Cue for gait velocity ($F[3, 42] = 7.609, p < .001, ES = .352$; Figure 3.2a), stride length ($F[3, 42] = 4.705, p = .006, ES = .252$; Figure 3.2b), and cadence ($F[3, 42] = 3.212, p = .032, ES = .187$; Figure 3.2c). Subjects adjusted their gait pattern to walk faster in the presence of MET ($t[14] = 3.128, p = .007$) and SM ($t[14] = 2.908, p = .011$) when compared to the NC trials. Subjects also demonstrated a tendency to increase their stride amplitude and step rate when listening to the MET and SM tracks, follow-up comparisons however, failed to reach significance ($p > .017$). Furthermore, subjects walked significantly faster and with longer strides in the MET (gait velocity, $t[14] = 3.485, p = .004$; stride length, $t[14] = 2.813, p = .014$) and SM (gait velocity, $t[14]=3.656, p \leq .001$; stride length, $t[14] = 3.136, p = .007$) conditions when compared to the NSM condition. Subjects did not

significantly alter their gait patterning between MET and SM conditions ($p > .05$).

Stride time variability was not affected by cue modality ($p > .05$; Figure 3.2d).

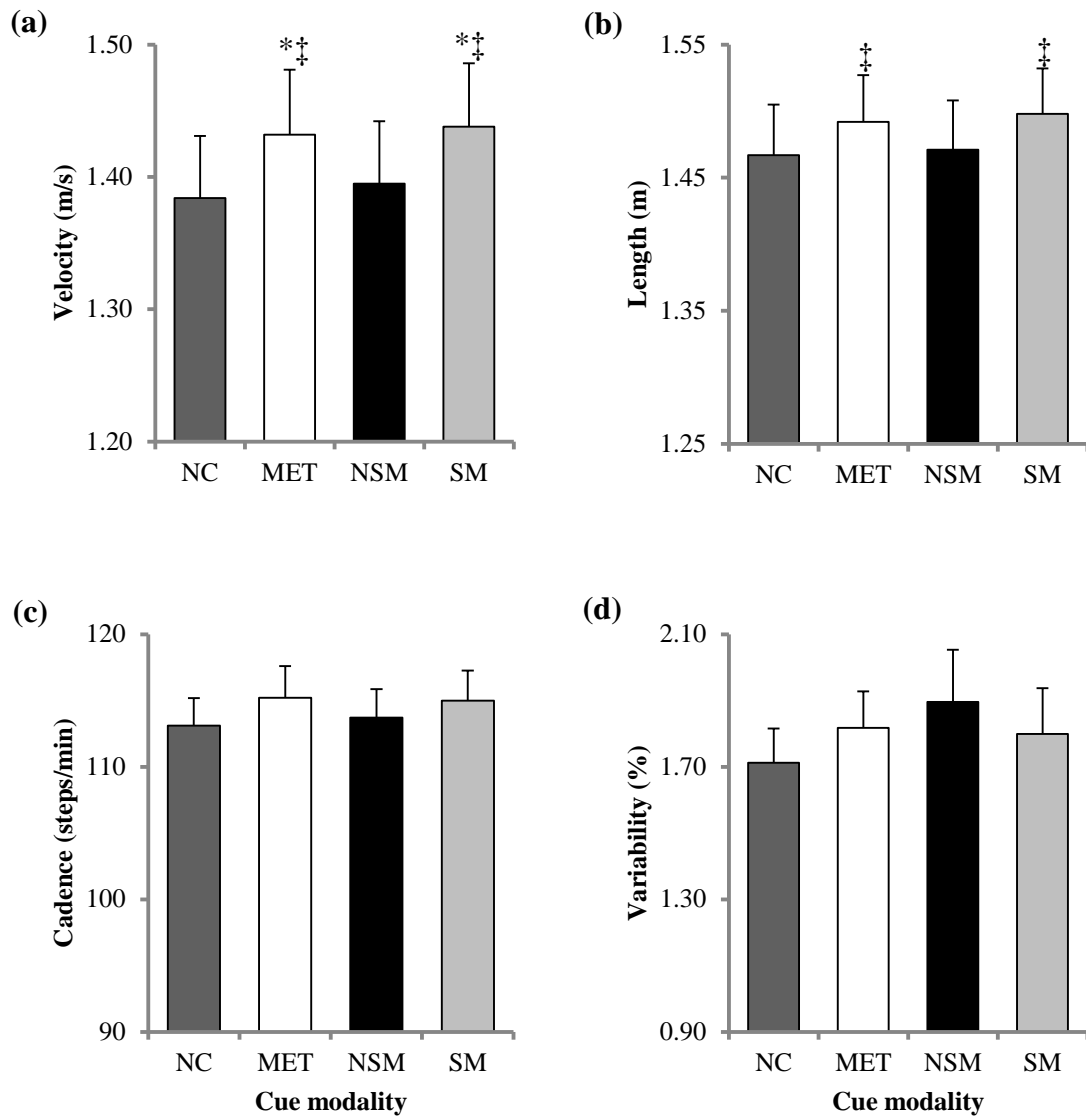


Figure 3.2 Effect of cue modality on average (a) gait velocity, (b) stride length, (c) cadence, and (d) stride time variability. Data presented are means and standard errors.

* $p \leq 0.017$ with respect to NC condition; ‡ $p \leq 0.017$ with respect to NSM condition.

3.4.2 Study 2: Cue frequency. The tempo of the provided cues was consistent between MET and MUS conditions at 90, 100, and 110 percent of the subjects preferred cadence ($p > .05$; Table 3.4). Enjoyment scores differed significantly between cue modalities at 90, 100, and 110 percent, with subjects enjoying the music conditions considerably more than the metronome conditions (90%, $t[9] = 9.791$, $p < .001$; 100%, $t[9] = 7.709$, $p < .001$; 110%, $t[9] = 7.344$, $p < .001$).

In the MET condition a main effect of Tempo indicated that subjects walked faster ($F[3, 27] = 3.773$, $p = .022$, $ES = .295$; Figure 3.3a) and with longer strides ($F[3, 27] = 3.482$, $p = .029$, $ES = .279$; Figure 3.3b) in response to increasing metronome tempo; follow-up comparisons however, failed to reach significance ($p > .05$). Cadence and stride time variability were not significantly altered by changes in MET presentation tempo ($p > .05$; Figures 3.3c and 3.3d respectively).

Subjects also adjusted their gait patterns in response to changes in music tempo as indicated by a main effect of Tempo for gait velocity ($F[3, 27] = 9.680$, $p < .001$, $ES = .518$; Figure 3.3a) and stride length ($F[3, 27] = 8.930$, $p < .001$, $ES = .498$; Figure 3.3b). Specifically, subjects walked significantly faster in the 90% ($t[9] = 6.332$, $p < .001$), 100% ($t[9] = 3.320$, $p = .009$), and 110% ($t[9] = 4.389$, $p = .002$) conditions when compared to the baseline (NC) condition (Figure 3.3a). Furthermore, subjects walked with a longer stride length in all music conditions when compared to the NC condition (90%, $t[9] = 4.482$, $p = .002$; 100%, $t[9] = 4.217$, $p = .002$; 110%, $t[9] = 4.049$, $p = .003$; Figure 3.2b). Walking speed and stride length did not differ between music conditions ($p > .017$). There was not an effect of Tempo for the measures of cadence or stride time variability ($p > .05$; Figures 3.3c and 3.3d respectively).

Table 3.4 *Summary of tempo data and enjoyment scores for Study 2.*

Parameter	MET			MUS		
	90	100	110	90	100	110
Tempo (bpm)	102.6(6.5)	113.3(7.5)	124.5(8.1)	101.8(7.1)	112.8(7.4)	124.5(7.9)
Enjoyment Score (0-10)	2.000(1.5)	2.300(1.9)	2.300(2.0)	9.000(.94)*	8.600(.97)*	8.800(1.1)*

MET and MUS values are presented as mean (standard deviation). * $p < 0.001$ with respect to equivalent MET condition.

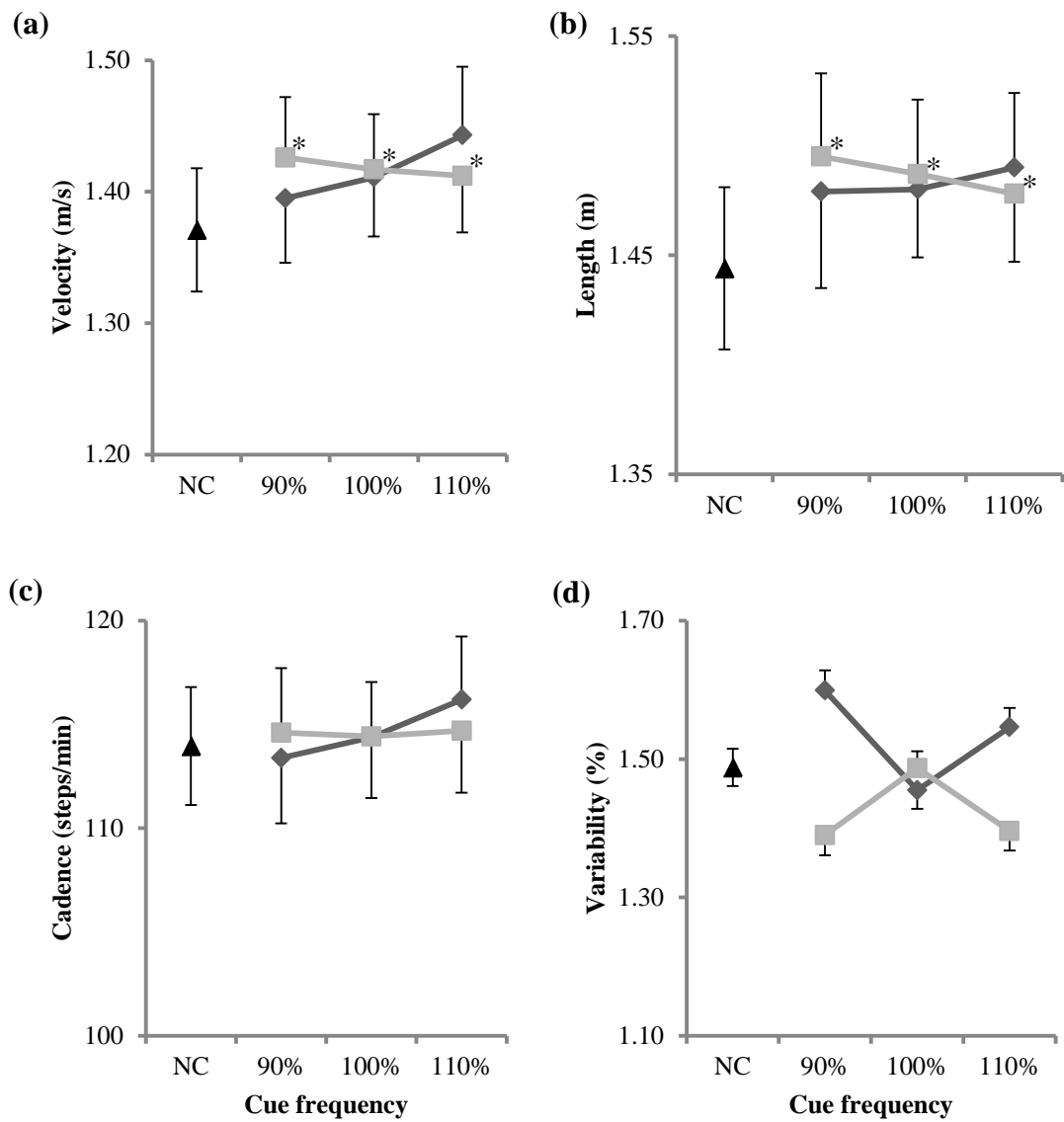


Figure 3.3 Effect of cue frequency on average (a) gait velocity, (b) stride length, (c) cadence, and (d) stride time variability. Black triangles represent the NC condition, dark diamonds and lines represent the MET conditions, light squares and lines represent the MUS conditions. Data presented are means and standard errors.

* $p \leq 0.017$ with respect to NC condition.

3.5 Discussion

This series of experiments explored how critical features of music selection can influence gait. The music used during these studies differed with respect to salience (familiarity and enjoyment) to the listener and tempo. Our findings indicated that music can influence spatiotemporal parameters of gait. Moreover, the physical response of the individual to the music selection is affected by the salience of the piece. Interestingly, the tempo of the music selection did not appear to differentially modulate the listeners' response to the cue. We suggest that the effects of music on gait, coupled with the high level of enjoyment indicated when listening to salient music whilst walking imply that salient music could provide an effective alternative to traditional auditory cues for use in cued therapeutic programs where increases in gait parameters such as velocity and stride length are considered beneficial.

Consistent with our hypothesis, the current findings indicated that music matched to the subjects preferred walking cadence modulated gait performance. The physical response of the subject to the music selection was however, influenced by the salience of the music. In the presence of tempo-matched salient music, gait velocity, stride length, and cadence increased in a manner comparable to when subjects were listening to a simple metronome tone. This finding is in accordance with previous work which has demonstrated improvements in gait performance amongst healthy and pathological older adult populations with a cadence-matched auditory cue (Arias & Cudeiro, 2008; Rochester et al., 2005; Willems et al., 2006). Conversely, non-salient music failed to modify gait patterning. In combination, these results are suggestive that therapeutic benefit and enjoyment need not be mutually exclusive. Indeed, enjoyment should be a central consideration when developing therapeutic exercise programs that require long-term participation, as exercise enjoyment has been

identified as an important determinant of program adherence and efficacy (Huberty et al., 2008; McAuley, Motl, et al., 2007; Wankel, Yardley, & Graham, 1985; Wininger & Pargman, 2003).

Metronome and salient music cues were effective in modifying spatiotemporal parameters of gait amongst the young adults enrolled in these studies; however, the observed improvements to gait were not differentially modulated by the presentation frequency of the cue. Increases in gait velocity, stride amplitude and/or cadence were comparable between cue tempi indicating that similar alterations to gait could be achieved using metronome or music cues equal to 90, 100 or 110 percent of the individuals preferred walking cadence. This finding was contrary to our hypothesis and the substantial body of research demonstrating that metronome cues provided at progressively increasing tempi differentially alter gait performance (Ford et al., 2007; Hurt et al., 1998; Kenyon & Thaut, 2000; Lim et al., 2005; Mauritz, 2002; Thaut et al., 2007; Thaut et al., 1997; Willems et al., 2006). A possible explanation for the contradictory results of the current series of studies may be that the subjects were not provided with explicit instructions to step in time with the beat of the music or metronome. The decision not to instruct subjects to synchronise their step with the cue was taken to maintain consistency with our earlier work (Brown et al., 2010; Brown et al., 2009); however, we recognise that this design decision conceivably restricted the benefits induced by the tempo of the cues.

Interestingly, stride time variability was largely unaltered by cue modality and cue tempo amongst the young adults. Stride-to-stride variability has been associated with fall risk amongst older adults with and without pathologies (Hausdorff, 2005; Hausdorff, Rios, & Edelberg, 2001; Nakamura, Meguro, & Sasaki, 1996; Plotnik, Giladi, Dagan, & Hausdorff, 2011; Schaafsma et al., 2003) and as a consequence is an

important consideration when developing novel cueing strategies. It is recognised however, that older adults and individuals with pathologies typically dedicate greater attentional resources to walking than healthy young adults (Lajoie, Teasdale, Bard, & Fleury, 1996; Woollacott & Shumway-Cook, 2002; Yogev-Seligmann et al., 2008); it is therefore conceivable that the cues applied in the current studies would increase stride time variability amongst subjects who have limited attentional resources available to attend to the environment and potential distracters. This possibility should be thoroughly investigated prior to implementing commercial music within a cueing program.

3.6 Conclusions

Contemporary commercial music influences gait performance amongst healthy young adults; however, music salience may be an important determinant in the efficacy of using commercial music as an auditory cue. Whilst our findings do not resolve the complexities of establishing selection criteria for music tracks in cued exercise programs the studies do provide a foundation on which to base future research directed towards clarifying the role of music tempo and other acoustical parameters (e.g. changes in pitch, harmony) in modulating gait performance.

Chapter 4: Walking with music is a safe and viable tool for gait training in Parkinson's disease: The effect of a 13-week feasibility study on single- and dual-task walking¹

4.1 Abstract

This study explored the viability and efficacy of integrating cadence-matched, salient music into a walking intervention for patients with PD. Twenty-two people with PD were randomised to a control (CTRL, n = 11) or experimental (MUSIC, n = 11) group. MUSIC subjects walked with an individualised music playlist three times a week for the intervention period. Playlists were designed to meet subject's musical preferences. In addition, the tempo of the music closely matched ($\pm 10-15$ bpm) the subject's preferred cadence. CTRL subjects continued with their regular activities during the intervention. The effects of training accompanied by "walking songs" were evaluated using objective measures of gait in conjunction with a standard clinical score. The MUSIC group improved gait velocity, stride time, cadence and motor symptom severity following the intervention. This is the first study to demonstrate that music listening can be safely implemented amongst PD patients during home exercise.

¹Chapter 4 is published in modified form; de Bruin, N., Doan, J.B., Turnbull, G., Suchowersky, O., Bonfield, S., Hu, B., & Brown, L.A. (2010). Walking with music is a safe and viable tool for gait training in Parkinson's disease: The effect of a 13-week feasibility study on single and dual task walking. *Parkinson's Disease*, 2010, 483530.

4.2 Introduction

The gait disturbances that characterise PD have been associated with increased fall risk, diminished mobility (Grimbergen et al., 2004; Stolze et al., 2004), loss of independence (Grimbergen et al., 2004; Shulman et al., 2008), and reduced quality of life (Rahman, Griffin, Quinn, & Jahanshahi, 2008; Schrag, Jahanshahi, & Quinn, 2000). Mobility impairments and fall risk amongst PD patients are further exacerbated when patients are engaged in a secondary task (Bloem, Valkenburg, Slabbekoorn, & van Dijk, 2001; Bond & Morris, 2000; Canning, 2005; Morris et al., 1996; O'Shea, Morris, & Iansek, 2002; Rochester et al., 2004), such as talking whilst walking. This phenomenon, known as dual task interference, is considered a common contributing factor to falls in the elderly, especially those with movement disorders and/or dementia (Beauchet et al., 2009). The inability to consistently manage gait deficits with pharmacological treatments has led to the development of rehabilitation strategies intended towards relieving gait impairments. One rehabilitation strategy that has frequently been reported as effectual for improving gait performance in PD is the use of rhythmic auditory cues (Lim et al., 2005; Nieuwboer et al., 2007; Picelli et al., 2010; Rochester et al., 2005; Rochester et al., 2007). Single session studies have established the effectiveness of auditory cueing in temporarily improving gait velocity, amplitude, frequency and variability across single- (Lim et al., 2005; Picelli et al., 2010) and dual-task (Rochester et al., 2005; Rochester et al., 2007) contexts. Furthermore, a number of studies have demonstrated the feasibility of incorporating auditory cues into exercise rehabilitation strategies to significantly improve gait performance and decrease motor symptom severity (Bryant et al., 2009; del Olmo & Cudeiro, 2005; Marchese et al., 2000; Miller et al., 1996; Nieuwboer et al., 2007; Rochester et al., 2010; Thaut et al., 1996). Although the efficacy of training with a

simple repetitive tone (Bryant et al., 2009; del Olmo & Cudeiro, 2005; Marchese et al., 2000; Nieuwboer et al., 2007; Rochester et al., 2010) or rhythmically accentuated music (Miller et al., 1996; Thaut et al., 1996) to facilitate parkinsonian gait has been widely documented, practical applications and the benefits of these rehabilitation strategies are constrained by several factors. First, there has been a lack of studies investigating how a musical piece or “walking song” should be constructed for individual patients thereby optimising the congruence of the music with walking and exercise, and maximizing the positive cueing effect. Second, even though the use of music at home during exercise may be considered beneficial and highly desirable, safety remains a major concern for patients. Previously, we reported that listening to music may have a distractive effect when initially combined with walking, possibly creating a dual task condition (Brown et al., 2009). It is possible; however, that this is a short-term phenomenon and that over time patients may become accustomed to the task.

To address these issues, in this study we implemented a 13-week home-based music and walking program. We selected commercially available music that was unaltered, and familiar and enjoyable to individual patients. The tempo of each musical piece was carefully evaluated to ensure it closely matched the preferred walking cadence of the respective patient. The temporal matching contrasts the aforementioned study, in which the intrinsic properties of the music were not controlled, potentially contributing to the gait deficits demonstrated by PD patients whilst walking with music (Brown et al., 2009). In the current study spatiotemporal parameters of gait and symptom severity were assessed pre-and post-intervention. Based on the substantiated effectiveness of rhythmic auditory cues in producing immediate and short-term improvements in parameters of gait across a variety of

functional gait activities (Bryant et al., 2009; del Olmo & Cudeiro, 2005; Lim et al., 2005; Marchese et al., 2000; Miller et al., 1996; Nieuwboer et al., 2007; Picelli et al., 2010; Rochester et al., 2010; Rochester et al., 2005; Rochester et al., 2007; Thaut et al., 1996) we hypothesised that a walking intervention that incorporated a music cueing program could be safely implemented and would result in improved gait performance across single and dual task test conditions post-intervention.

4.3 Methods

4.3.1 Subjects. Thirty-three patients with mild to moderate PD were enrolled from two research centres: University of Lethbridge, Lethbridge, Canada (n = 12) and Dalhousie University, Halifax, Canada (n = 21). Following enrolment, patients were randomly allocated to a control (CTRL) group (n = 17) or an experimental (MUSIC) group (n = 16). The Lethbridge subjects provided data (Unified Parkinson's Disease Rating Scale (UPDRS); Fahn & Elton, 1987, Gait and Balance Scale (GABS); Thomas et al., 2004, Activities-specific Balance Confidence scale (ABC); Powell & Myers, 1995, and Parkinson's Disease Questionnaire-39 (PDQ-39); Jenkinson, Fitzpatrick, Peto, Greenhall, & Hyman, 1997) for a companion study to be reported subsequently. The GABS, ABC and PDQ-39 data are not included in this study.

Eligibility criteria were diagnosis of PD (United Kingdom Brain Bank Criteria; Fahn, 1987), stage II-III on the Hoehn and Yahr scale (Hoehn & Yahr, 1967), stable medication regimen, independently mobile without the use of a walking aid, and intact hearing. Patients were excluded from the study if diagnosis was less than one year, if they had undergone deep brain stimulation surgery, if they experienced regular freezing episodes (self-report), neurological disorders or co-morbidities likely to affect gait, scored 24 or less on the Mini-Mental Status

Examination (MMSE; Folstein, Folstein, & McHugh, 1975) and/or already walked with music.

4.3.2 Ethics statement. The study was performed with approval by the University of Lethbridge Human Subject Research Committee and The Dalhousie University Health Sciences Research Ethics Board in accordance with the Declaration of Helsinki. All subjects were informed of the nature of the study and provided informed written consent prior to the start of the study.

4.3.3 Intervention. The CTRL group continued with any regular activities for the 13-week intervention period. The MUSIC group walked at least 30 minutes, three times a week at a comfortable pace whilst listening to an individualised music playlist through head/ear-phones on an iPod® (Apple Inc., Cupertino, CA) in addition to maintaining regular activities. Subjects walked on their own in the community and were asked to refrain from dual-tasking (i.e. conversing with companions or walking with pets) whilst participating in the music accompanied walks. Each of the subjects in the CTRL and MUSIC group maintained an 'Activities and Falls' diary in which physical activities, activity duration, and any falls experienced were documented each day. All subjects were contacted bi-weekly to monitor and ensure compliance.

4.3.4 Pre- and post-intervention assessment. Outcome measures were assessed immediately prior to randomisation (pre-intervention) and after 13 weeks (post-intervention). Subjects were tested on medications, at the same time of day for pre- and post-intervention assessments. Subjects walked the length of a 10 metre walkway at a self-selected pace in six different test conditions. Test conditions were differentiated by the presence of music accompaniment (no music/music) and the requirement to perform a simultaneous cognitive task (single-task/dual-task) or

negotiate a three-dimensional foam block obstruction (no obstacle/obstacle). This paper explores the training effects of a 13-week music accompanied walking program on single- and dual-task walking; therefore the results reported are for single- and dual-task walking trials without music. In addition, due to the differences in motor patterning between unobstructed and obstructed walking, the effects of the walking intervention on obstacle negotiation will be addressed in a separate paper.

The cognitive task consisted of serial 3 subtractions from a random 3 digit number. A new starting number was provided for each dual-task trial immediately prior to trial commencement. Subjects were instructed to prioritise walking and the cognitive task equally. Subjects completed 6 trials in each condition (N = 36 trials; Figure 4.1). Task presentation was randomised to control for order and practice effects. Music conditions were counterbalanced between subjects. One practice trial was performed for each task prior to the start of the testing session. A trained researcher supervised all subjects during testing to ensure subject safety. Frequent rests were provided to avoid fatigue.

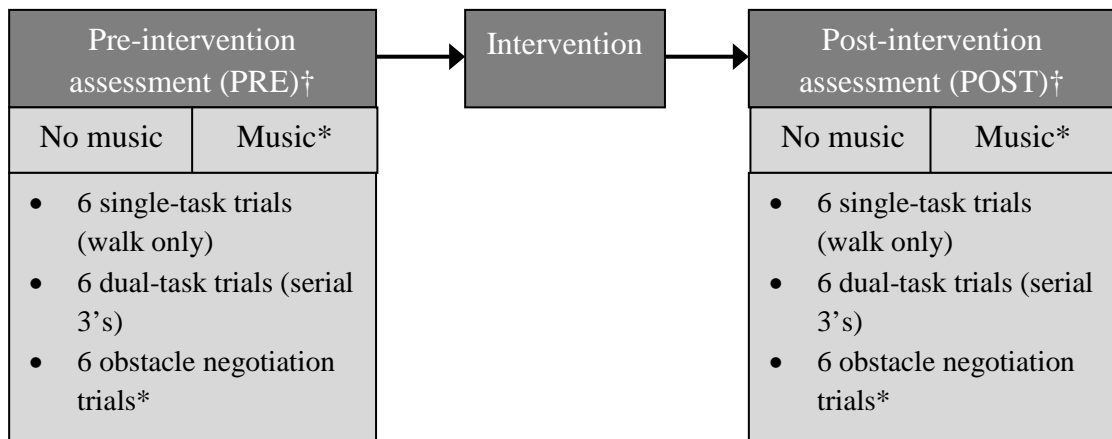


Figure 4.1 Experimental design. † Trials randomised. * Not included in current analysis.

4.3.5 Music. The cadence of each subjects' preferred walking speed was determined during the screening visit. The length of the walkway used to determine preferred cadence was 10 metre. Following randomisation, MUSIC subjects participated in a telephone interview with a music specialist (S.B.), detailing their music listening habits and preferences. An individualised music playlist was created for each subject with a specific arrangement of tempo-to-cadence matched songs that were identified to be salient to the patient. The music specialist defined music salience based on genre, artist and song preferences. The range of tempos for each playlist closely matched (± 10 -15 beats per minute) the preferred walking cadence of each respective patient. The tempo of each piece was determined independently by two raters using a metronome; agreement between raters was absolute. Each playlist was loaded to a personal music player (iPod Nano or Shuffle based on personal preference) and subjects were offered a choice of earbuds or headphones to maximise comfort. Playlists were approximately one hour in duration, and subjects were asked to play through the playlist in the sequence provided rather than setting the music player in 'shuffle' mode. Subjects were asked to refrain from listening to the music outside of the walking program. Prior to the commencement of the intervention subjects were provided with a familiarisation period on the iPod. The familiarisation period was concluded when the subject indicated confidence in operating the personal music player independently. Subjects were also informed that they could request changes to their playlist at any stage of the intervention.

4.3.6 Apparatus. Kinematic data were collected using the technology available at each research centre. Gait parameters were assessed using a 6.5 metre instrumented GAITRite® mat (100Hz; Dalhousie University; CIR Systems Inc, Havertown, PA) that was placed at the centre of a 10 metre walkway, or alternatively

using a six camera motion analysis system (120Hz; University of Lethbridge; Vicon-Peak®, Peak Performances Technologies, Englewood, CO). Seventeen passive markers were placed on the subjects for use with the camera motion analysis system as previously described (Brown et al., 2009). The validity and reliability of the GAITRite and Vicon systems for measuring spatiotemporal parameters of gait have previously been established (Bilney, Morris, & Webster, 2003). In addition, the inter-system reliability has been determined, with intraclass correlation coefficients of between 0.92 and 0.99 indicating good agreement between the GAITRite and Vicon systems for averaged spatial and temporal gait data. Absolute differences between the systems were reported as 0.02m/s; 2.03steps/min, and 0.02m for gait velocity, cadence, and stride length, respectively (Webster, Wittwer, & Feller, 2005). An iPod Nano with microphone, attached to the subjects' shirt, was used to capture verbalizations during the dual task trials.

4.3.7 Outcome measures. Aligned with the main goal of many gait training interventions, the primary outcome measure for this study was gait velocity (m/s) with secondary outcome measures consisting of stride time (s), stride length (m), and cadence (steps/minute). Error rates (subtraction errors: number of subtractions; %) on the dual task were also evaluated. Additionally, motor symptom severity was assessed using the UPDRS (III) motor section. All UPDRS (III) motor assessments were performed by a trained evaluator. The evaluator was blinded to subject group assignment; the order of assessment among groups was randomised within and between days.

Descriptive measures obtained pre-intervention included the Modified Baecke Questionnaire for Older Adults (Voorrips, Ravelli, Dongelmans, Deurenberg, & Van Staveren, 1991) and MMSE (Folstein et al., 1975). An eight item questionnaire was

administered to the MUSIC group post-intervention to determine music and intervention tolerance and adherence. The “Activities and Falls” diary was used to determine compliance to the intervention, walk duration, activity level and number and causes of falls during the intervention period.

4.3.8 Data processing. Raw marker data collected using the camera motion analysis system were filtered at 10Hz using a low pass fourth-order Butterworth filter and then processed using custom written algorithms (Matlab, Version R2007a; The Mathworks Inc, Redmond, WA). A seven segment model was used to calculate location of whole body centre of mass (COM) in the anterior-posterior (AP) direction. The finite differences method was then used to determine AP COM velocity. Kinematic data were cropped into gait cycles using the event of right heel contact. Mean values across gait cycles were calculated for each trial and trials were averaged across each test condition for each subject.

Verbal data collected during the dual-task trials were scored manually to determine relative error rates, based on a ratio of the number of subtraction errors to the number of subtractions during the trial. Delayed responses were considered correct or incorrect as appropriate. Mean values were calculated pre- and post-intervention.

4.3.9 Statistical analysis. Data were analysed using SPSS Statistics 17.0 for Windows (SPSS Inc., Chicago, IL). Subject characteristics, baseline measures, falls and walk durations were summarised descriptively and compared between groups using independent *t*-tests or chi-square tests. Responses to the eight item Post-intervention Questionnaire were summarized descriptively for the MUSIC group.

Disease severity could not be considered homogeneous between groups pre-intervention. Accordingly, separate 2-factor [Time (PRE/POST) x Task (SINGLE/DUAL)] Repeated-Measures Analyses of Variance (RM-ANOVA) were used to establish the effect of time and task on primary outcome measures within each group. Significant interactions were followed up with paired *t*-tests. Unified Parkinson's Disease Rating Scale motor scores and error rates were assessed using paired *t*-tests. Given the exploratory nature of the study Bonferroni corrections were not applied to multiple comparisons. Statistical significance was set at 0.05. Effect size (ES) was reported as partial η^2 values.

4.4 Results

Thirty-three PD patients were enrolled into the study; complete data collected from twenty-two subjects were used in final analysis (see Figure 4.2 for study flow chart). Subject demographics and clinical characteristics at baseline are provided in Table 4.1.

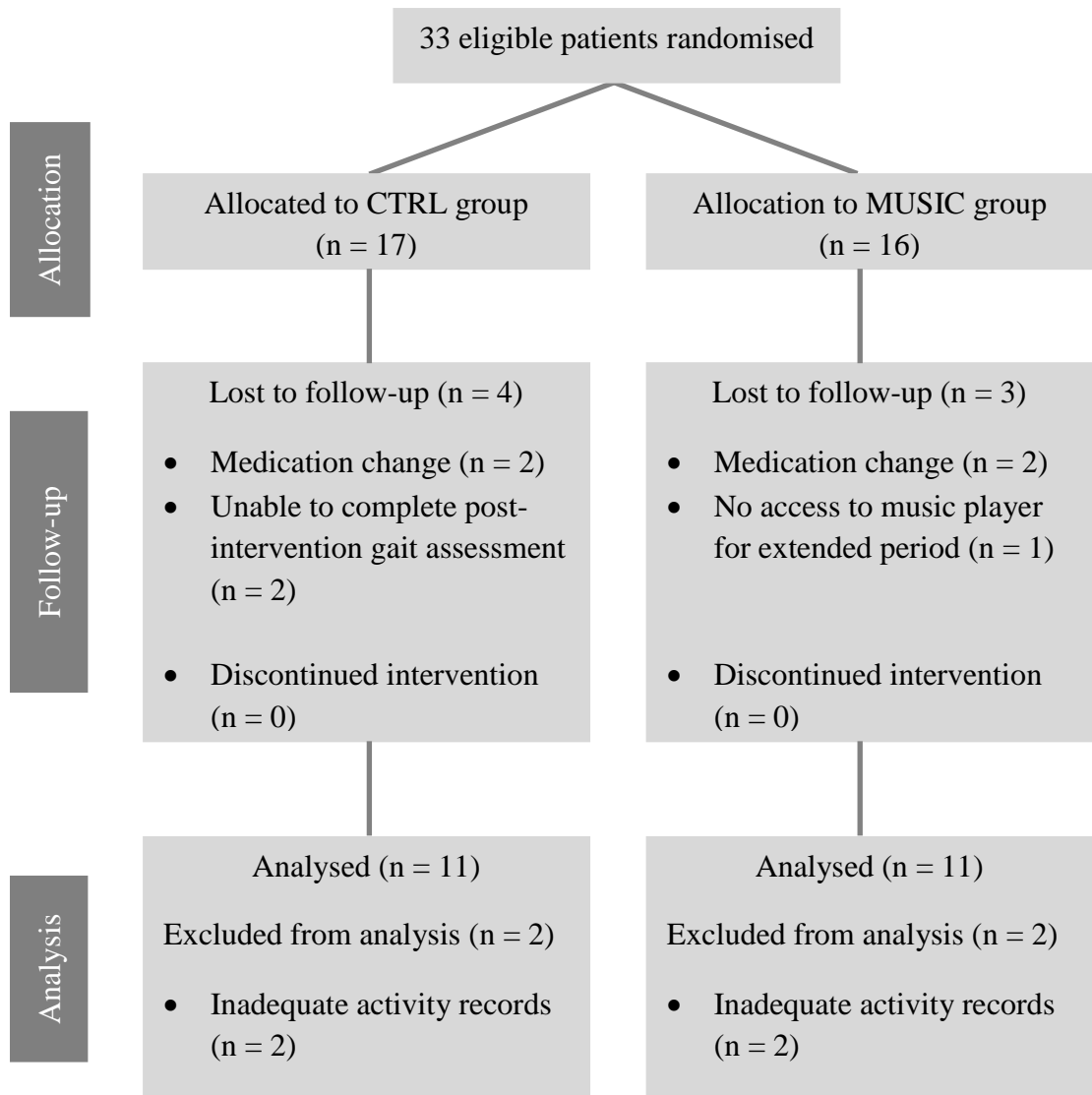


Figure 4.2 Study flow chart.

Table 4.1. *Subject demographics and clinical characteristics at baseline*

Characteristic	CTRL	MUSIC	<i>p</i>
No. of subjects	11 (4 Lethbridge)	11 (3 Lethbridge)	
Sex (M/F)	5/6	6/5	.67
Age (years)	67.0 (8.1)	64.1 (4.2)	.33
Disease duration (years)	4.5 (3.3)	6.4 (4.2)	.23
MMSE	28.4 (1.8)	29.3 (1.3)	.20
Hoehn and Yahr	2.1 (0.4)	2.3 (0.4)	.43
Baecke score	10.2 (4.8)	8.9 (3.8)	.48
UPDRS (III) score	20.4 (5.0)	25.5 (9.3)	.13

Values are mean (standard deviation) for continuous variable, and number for nominal variables.

F: Female; M: Male; MMSE: Mini Mental Status Examination; UPDRS: Unified Parkinson's Disease Rating Scale. MMSE, Hoehn and Yahr, and UPDRS scores were measured with subjects on anti-parkinsonian medication.

4.4.1 The effect of task on gait parameters. Descriptive statistics for all outcome measures are provided in Tables 4.2 and 4.3 for the CTRL and MUSIC subjects, respectively. A main effect for Task indicated that CTRL subjects walked slower ($F[10] = 7.749, p = .019, ES = .437$; Figure 4.3a), with shorter strides ($F[10] = 8.661, p = .015, ES = .464$; Figure 4.3c), and decreased cadence ($F[10] = 5.021, p = .049, ES = .344$; Figure 4.3d), and had a tendency towards increased stride time ($F[10] = 3.279, p = .100, ES = .247$; Figure 4.3b) in the dual-task condition. Similarly the MUSIC group walked with decreased velocity ($F[10] = 25.413, p = .001, ES = .718$; Figure 4.3a), stride time ($F[10] = 8.646, p = .015, ES = .464$; Figure 4.3b), stride length ($F[10] = 30.325, p < .001, ES = .752$; Figure 4.3c), and cadence ($F[10] = 10.688, p = .008, ES = .517$; Figure 4.3d) when walking in the dual-task condition.

Table 4.2 *Summary of descriptive statistics and change scores for the CTRL group for outcome measures pre- and post-intervention.*

Measure	SINGLE			DUAL			T	Ta	T x Ta
	PRE	POST	change	PRE	POST	change			
Velocity (m/s)*	1.27(0.16)	1.25(0.17)	0.02	1.03(0.41)	1.01(0.42)	0.03	.232	.019	.869
Stride time (s)	1.06(0.11)	1.06(0.13)	0.002	1.51(0.88)	1.53(0.90)	-0.01	.876	.100	.906
Stride length (m)*	1.33(0.13)	1.30(0.14)	0.03	1.25(0.20)	1.23(0.20)	0.02	.167	.015	.394
Cadence (steps/min)*	114(11.7)	115(13.1)	-0.62	96.3(32.8)	94.7(35.5)	1.64	.786	.049	.459
Error rate (%)	NA	NA	NA	13.4(19.7)	16.2(19.4)	-2.80	.631	NA	NA
UPDRS (III) score	20.4(5.03)	18.6(7.38)	1.82	NA	NA	NA	.286	NA	NA

PRE and POST values are presented as mean (standard deviation). Change values are PRE minus POST and are presented as mean. * A negative change value indicates an improvement in measure. T: Time; Ta: Task.

Table 4.3 *Summary of descriptive statistics and change scores for the MUSIC group for outcome measures pre- and post-intervention*

Measure	SINGLE			DUAL			T	Ta	T x Ta
	PRE	POST	change	PRE	POST	change			
Velocity (m/s)*	1.28(0.22)	1.31(0.22)	-0.03	1.09(0.26)	1.16(0.24)	-0.07	.002	.001	.081
Stride time (s)	1.07(0.07)	1.06(0.07)	0.02	1.20(0.15)	1.11(0.08)	0.08	.019	.015	.062
Stride length (m)*	1.36(0.17)	1.37(0.18)	-0.01	1.27(0.20)	1.28(0.21)	-0.01	.524	.000	.887
Cadence (steps/min)*	112(7.86)	114(7.85)	-1.95	102(12.0)	108(7.76)	-6.53	.007	.008	.056
Error rate (%)	NA	NA	NA	13.2(12.8)	7.42(9.50)	5.76	.155	NA	NA
UPDRS (III) score	25.5(9.28)	19.9(9.05)	5.55	NA	NA	NA	.002	NA	NA

PRE and POST values are presented as mean (standard deviation). Change values are PRE minus POST, and are presented as mean. * A negative change value indicates an improvement in measure. T: Time; Ta: Task.

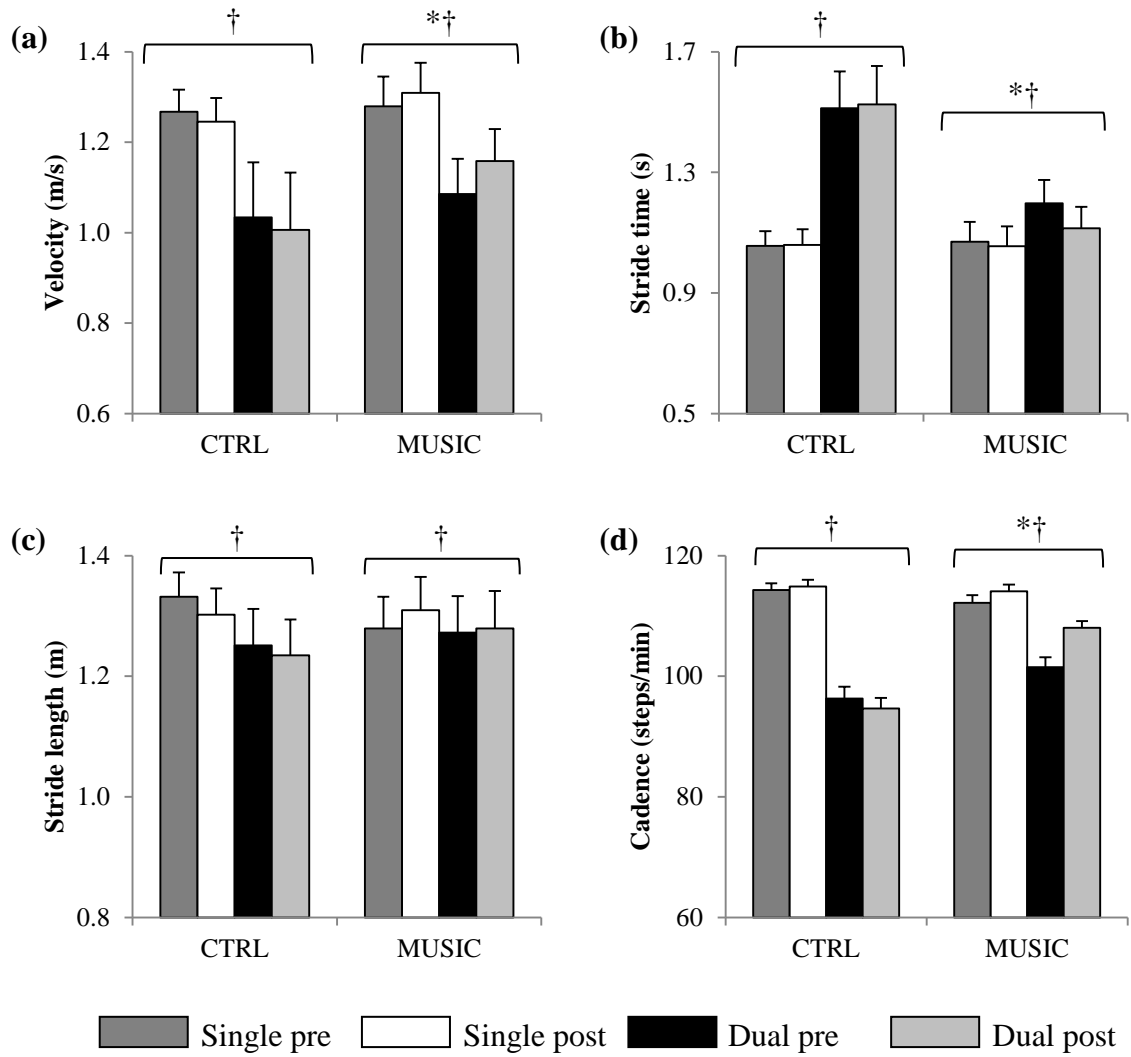


Figure 4.3 Effect of intervention on gait parameters in single- and dual-task conditions. Effect of intervention on (a) velocity, (b) stride time, (c) stride length, and (d) cadence, during single-task and dual-task conditions, pre- and post-intervention amongst CTRL and MUSIC groups (means and standard errors). * Significant effect of Time. † Significant effect of Task.

4.4.2 The effect of intervention on outcome measures. The 13-week intervention did not have an effect on the outcome measures of the CTRL group ($p > .05$). In addition, Time-by-Task interactions did not reach significance ($p > .05$), indicating that the changes to gait parameters observed among the CTRL group following the 13-week intervention were consistent across single and dual task conditions. In contrast, the MUSIC group demonstrated a significant increase in velocity ($F[10] = 17.474, p = .002, ES = .636$; Figure 4.3a) and cadence ($F[10] = 11.629, p = .007, ES = .538$; Figure 4.3d), and a decrease in stride time ($F[10] = 7.740, p = .019, ES = .436$; Figure 4.3b) following the 13-week intervention. Time-by-task interactions approaching significance were observed for velocity ($F[10] = 3.756, p = .081, ES = .273$; SINGLE = 2.34% increase; DUAL = 6.68% increase; Figure 4.3a), stride time ($F[10] = 4.417, p = .062, ES = .306$; SINGLE = 1.42% decrease; DUAL = 6.86% decrease; Figure 4.3b), and cadence ($F[10] = 4.654, p = .056, ES = .318$; SINGLE = 1.74% increase; DUAL = 6.86% increase; Figure 4.3d) suggesting that the intervention had a differential effect on the magnitude of improvements to single- and dual-task gait performance amongst the MUSIC group. A non-significant main effect of Time for error rate ($p > .05$), indicated that the MUSIC group did not alter their error rate for the secondary arithmetic task following the intervention.

Following the 13-week intervention, the MUSIC group demonstrated a statistically significant improvement in UPDRS (III) score ($t[10] = 4.045, p = .002$; 5.6 point reduction); the CTRL group also experienced a decrease in UPDRS score, however, the improvement for the CTRL group failed to reach significance ($t[10] = 1.128, p = .286$; 1.8 point reduction).

4.4.3 Feasibility of intervention. Each group experienced 9 falls during the intervention period. Two separate subjects experienced falls in each of the groups. The falls did not occur during physical activity. Compliance with the intervention was good; two subjects in the MUSIC group took a one-week break due to scheduling conflicts. MUSIC subjects reported mean walk duration of 115 ± 28 minutes per week with their individualised music, with 90 minutes per week being the suggested weekly walk duration. The overall mean walk duration during the intervention did not differ significantly between groups ($t[20] = 1.073, p = .296$; CTRL = 185 ± 139 minutes per week; MUSIC = 138 ± 47 minutes per week).

Subjects rated the experience of exercising to their own programmed music as 9.0 on a 10 point rating scale. In addition, ten out of the 11 subjects in the MUSIC group indicated that they were comfortable enough with the design and the operation of the personal music player that they would consider using it again. One subject experienced difficulties with the complexity of the music player and the earphone cables, but managed to complete the intervention. All MUSIC subjects indicated that they liked the music that was selected for them, with three subjects requesting partial or complete music changes during the intervention. Furthermore, nine of the 11 MUSIC subjects reported that they walked more than they expected to as a result of using the music, with two subjects reporting that the music had motivated them to try other exercises outside of walking. When asked to describe the benefits, if any, derived from walking with music responses included, 'I walked with an increased pace, even after turning the music off', 'I stood taller and swung my arms more', 'I walked smoother, it was more even', 'I had an improved emotional state', 'exercising was less monotonous', and 'the music provided extra motivation to exercise'. The majority (9/11) of patients assigned to the MUSIC group did not report any

unfavourable effects of the intervention, however, one subject reported some cramping in their thigh at night after walking while another patient reported feeling more tired during the intervention when they came in from walking. Nine out of the 11 subjects in the MUSIC group planned to continue exercising with music in the future.

4.5 Discussion

This study investigated the feasibility and efficacy of using cadence-matched salient music as a gait training tool for PD patients. In agreement with our hypothesis, the findings of this study indicate that PD patients who trained for 13 weeks with a music program improved gait performance. In addition, the high compliance rate to the intervention and the limited reports of adverse effects provide the possibility that salient music may be a beneficial compliment to a walking activity intervention for use in the parkinsonian population.

The CTRL group maintained gait performance across all measures and task conditions following the intervention. Conversely, and in agreement with previous intervention studies using rhythmic auditory cues (del Olmo & Cudeiro, 2005; Miller et al., 1996; Nieuwboer et al., 2007; Thaut et al., 1996) subjects who had walked with cadence matched, salient music demonstrated improved gait performance following the intervention. In the single-task condition the MUSIC group demonstrated marginal improvements in gait velocity, cadence, and stride time post-intervention. The same pattern of improvement was observed with larger relative magnitude in the dual-task condition. This differential effect of the intervention by task was supported by strong two-way (Time x Task) interactions for the measures of velocity, stride time, and cadence. Consistent with prior reports that rhythmic auditory cues tend to be more

effective in improving temporal as opposed to spatial parameters of gait (Howe et al., 2003; Morris et al., 1994; Suteerawattananon, Morris, Etnyre, Jankovic, & Protas, 2004), stride length remained largely unchanged in both conditions following the intervention. The enhanced gait performance demonstrated by the MUSIC group was accompanied by a significant improvement in motor symptom severity following the intervention. Further analysis revealed that the observed improvements did not reflect posture and gait items of the UPDRS, but instead were confined to the components of the UPDRS that contribute to the akinesia subscale (Q23-26).

The number of falls experienced during the intervention period was constant across the two groups. Furthermore, the reported falls occurred whilst patients were carrying out activities of daily living within their homes and not whilst patients were engaged in the walking intervention. This implies that safety was not further compromised by the intervention for the group who listened to music whilst walking. In addition, the use of a personal music player to provide the individualised playlist during the intervention was well-accepted by the subjects as indicated by patient responses in the Post-intervention Questionnaire. The subjective ratings of improved gait performance and/or emotional state were reported by all subjects in the MUSIC group, providing additional insight to the benefits provided by the intervention and provide further support for the feasibility of using salient music as a practical and sustainable cueing strategy. The fatigue and cramping reported by two patients in the MUSIC group are consistent with common symptoms of PD (Ford, 2010; Friedman et al., 2007; Goetz, Tanner, Levy, Wilson, & Garron, 1986) and therefore may reflect the symptom profile of the disease rather than any detriment imposed by the walking program.

The mechanism through which cadence-matched, salient music improves gait performance and motor symptoms in PD patients is equivocal. The improvement in uncued gait and inconsistent changes in stride time variability do not support the frequently postulated suggestion that rhythmic auditory cues act as an external pacemaker. One alternative explanation in agreement with the work of Sacrey et al. (2009) is that the music may have enhanced gait performance through increasing the patients' affective arousal. The arousal potential of the music was intentionally high, with pieces selected based on familiarity and enjoyment. The improvement in dual-task gait performance for the MUSIC group following a period of training with music may be representative of benefits of dual-task training. Practicing two tasks concurrently allows the improvement of task-coordination skills (Silsupadol et al., 2009) therefore if listening to music is a cognitively demanding task, as we have suggested (Brown et al., 2009), it becomes possible that the intervention may inadvertently provide dual task training.

4.5.1 Limitations. This study included a comparatively small sample of PD subjects; furthermore the subjects were relatively heterogeneous between groups when considering baseline disease severity (motor section of UPDRS). The limited sample size used in this study limits both the statistical power of the statistical analyses used in this study, as well as the generalizability of our findings to the wider patient community. In addition, the heterogeneity of the sample groups at baseline necessitates cautious interpretation of the findings, with the possibility that the observed improvements in gait performance and symptom severity demonstrated by the MUSIC group could simply represent a placebo effect, or in the case of symptom severity a regression to the mean. Based on similar results following training with rhythmic auditory tones (Rochester et al., 2010), we propose, as an alternative, that

these preliminary results support the notion that a walking program accompanied by cadence-matched, salient music can improve single- and dual-task gait performance amongst PD patients with mild to moderate disease severity.

A second major limitation of this study was that the CTRL group continued with regular activities as opposed to completing the walking program without music. This design decision reflected the characteristics of the local PD community who are actively encouraged to maintain a regular walking routine. As such, our available sample of convenience was comprised of individuals who included walking as part of their regular routine. Therefore, we are unable to elucidate whether the improvements to gait observed in this study reflect walking with music or the documented benefits of sustained walking. Modified Baecke questionnaire scores, however, indicated that each group had similar activity levels prior to the study, with the majority of subjects being regular walkers. In addition, the two groups spent a comparable amount of time walking during the intervention period (CTRL = 2289 ± 1696 minutes; MUSIC = 1791 ± 647 minutes; $t[20] = .908, p = .375$). These data lend support to the possibility that the improvements to gait performance observed in the MUSIC group were due to the accompaniment of cadence-matched, salient music. Future studies should incorporate a walking control group to verify this conjecture. Despite the limitations of the current study the findings should be used to direct the design of larger-scale randomized control trials investigating the efficacy of incorporating cadence-matched salient music into a gait training program. Further investigations should also utilise planned follow-up assessments to establish the optimal training frequency and duration necessary to retain improvements to gait performance and symptom severity.

In conclusion, our results indicate that the use of cadence-matched, salient music to accompany walking is a feasible and enjoyable intervention for use amongst patients with mild to moderate PD. Further research is warranted to elucidate the effect of training with a salient music accompaniment on gait performance.

Chapter 5: Training-related changes to obstacle crossing gait performance amongst people with Parkinson's disease

5.1 Abstract

Impaired obstacle crossing has been identified as one of the major environmental risk factors for falls amongst people living with PD, however, gait training interventions continue to focus on unobstructed walking. This study examined whether the demonstrated benefits of a music-accompanied walking program on unobstructed walking translate to complex gait activities, such as obstacle crossing. Nineteen people with PD were randomised to a control (CTRL, n = 9) or experimental (MUSIC, n = 10) group. The CTRL group continued with their regular activities for the 13-week intervention period. The MUSIC group walked with an individualised music playlist three times a week during the intervention. Gait performance was measured using standard spatiotemporal measures of gait during unobstructed and obstructed walking conditions pre- and post-intervention. Following the gait training intervention the MUSIC group demonstrated improvements in step velocity, step length, and step time when approaching the obstacle. The findings of this study support the possibility that gait training programs designed to improve unobstructed gait may have potential to provide benefit for more challenging gait activities such as obstacle crossing.

5.2 Introduction

Falls are one of the most serious consequences of the gait disturbances and postural instability associated with PD. It is estimated that two in three people living with PD will experience a fall during the span of one year (Ashburn et al., 2001; Wood et al., 2002), with almost half of these individuals being at risk for recurrent falls (Kerr et al., 2010; Marinolli, Korpelainen, Sotaniemi, Myllyla, & Korpelainen, 2011). This high prevalence of falls amongst people with PD is responsible for a fall-related injury rate that is almost three times greater than amongst non-parkinsonian older adults (Melton et al., 2006). Furthermore, falls contribute to many other sequelae that negatively impact quality of life amongst people with PD, such as, a fear of falling (Adkin, Frank, & Jog, 2003; Bloem, Grimbergen, Cramer, Willemsen, & Zwinderman, 2001), self-imposed activity restriction (Fletcher & Hirdes, 2004; Nilsson, Drake, & Hagell, 2010), an associated increase in dependency (Grimbergen et al., 2004; Shulman et al., 2008) and an increased need for institutional care (Hely et al., 1999; Temlett & Thompson, 2006).

The aetiology of falls amongst people with PD is multifaceted; however, complex gait activities, such as multi-tasking (i.e. walking whilst talking) and obstacle avoidance are most commonly identified as contributing factors to falls in this population (Stolze et al., 2004; Willemsen, Grimbergen, Slabbekoorn, & Bloem, 2000). People with PD have been shown to approach and cross obstacles with shorter and slower steps when compared to healthy age-matched adults (Brown et al., 2010; Galna et al., 2010; Nocera et al., 2010; Stegemoller et al., 2012; Vitorio et al., 2010). This obstacle crossing strategy is suggested to be a reflection of the impairments in movement amplitude regulation experienced by people with PD (Morris, et al., 1996) and has potential negative implications for patient safety. Impaired step length

regulation results in people with PD stepping closer to the obstacle both before (Vitorio et al., 2009) and after (de Bruin et al., 2010; Galna et al., 2009; Vitorio et al., 2009) crossing increasing the risk of either tripping or stepping on the obstacle.

The ability to safely and successfully modify gait patterning to negotiate the environment and respond to challenging task demands is critical to the maintenance of overall mobility and independence in the home and community. Whilst improved efficacy and automaticity of the gait cycle must necessarily remain a treatment priority for people with PD, consideration should also be given to the possibility of extending rehabilitation programs to incorporate complex gait tasks, such as negotiating obstacle contingencies. Expanding rehabilitation programs to include functional gait activities could carry the benefit of enhancing the mobility repertoire to improve capacity for function in this population. Recent work from our group has found that a music-accompanied walking program is a safe and enjoyable intervention that is effective in improving single- and dual-task walking amongst people with mild to moderate PD (de Bruin et al., 2010). The objective of the present study was to examine whether the benefits of the gait training intervention extend beyond the relative simplicity of unobstructed gait to provide advantage for obstacle negotiation, a task that has strong implications for patient safety and functionality. In line with our previous work, we hypothesised that the hypokinetic stepping pattern exhibited during obstacle crossing would be improved following the 13-week music-accompanied walking program.

5.3 Methods

All subjects in this study have provided a subset of data for an accompanying study (de Bruin et al., 2010).

5.3.1 Subjects. Thirty-three people diagnosed with idiopathic PD were recruited from two research centres; University of Lethbridge, Lethbridge, Canada ($n = 12$) and Dalhousie University, Halifax, Canada ($n = 21$). Recruitment was according to the following inclusion criteria: mild to moderate disease severity (Hoehn & Yahr stages II-III; Hoehn & Yahr, 1967); stable medication usage for a minimum of four weeks prior to inclusion in study; independently mobile without the use of a walking aid; and Mini-Mental Status Examination (MMSE; Folstein, et al., 1975) scores of 24 or higher. Specific exclusion criteria for subjects were: diagnosis of PD less than 12 months prior to inclusion in study; having received surgical intervention for treatment of PD; the presence of a neurological disorder or comorbidity likely to affect gait or their ability to complete the intervention; and severe hearing deficits. All subjects provided informed written consent prior to enrolment into the study as approved by the University of Lethbridge Human Research Committee and the Dalhousie University Health Sciences Research Ethics board.

5.3.2 Procedures. Following enrolment and initial assessment, subjects were randomly assigned to a control (CTRL) or experimental (MUSIC) group. The study used a repeated measures design. Outcome measures were assessed immediately prior to randomization (PRE) and within 48 hours of completing the 13-week intervention (POST). Assessments were carried out during the self-reported “ON” period of the medication cycle (approximately 1 hour following medication intake), with PRE- and POST-assessments being scheduled for the same time of day.

Subjects were asked to walk the length of a 10 metre walkway at a self-selected pace in six different walking conditions. Walking conditions were differentiated by the presence of music (no music/music), the necessity to perform a

concurrent cognitive task (single-task/dual-task), and the requirement to negotiate a physical obstacle (no obstacle/obstacle). Subjects performed six trials in each walking condition, for a total of 36 trials (Figure 5.1). Trials were blocked by the presence of music and blocks were counterbalanced between subjects. Walking conditions were randomised within each block of trials to control for trial and order effects. This paper addresses the training effects of a music-accompanied gait training intervention on spatiotemporal parameters of obstacle approach, crossing, and recovery. Subjects had the opportunity to perform one practice trial per condition prior to the start of each assessment. Subjects were guarded against falls by a trained research assistant. Rest breaks were provided as required.

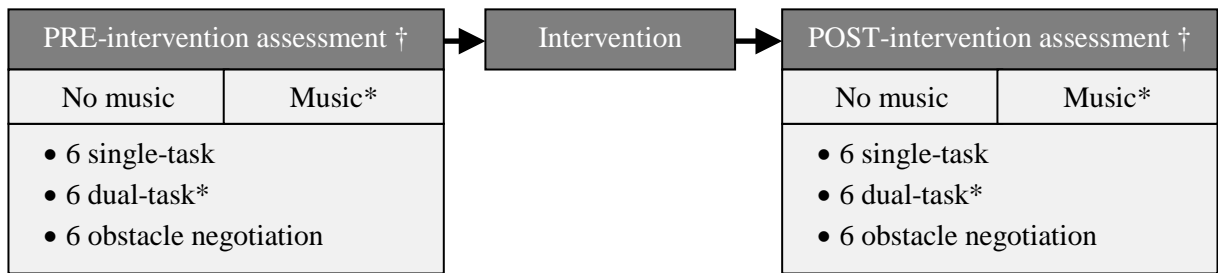


Figure 5.1 Experimental design for PRE- and POST-intervention gait assessments.

† Trials randomised. * Not included in current analysis.

5.3.3 Apparatus. Gait parameters were assessed using a 6.5 metre GAITRite mat (100 Hz; Dalhousie University; CIR Systems Inc., Haverton, PA) placed at the centre of the 10 metre walkway or alternatively using a six-camera motion analysis system (120 Hz; University of Lethbridge; Vicon-Peak, Peak Performance Technologies, Englewood, CO). Seventeen passive markers were placed on major anatomical landmarks for use with the motion analysis system. Passive marker placement for use with the motion analysis system has previously been described in detail (Brown et al., 2010; Brown et al., 2009; de Bruin et al., 2010).

The obstacle was a dense foam block (0.115m high x 0.155m deep x 0.605m width) placed at the midpoint of the walkway prior to trial commencement during the obstacle negotiation trials. Sagittal video of obstacle crossing was captured using a digital video camera.

5.3.4 Intervention. Subjects assigned to the CTRL group were encouraged to continue with their regular activities for the intervention period. Subjects randomised to the MUSIC group supplemented their regular activities with ~ 39, 30 minute walks (three times per week for 13 weeks), which were accompanied by a personalised music playlist provided through head/earphones and a personal music player. Walks were self-directed and completed in the subject's location of choice. The MUSIC group were requested to avoid dual-tasking (i.e. conversing with companions or walking with pets) during their music accompanied walks. All subjects completed a daily 'Activities and Falls Diary', documenting the type and duration of physical activities, as well as details of any falls experienced. Subjects were contacted bi-weekly by the study coordinator to monitor and ensure compliance.

5.3.5 Music. Individualised music playlists provided to the MUSIC group for the intervention period were approximately one hour in duration and were preloaded to a personal music player. Music tracks were selected if the track matched the subjects indicated genre or artist preferences. In addition, it was necessary that the tempo of the track matched the subject's preferred walking cadence (preferred cadence \pm 10-15 bpm), as determined during the screening visit. The tempo of each track was determined independently by two raters using a metronome. Subjects were provided with a familiarisation period on the personal music player and were also advised that they could request changes to their music playlist at any stage in the intervention.

5.3.6 Outcome measures. The first leg to cross the obstacle was designated the lead limb and the second leg to cross the obstacle was the trail limb (Chen et al., 1994). Subjects self-selected their lead limb in all obstacle negotiation trials. In accordance with the principal aim of the gait training intervention, the primary measure of interest was velocity (m/s) with secondary measures of interest consisting of step length (m), step time (s), and obstacle contacts (%). Step velocity, length, and time were calculated for four consecutive steps for the obstacle negotiation trials; two approach steps (lead and trail), the crossing step, and a recovery step (Figure 5.2). The same spatiotemporal parameters were calculated for the equivalent four steps for the unobstructed (single-task) trials.

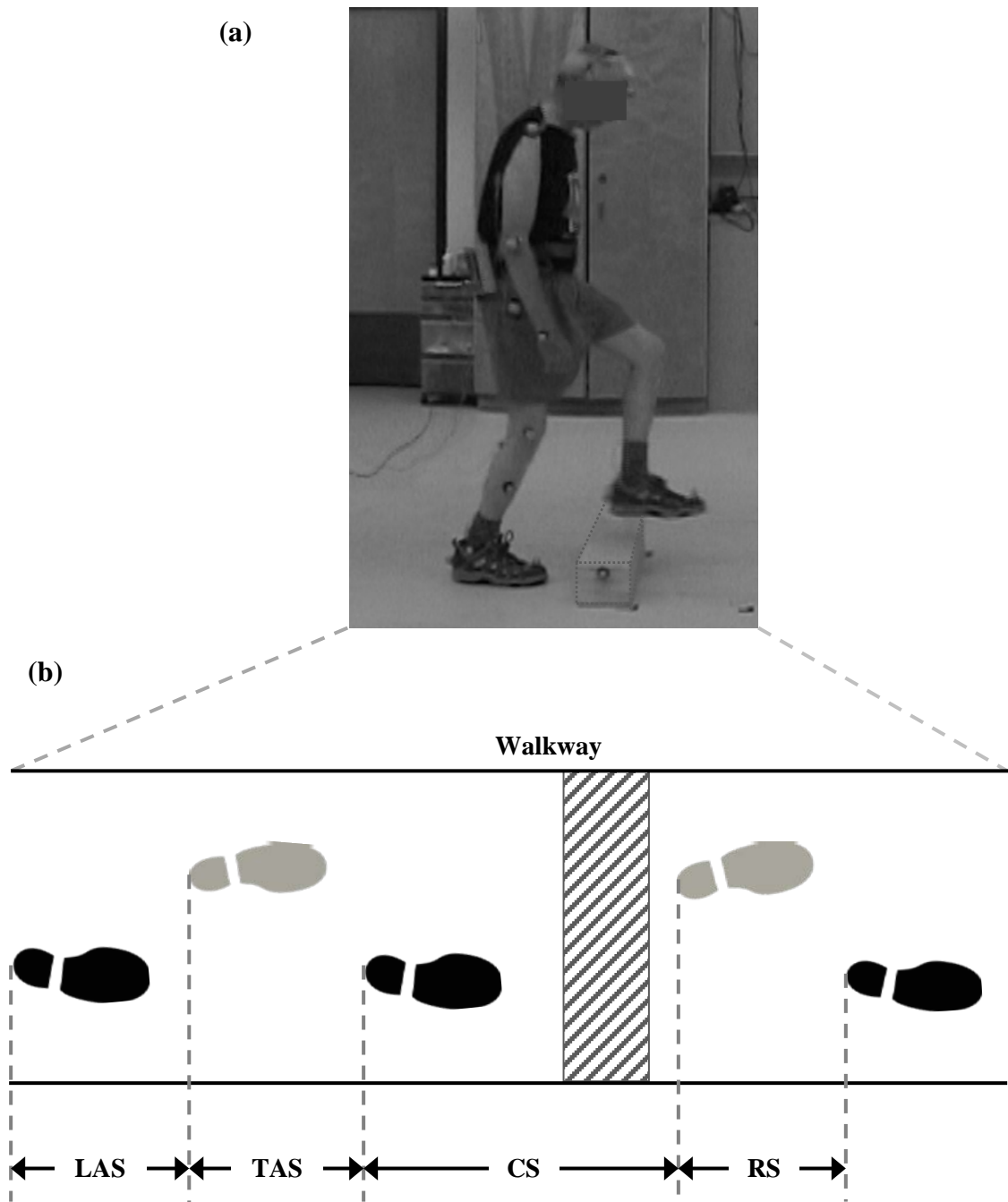


Figure 5.2 (a) Sagittal view of a subject crossing the obstacle, and (b) Expanded top-down view of steps for obstacle negotiation trials. Obstacle is indicated by diagonal lines; grey footprints indicate lead foot; black footprints indicate trail foot. Steps are lead approach step (LAS), trail approach step (TAS), crossing step (CS), and recovery step (RS).

Additional descriptive measures collected during the PRE-intervention assessment included the MMSE and the Modified Baecke Questionnaire for Older Adults (Voorrips et al., 1991) in addition to demographic data. The ‘Activities and Falls Diary’ was used to confirm compliance to the intervention and activity and fall levels. Motor symptom severity was assessed PRE-and POST-intervention by a blinded evaluator using the motor section of the UPDRS, these data have been reported previously (de Bruin et al., 2010).

5.3.7 Data processing. Procedures used to calculate spatiotemporal parameters of gait from raw motion analysis data have been described previously (Brown, et al., 2009; de Bruin, et al., 2010). Due to a first-trial effect ($p < .01$), mean values for spatiotemporal measures were calculated for the last five obstacle negotiation trials PRE- and POST-intervention. Obstacle contacts were identified using a custom written algorithm (Matlab version R2009a, The MathWorks; Natick, MA) that identifies changes to the static position of the obstacle. Sagittal videos were also scored manually to confirm the number of obstacle contact events.

5.3.8 Data analysis. Baseline characteristics and measures were summarised descriptively and compared between groups using independent t -tests for continuous variables and the chi-square test for nominal variables. The effects of the intervention period on spatiotemporal parameters of the approach, crossing and recovery steps were evaluated using separate mixed design three-factor [Time (PRE/POST) x Step (LAS/TAS/CS/RS) x Group (CTRL/MUSIC)] Repeated-Measures Analyses of Variance (RM-ANOVA). Obstacle contacts were assessed using a mixed two-factor [Time (PRE/POST) x Group (CTRL/MUSIC)] RM-ANOVA. Given the exploratory nature of the study Bonferroni corrections were not applied to multiple post-hoc comparisons and a significance level of 0.05 was used in all analyses. Partial η^2 values

were used to report the effect size. Analyses were performed using SPSS Statistics 18.0 for Windows (SPSS Inc. Chicago, IL).

5.4 Results

Thirty-three eligible subjects were enrolled in the study. All subjects completed the intervention, however, seven subjects (CTRL = 4; MUSIC = 3) were excluded from follow-up due to significant medication changes (n = 4), inability to complete POST-intervention gait assessment (n = 2) or a lack of access to the music player for an extended period during the intervention (n = 1). A further seven subjects (CTRL = 4; MUSIC = 3) were excluded from analysis due to inadequate maintenance of activity records (n = 4) and equipment malfunctions (n = 3). Demographic data and clinical characteristics for the nineteen subjects that contributed to the final dataset are shown in Table 5.1. Adherence to the intervention was very good; two subjects in the MUSIC group missed three walking sessions each due to scheduling conflicts. The MUSIC group completed an average of 43.5 (\pm 6.8) walking sessions during the 13-week intervention period, resulting in 1120 (\pm 323) minutes of walking with music per subject.

Table 5.1. *Subject characteristics at baseline.*

Characteristic	CTRL	MUSIC	<i>p</i>
Demographics			
No. of subjects	9	10	
Age (years)	64.8 (7.1)	64.7 (4.9)	.98
Sex (M/F)	4/5	6/4	.50
Clinical characteristics			
Disease duration (years)	5.0 (3.4)	5.9 (4.0)	.60
MMSE	28.7 (1.6)	29.6 (0.8)	.12
H & Y	2.1 (0.4)	2.3 (0.4)	.48
UPDRS (III)	19.8 (4.0)	25.5 (9.8)	.12

Values are mean (standard deviation) for continuous variable, and number for nominal variables.

F: Female; H & Y: Hoehn and Yahr stage; M: Male; MMSE: Mini Mental Status Examination; UPDRS: Unified Parkinson's Disease Rating Scale. MMSE, H & Y, and UPDRS scores were measured with subjects 'on' anti-parkinsonian medications.

The CTRL group crossed the obstacle successfully without contacting the obstruction in 100 percent of the obstacle negotiation trials. The MUSIC group had a 100 percent success rate PRE-intervention, however, one person in the MUSIC group stepped on the obstacle with the heel of their lead foot in a single trial in the POST-intervention assessment (98 percent success rate). The incidence of obstacle contacts did not differ significantly between groups or testing sessions ($p = .36$).

A main effect for Step indicated that subjects modulated their walking speed ($F[3, 51] = 12.821, p < .001, ES = .430$), step length ($F[3, 51] = 45.932, p < .001, ES = .730$) and step time ($F[3, 51] = 73.651, p < .001, ES = .812$) according to whether they were approaching, crossing or recovering from crossing the obstacle. Subjects walked significantly faster in the approach and crossing steps when compared to the RS ($p \leq .009$). As expected, step length was longer in the CS than in either of the approach steps ($p < .001$) or the RS ($p < .001$). Lastly, step time was significantly shorter for the approach steps than the CS and RS ($p < .001$).

The intervention had a differential effect on the obstacle approach and crossing behaviours of the groups, as indicated by significant Time x Step x Group interactions for step velocity ($F[3, 51] = 3.793, p = .016, ES = .182$; Figure 5.3a) and step length ($F[3, 51] = 3.187, P=.031, ES = .158$; Figure 5.3b). Specifically, gait performance was maintained from pre- to post-intervention by the CTRL group ($P > .05$). In contrast, the MUSIC group significantly increased step velocity whilst approaching the obstacle (LAS, 10.2% increase, $t[9] = 2.611, p = .028$; TAS, 8.0% increase, $t[9] = 3.518, p = .007$) following the intervention. Step velocity for the crossing and recovery steps was however, unchanged from pre- to post-intervention ($p > .05$). The MUSIC group also showed a tendency to increase the length of the trail approach step ($t[9] = 2.258, p = .050, 4.9\%$ increase) and decrease the crossing step

length ($t[9] = 2.175, p = .058, 4.0\%$ decrease) following the intervention. The lead approach step and recovery step were unaffected by the intervention ($p > .05$). A non-significant Time x Step x Group interaction for step time suggested that step time was maintained for both groups following the intervention period ($p > .05$; Figure 5.3c).

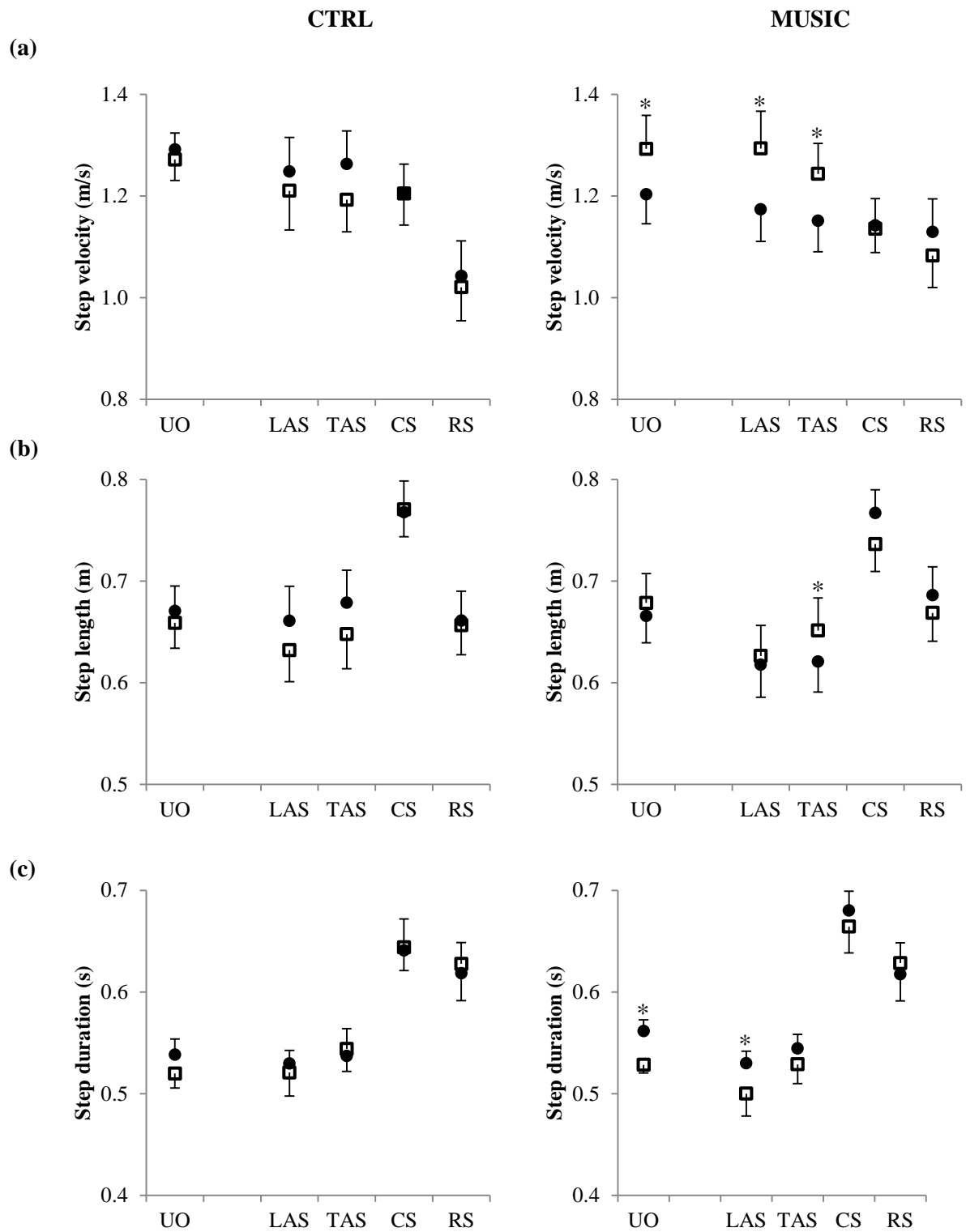


Figure 5.3 Step (a) velocity, (b) length, (c) time for unobstructed walking (UO) and the LAS, TAS, CS, and RS steps, PRE- and POST-intervention. Dark circles represent the PRE-intervention data; open squares represent the POST-intervention data. Asterisk (*) indicates significant PRE- to POST-intervention changes ($p \leq .05$). Data are means and standard errors.

5.5 Discussion

The capacity to safely negotiate an obstacle is an essential skill for overall mobility and independence that is known to be compromised amongst people with PD (Brown et al., 2010; Galna et al., 2010; Martens & Almeida, 2012; Nocera et al., 2010; Stegemoller et al., 2012; Vitorio et al., 2010). Indeed, impaired obstacle negotiation has been identified as a common mediator of falls in this population (Stolze et al., 2004; Willemsen et al., 2000). The present study examined whether the documented benefits of a music-accompanied gait training program for unobstructed gait (de Bruin et al., 2010) also translated to benefit obstacle crossing behaviours.

The intervention period resulted in differential effects on obstacle crossing behaviours between the CTRL and MUSIC groups. The CTRL group largely maintained spatial and temporal parameters of obstacle crossing following the intervention period; they did however, demonstrate a tendency to decrease approach step speed and length. This outcome parallels the pattern of change observed for the CTRL group during unobstructed walking (de Bruin et al., 2010). In contrast, the MUSIC group approached the obstacle significantly faster, with increased step length and decreased step time following the music-accompanied gait training program. Similar to the CTRL group, these gait adaptations reflected the improvements observed during unobstructed walking (de Bruin et al., 2010). The results for the obstacle crossing and recovery steps did not however, support our hypothesis that the characteristic hypometric gait patterns observed at baseline would be improved following the walking program. In fact, the MUSIC group maintained crossing and recovery step velocity from pre- to post-intervention. For the obstacle crossing step, the conservation of step velocity was achieved by a decreased step length (4.0%) and decreased step time (3.4%).

Interpreting the safety implications of a shortened obstacle crossing step is difficult. A shorter crossing step could be a consequence of stepping closer to the back of the obstacle with the lead limb, stepping closer to the front of the obstacle with the trail limb, or indeed a combination of both. Any of these possibilities could increase the likelihood of contacting the obstacle during crossing. Placing the lead foot closer to the back of the obstacle following crossing has been associated with an increased risk of stepping on the obstacle (as was observed in the single obstacle contact in this study) during foot placement. Whilst stepping closer to the front of the obstacle with the trail foot increases the likelihood of tripping on the obstacle (Chou & Draganich, 1998). Conversely, a shorter crossing step in combination with a decreased step time would result in less time spent in the unstable single limb support phase of the gait cycle, potentially promoting stability during obstacle crossing. Future research should examine the spatial parameters of the obstacle crossing step (i.e. pre- and post-obstacle distances and vertical clearance heights) to allow us to fully elucidate the potential consequences of the documented gait adaptations post-intervention.

Obstacle negotiation requires both proprioceptive and visual information for safe and successful crossing. Indeed, the safe placement of the lead foot during the obstacle crossing step requires online visual processing, whilst crossing the obstacle with the trail foot (recovery step) uses visual information in a feed-forward manner in combination with proprioceptive feedback (Mohagheghi et al., 2004; Patla & Greig, 2006; Patla & Vickers, 1997) to achieve safe foot placement. People with PD display increased visual dependence during the online control of locomotion when compared to non-parkinsonian older adults (Azulay et al., 2002; Azulay et al., 2006), possibly to compensate for the proprioceptive processing deficits (Boecker et al., 1999; Martens & Almeida, 2012; Mongeon et al., 2009; O'Suilleabhain et al., 2001; Zia et al., 2000)

and impaired sensorimotor integration (Almeida et al., 2005; Machado et al., 2010) experienced by this population. Therefore, this presents the possibility that the limited changes observed during the crossing and recovery steps in this study are a result of the heightened attentional demands associated with the visual regulation of stepping patterns during the obstacle crossing and recovery steps.

Regardless of the adaptations to obstacle crossing parameters made by the CTRL and MUSIC groups, there was only one incident of obstacle contact and the obstacle contact did not result in a loss of balance. In this study, the obstacle was clearly visible from trial onset, evidently allowing the patients sufficient time to plan and adjust their steps to safely accommodate the obstruction in their travel path. It is important to note, however, that the laboratory setting used for the gait assessments in this study does not accurately reflect the environment in which patients will typically encounter obstacles in their home or community. In the daily environment patients may be concurrently attending to additional tasks and distracters whilst avoiding an obstacle. These complex walking scenarios would increase the attentional demands of the task beyond those experienced in the controlled laboratory environment and the complexity of the environment would likely limit the attention that the patient directs toward the visual information available on the obstacle, therefore increasing the risk of obstacle contact (Martens & Almeida, 2012). The intervention implemented in this study, however, likely provided patients with the opportunity to practice walking and even obstacle negotiation in complex, attentionally demanding situations. Indeed, patients were required to complete walking sessions independently in the local community without therapist supervision. This form of community walking conceivably challenged the subjects to walk in a variety of unpredictable, dynamic environments (i.e. uneven terrain, changing ambience, abrupt and unplanned direction

changes, and stopping and starting) with environmental distracters (i.e. other walkers or trail users and road traffic) which would conceivably increase the motoric and attentional demands of walking beyond those experienced in a stable and predictable home or clinical environment. We suggest that the complexity of the environment encountered during the walking sessions, coupled with the music accompaniment encouraged subjects to practice flexibly allocating attentional resources whilst simultaneously maintaining safe gait, thereby providing a form of complex gait training that addresses the need to improve daily functional performance.

In conclusion, the results of this study tentatively suggest that it may be possible to develop an individualised and sustainable rehabilitation intervention that not only effectively improves unobstructed gait performance for people living with PD, but may also extend benefit to certain aspects of complex gait activities such as obstacle crossing. Future studies should confirm and extend these results to include additional kinematic measures of obstacle crossing that may serve to clarify the safety implication of these findings in this population.

Music can lift us out of depression or move us to tears – it is a remedy, a tonic, orange juice for the ear. But for many of my neurological patients, music is even more – it can provide access, even when no medication can, to movement, to speech, to life. For them, music is not a luxury, but a necessity.

Oliver Sacks, *Musicophilia* (2007)

Chapter 6: General Discussion

Music has long been appreciated for its capacity to produce physiological and psychological responses in humans (Murrock, 2005). Indeed, the relationship between music and movement has been described throughout history and across cultures.

Historically, work songs served to coordinate physical work (i.e. agricultural work songs, sea shanties), cadence calls synchronised marching in the military, and dance was an important aspect of spiritual and social occasions (Thaut, Kenyon, et al., 1999). More recently, sport and exercise have been coupled with music, from people running or walking whilst listening to music from a personal music player to music being played free-form in the gym or in exercise classes.

The advancement in non-invasive neuroimaging techniques has helped to elucidate the physiological basis for the rhythmic synchronisation of behaviour. The recognition that music listening activates motor regions of the brain (Chen, Penhune, & Zatorre, 2008) has transformed the therapeutic role of music in the field of rehabilitation, leading to the development of a number of sensorimotor rehabilitation techniques that use auditory rhythm to regulate motor function in populations that experience motor dysfunction. Rhythmic auditory stimulation is one such neurologic rehabilitation technique that has been effectively applied during single sessions and long-term interventions to improve motor function in a variety of pathological populations including stroke (Bradt et al., 2010; Ford et al., 2007; Hayden, Clair,

Johnson, & Otto, 2009; Malcolm, Massie, & Thaut, 2009; Mauritz, 2002; Thaut et al., 2007; Thaut et al., 1997), traumatic brain injury (Goldshtroum, Knorr, & Goldshtroum, 2010; Hurt et al., 1998; Kenyon & Thaut, 2000), Huntington's disease (Bilney, Morris, Churchyard, Chiu, & Georgiou-Karistianis, 2005; Delval, et al., 2008; Thaut, Miltner, et al., 1999; Wittwer, Webster, & Hill, 2012), Multiple Sclerosis (Baram & Miller, 2007), and PD (Bryant et al., 2009; del Olmo & Cudeiro, 2005; Lim et al., 2005; Nieuwboer et al., 2007; Picelli et al., 2010; Rochester et al., 2010; Rochester et al., 2005; Rochester et al., 2007). Despite the widely documented efficacy of cued exercise programs in improving motor performance amongst people with movement pathologies, exercise participation and adherence is frequently reported to be low amongst these individuals (Ene et al., 2011; Fertl et al., 1993) which potentially compromises the benefits of long-term training interventions. Poor exercise or program adherence amongst people with movement pathologies is commonly attributed to a lack of motivation in addition to fatigue, disorders of affect and disease-related limitations (Hale, Smith, Mulligan, & Treharne, 2012; Hassett, Tate, Moseley, & Gillett, 2011; Jurkiewicz, Marzolini, & Oh, 2011; Motl, Snook, McAuley, & Gliottoni, 2006; Quinn et al., 2010). Given the potential for music to influence emotions and motivation as well as movement, the experiments in this thesis sought to first determine the feasibility of using commercially available music as an alternative to traditional auditory cues and subsequently to establish the viability and efficacy of using cadence-matched salient music as a gait training tool amongst people with PD. This thesis represents the first steps towards a long-term goal of developing an individualised and engaging gait rehabilitation program that whilst functionally and ecologically relevant also maximises functional gait performance amongst people living with PD.

6.1 Music Salience Influences Gait Performance

The first series of experiments presented in this thesis investigated the potential of using commercially available music to influence gait patterning amongst healthy young adults. The music presented to the subjects differed with respect to its salience to the listener, as well as the presentation frequency (90, 100, and 110 percent of the participants' baseline step rate). Due to the inherent rhythmicity of the music and the documented physiological effect of auditory rhythm on the motor system (Thaut, 2005) it was hypothesised that commercially available music would be effective in influencing gait patterning. Based on the suggestion that music that is meaningful to the listener increases affective arousal (Blood & Zatorre, 2001; Hargreaves & North, 1997) it was hypothesised that salient music would maximally influence gait patterning amongst young adults. Lastly, in agreement with the principles of stepwise limit cycle (step rate) entrainment (Thaut, 2005) and the extensive body of literature documenting the modulation of gait patterning with auditory cues of differing tempi (Ford et al., 2007; Hurt et al., 1998; Kenyon & Thaut, 2000; Lim et al., 2005; Mauritz, 2002; Thaut & McIntosh, 1999; Thaut et al., 1997; Thaut, Miltner, et al., 1999) it was expected that step rate would be adjusted to closely match the presentation frequency of the music.

In accordance with the hypothesis, when auditory cues were presented at a tempo that matched the subject's natural limit cycle (i.e. baseline step rate) gait patterning was differentially modulated by cue modality. Specifically, the subjects walked faster and with larger strides when listening to the metronome or salient music cues. In contrast, when participants were listening to non-salient music whilst walking their gait patterning was comparable to when they walked without an auditory cue. Whilst alterations to gait performance were comparable for the metronome and salient

music cues the self-reported level of enjoyment was significantly higher when subjects' were listening to salient music. The subjects' enjoyment of the cueing strategy is an important consideration when designing and implementing a novel rehabilitation program as the maintenance of therapeutic benefits will likely necessitate long-term adherence to the intervention program. The metronome cue implemented in this study was consistently associated with low levels of enjoyment, with subjects repeatedly reporting that the cue was monotonous. Exercise adherence has been associated with positive exercise experiences (Hamburg & Clair, 2003; Huberty et al., 2008; McAuley et al., 2007; Wankel et al., 1985; Wininger & Pagman, 2003) and maintained interest in the activity (Johnson et al., 2001). It is therefore conceivable that the positive experiences associated with listening to salient music selections may contribute to long-term adherence to a music-accompanied walking program.

Beyond the perceived enjoyment of listening to and walking with salient music it has previously been reported that passively listening to pleasant music increases the activity of a network of subcortical structures including the VTA, nucleus accumbens, and hypothalamus (Brown, Martinez, & Parsons, 2004; Menon & Levitin, 2005). The VTA and nucleus accumbens have been identified as components of the mesolimbic reward network. Increased activity in the VTA and nucleus accumbens is likely associated with an increase in DA levels in the brain which would mediate the reinforcing and rewarding features of music listening in a manner similar to that seen with natural rewards such as food, water, and sex. The increase in activity of the hypothalamus is associated with autonomic responses to the music (i.e. changes to heart rate, respiration rate). The increase in autonomic and affective arousal induced by the salient music cues conceivably influences motor activity through

increasing the availability of DA in numerous brain regions including the basal ganglia.

Standard RAS treatment protocols used in gait therapy and rehabilitation typically apply stepwise limit cycle entrainment (SLICE). The frequency of the RAS is initially set at the individuals' natural movement frequency and once movement parameters have been optimised and stabilised at this frequency new limit cycles are entrained in a step-wise process at a lower or higher cadence depending on the goals of the protocol. In an attempt to reproduce this protocol design, subjects were presented with cues at 90, 100, and 110 percent of their preferred cadence. Interestingly, and contrary to our expectations alterations to gait patterning were not differentially affected by the presentation frequency of the cue. The young adults recruited for this study were healthy, active kinesiology undergraduate students who were self-declared to be free from any known neurological or orthopaedic conditions that could influence their gait performance. It is possible that the contradictory findings are the result of a 'ceiling effect'. The subjects recruited for this study were likely walking optimally, with a stable natural limit cycle in the absence of cues which could limit the changes induced by auditory rhythms of different tempi. A second possible explanation for unexpected results related to cue tempo was that due to a lack of focused instructions participants chose not to pace themselves with the auditory rhythm. In this series of studies subjects were not provided with explicit instructions to step to the beat of the music or the metronome tone, but rather were told to 'listen to the cue whilst walking'. Whilst it is possible that the decision not to instruct subjects to synchronise their stepping with the perceived beat may have limited the benefits produced by the tempo of the cues previous studies have suggested that humans have a natural tendency to synchronise rhythmic body movements with the

timing of perceived beats even in the absence of overt instructions (Large, 2000; Snyder & Krumhansl, 2001).

The finding that salient music was effective in influencing gait performance amongst young adults is in agreement with previous work from our group that found that self-selected salient music modulated gait amongst healthy older adults (Brown et al., 2009; Brown et al., 2010). Novel exposure to salient music whilst walking was however, detrimental to gait performance amongst people with mild to moderate PD (Brown et al., 2009; Brown et al., 2010). We suggested that these divergent findings likely reflect the differing levels of gait automaticity expressed by the different study populations. Listening to music appeared to effectively act as an additional task for people with PD, creating a dual- or multi-task scenario for the patient and diverting attentional resources away from the primary task of walking. As previously mentioned, people with PD necessarily use more conscious control mechanisms for walking to compensate for the dysfunctional basal ganglia (Morris et al., 1994; Yogev-Seligmann et al., 2008). Whilst using a conscious control mechanism may facilitate successful movement execution, it also diminishes the availability of residual attentional resources to attend to distracters, additional tasks, or environmental demands. In contrast, the gait of healthy young adults is largely under the automatic control of the basal ganglia necessitating limited involvement of central cognitive processes. The younger adults will consequently have sufficient residual attentional resource capacity to attend to additional attentionally demanding tasks (i.e. music listening) with little to no impairment of gait performance (dual-task interference). As such, the results of this study should be interpreted with caution as the cognitive demands of the proposed cueing strategy are likely dependent on the user.

6.2 Salient Music is a Safe and Efficacious Tool for Gait Training in PD

The second study presented in this thesis explored the efficacy and feasibility of using cadence-matched salient music as a gait training tool amongst people with mild to moderate severity PD. The hypothesis for this study, based on the established efficacy of cued gait interventions in improving parkinsonian gait across a range of functional gait activities (Bryant et al., 2009; del Olmo & Cudeiro, 2005; Lim et al., 2005; Nieuwboer et al., 2007; Rochester et al., 2010) was that a music-accompanied walking program could be safely implemented amongst people with PD and that moreover the program would be effective in improving single- and dual-task gait performance.

Consistent with our hypothesis and the literature, participants significantly improved temporal parameters of gait following a 13-week period of training with salient music that was tempo-matched to the subject's baseline movement frequency. Specifically, the subjects who had walked with music during the intervention period walked faster, with a decreased stride time and increased step rate following the intervention. The pattern of gait improvement post-intervention was consistent across single- and dual-task walking however; in agreement with previous research (Baker, Rochester, & Nieuwboer, 2007, 2008; Rochester et al., 2005; Rochester et al., 2007) the improvement was more pronounced when participants were requested to concurrently complete a secondary cognitive task whilst walking. Improvements to gait performance were accompanied by a significant decrease in motor symptom severity (as determined by UPDRS (III) scores); however, these improvements were not in the posture and gait measures of the scale, but rather reflected improvements in measures that contribute to the akinesia subscale. Whilst unexpected, these results are in agreement with work of Pacchetti et al (2000) which reported significant

improvements to measures of bradykinesia and akinesia amongst people with PD following three months of active music therapy. The authors suggested that the reported improvements to these measures may have been a result of the external rhythmic cues acting as a timekeeper for the patients; however, the authors also suggested the possibility that the affective arousal effect of the music may activate the dopaminergic mesolimbic neurons that project to the nucleus accumbens which may in turn briefly activate the cortical-basal ganglia motor loop through a limbic-motor system interface thereby providing motor facilitation.

We are unable to elucidate the mechanism through which cadence-matched, salient music improved gait performance and motor symptom severity from this study. The observed improvements in uncued single-task gait performance are consistent with the theory of auditory-motor coupling and extensive research demonstrating the efficacy of cadence-matched metronome cues in improving gait (Bryant et al., 2009; del Olmo & Cudeiro, 2005; Lim et al., 2005; Nieuwboer et al., 2007; Rochester et al., 2010). Based on the findings of the first study in this thesis, however, it is conceivable that the salience of the music also contributed benefit to gait performance. One possibility that has been mentioned previously is that music, particularly music that is salient to the individual may be ‘activating’, increasing an individual’s affective and autonomic arousal (Blood & Zatorre, 2001; Hargreaves & North, 1997). Increases in affective arousal are associated with an increase in DA concentrations in the brain, through increased activity in the mesolimbic pathway (Menon & Levitin, 2005), in populations that experience DA deficiencies such as people with PD increased availability of DA may positively influence motor performance. A second possibility for the influence of music salience on gait is based on the suggestion that similar to the visual system the auditory system is comprised of

two parallel pathways; primary and secondary. The primary (lemniscal) pathway is thought to be responsible for tonotopic organisation, whereas the secondary (nonlemniscal) pathway plays a role in temporal pattern recognition, auditory cue learning, and memory and furthermore has widespread connections to motor and limbic systems (Hu, 2003). It has been speculated that familiar and enjoyable music may preferentially target the secondary auditory pathway, thereby facilitating motor performance and inducing emotional responses to the music.

The improvement in dual-task gait performance following the intervention period did not reflect a change in task prioritisation from the secondary task (serial-3 subtractions) to the primary task of maintaining safe and effective gait for the patients, as secondary task performance was maintained following the intervention. An alternative explanation for the improvements to dual-task gait that has been proposed by Brauer and Morris (2010) is that repeated practice of two or more tasks concurrently, in the case of this study, walking and listening to music, may over time reduce the attentional demands associated with each individual task (i.e. improve gait automaticity). This in turn may allow a generalised improvement in the capacity to divide or appropriately allocate attentional resources between concurrent tasks. The intervention implemented in this study required people to listen to music whilst walking in a complex environment that carried the potential for changing terrain, changing light and weather conditions, and environmental stimuli and distracters. We suggest that the intervention may have inadvertently provided an effective form of dual-task gait training for the subjects, encouraging them to flexibly allocate cognitive resources to multiple tasks and/or stimuli whilst simultaneously maintaining safe gait.

Assessing the feasibility of the unsupervised, home-based intervention was also a critical component of this study. The safety of the intervention was determined

from the subjects self-reported fall rate (Activities and Falls diary). Each study group reported an average of 0.15 falls per week during the 13-week intervention period, this fall rate is comparable to that widely reported in the literature (0.14 falls per week; Ashburn et al., 2001; Wood et al., 2002) suggestive that the gait training program did not increase the fall risk for this population and furthermore could be safely implemented in an unsupervised community setting amongst people with PD.

Adherence to the intervention was very strong with participants completing more than 98 percent of the scheduled walking sessions. Attrition levels in similar populations have typically been reported to be in the region of five to eight percent (Morris et al., 1994; Morris et al., 1996; Morris et al., 2000). The high adherence observed in this study agrees with the work of Clair and colleagues (Hamburg & Clair, 2003; Johnson, et al., 2001) who have reported improved exercise adherence amongst non-parkinsonian older adults in exercise programs with music accompaniment when compared to programs without music. Also, in line with previous research investigating walking levels amongst people with PD during a home-based cued gait training program (Lim et al., 2010) the participants in this study reported walking on average 28 percent longer than requested when walking with music each week. The unanimously positive subjective responses of the participants following the conclusion of the training program suggest that the strong adherence to the training regime may also be attributable in part to both the perceived improvements to gait performance as well as the music accompaniment in this intervention. It has been suggested that adherence to an exercise program occurs when the exercise is connected with positive experiences and when the individuals' interest is captured and then maintained (Hamburg & Clair, 2003; Johnson et al., 2001). Participants in this study specifically indicated that they felt that the music

accompaniment made ‘exercise less monotonous’ and provided ‘extra motivation to exercise.

The increased prevalence and severity of gait impairments with disease progression (Kang, Bronstein, Masterman, Redelings, Crum, & Ritz, 2005) suggests that people with PD will likely need to be engaged in a gait rehabilitation program for years or even decades to optimise and maintain functional mobility. As such, it is important that patient feedback is collated and critically examined as an integral component of protocol design as the users’ perceptions of the strategy will influence their willingness and motivation to continue to participate in the therapy.

6.3 Music-accompanied Gait Training Influences Complex Gait Activities in PD

The final study presented in this thesis examined whether the documented benefits of the music-accompanied walking program to unobstructed walking (de Bruin et al., 2010) translate to complex gait activities, specifically obstacle crossing. It has been reported that people with PD adopt a conservative obstacle crossing strategy that is reflective of the bradykinesia exhibited during unobstructed gait (Brown et al., 2010; Galna et al., 2010; Nocera et al., 2010; Stegemoller et al., 2012; Vitorio et al., 2010). Therefore, it was expected that the observed improvements to bradykinetic steady-state gait would be replicated in obstructed gait trials following the 13-week music-accompanied gait training intervention.

Subjects who completed the music-accompanied gait training program demonstrated an improvement in spatiotemporal parameters of obstacle crossing behaviour following the intervention. Whilst this finding was consistent with the hypothesis for this study it is important to note that the gait improvements were limited to the steps approaching the obstacle, with small non-significant changes in

gait patterning being observed for the crossing and recovery steps. More specifically, step velocity, step length and step time were improved for a minimum of two steps prior to obstacle crossing in the post-intervention assessment. These improvements to spatiotemporal gait parameter reflected the training-related improvements observed during unobstructed gait (de Bruin et al., 2010). Shortening step lengths prior to obstacle crossing have previously been associated with an increased risk of falls (Chen et al., 1994), therefore it is plausible that the increases in approach step amplitude that were reported in this study may have positive implications for patient safety.

The motoric and attentional demands of obstacle negotiation exceed those of steady-state gait (Siu, Catena, et al., 2008) and moreover the demands vary according to the environment (Brown et al., 2006; Brown, McKenzie, & Doan, 2005; McKenzie & Brown, 2004) and the phase of obstacle crossing (i.e. approach, crossing, recovery; Brown et al, 2005). The findings of this study are suggestive that people living with PD find the crossing and recovery steps particularly challenging and moreover, that the strategies used during these phases of obstacle crossing are not influenced by a period of gait training. Safe obstacle crossing typically requires online visual processing for placement of the lead foot after the obstacle, whilst in non-parkinsonian adults the recovery step would necessitate using visual information in a feed forward manner in conjunction with proprioceptive information to safely place the trail foot over the obstacle (Mohagheghi et al., 2004; Patla & Greig, 2006; Patla & Vickers, 1997). People with PD display increased visual dependence during steady-state gait (Azulay et al., 2002; Azulay et al., 2006) possibly as a means to compensate for the proprioceptive deficits experienced by this population (Boecker et al., 1999; Martens & Almeida, 2012; Mongeon et al., 2009; O'Suilleabhain et al., 2001; Zia et

al., 2000). Therefore, it is conceivable that the increased cognitive involvement necessary to ensure safe foot placement during obstacle negotiation limits the potential to improve the spatiotemporal parameters of the crossing and recovery phases of obstacle crossing amongst people with PD.

A single obstacle contact was observed during this study. The obstacle contact occurred following the intervention period and was the result of the participant stepping on the obstacle with the lead foot during foot placement. The high success rate in safely negotiating the obstacle is consistent with the findings of previous studies investigating the avoidance of fixed obstacles in the path of travel where the obstacle to be negotiated is visible for at least two steps prior to crossing (Brown et al., 2010; Chen et al., 1991; Galna et al., 2010; Hahn & Chou, 2004; McFadyen & Prince, 2002; Nocera et al., 2010; Stegemoller et al., 2012). This experimental paradigm appears to provide the participants with sufficient time to make the necessary adaptations to their stepping pattern to safely negotiate the obstacle. It would be valuable to include time-critical obstacle avoidance scenarios in future studies to maximise the ecological validity of the testing paradigm. In addition, obstacle clearance parameters (pre-obstacle distance, post-obstacle distance, and vertical foot clearance) were not recorded in this study, therefore inferences about fall risk following the training intervention should be made with caution. Whilst the people with PD included in this study may have largely maintained walking speed, step amplitude and step duration during the crossing step following the intervention they may have adapted spatial parameters of obstacle crossing that in turn could influence the safety of the obstacle crossing strategy. The measures collected during this study may not be sufficient to conclusively determine whether obstacle

negotiation performance was improved or compromised by the music-accompanied gait training intervention.

6.4 Implications of Results

Salient music appears to be an effective alternative to the traditional auditory cues used increasingly within parkinsonian gait training interventions. Despite initial concerns that listening to salient music concurrent to walking is a cognitively demanding activity for people with PD (Brown et al., 2009; Brown et al., 2010) it appears that people with mild to moderate severity PD are able to overcome this dual-task interference with practice. Moreover, a long-term gait training intervention that incorporates cadence-matched salient music appears to improve motor symptom severity and provides benefit across a range of complex gait activities that have previously been identified as mediators of falls for people with PD (Bloem et al., 2004; Stolze et al., 2004; Wood et al., 2002).

The observed modulation of gait performance amongst the young adults and people with PD in the studies included in this thesis provide support for the theory that music can modulate motor control through the theorised neuronal coupling between the auditory and motor systems. The rhythmic content of music can be used to improve gait performance in two ways; either as an immediate entrainment stimulus that is provided to improve online gait performance or alternatively as a facilitatory stimulus for the long-term training of functional gait patterns that are maintained in the absence of the rhythmic stimulus (Thaut, 2005). The experiments included in this thesis were not designed to elucidate the mechanisms through which these improvements to gait performance are achieved, however, we can speculate that the perception of an auditory rhythm activates sensorimotor regions of the brain,

ultimately entraining the motor response to the given rhythmic time information (Chen et al., 2008a; Chen et al., 2006; Jancke, Loose, Lutz, Specht, & Shah, 2000; Levitin & Menon, 2003; Lewis et al., 2004; Rao et al., 1997). The cues, whether they are a metronome tone or the ‘beat’ in a piece of music provide a continuous time reference that in turn provides anticipatory cueing in the execution of goal-directed movements (Nieuwboer et al., 2007). Whilst cueing strategies are initially employed as compensatory rehabilitative strategies, providing an external timer that allows the bypassing of the dysfunctional basal ganglia and provides a temporal marker to which a rhythmic movement such as gait can be entrained (immediate entrainment), with appropriate training the cueing approach may become a restitutive strategy providing sustained gait benefits to the patient in the absence of the stimulus. Restitution of function is theorised to be a consequence of neuroplasticity that is driven by training and learning (Nudo, Wise, SiFuentes, & Milliken, 1996; Rossini et al., 1998). Caution should be exercised however, that the cue does not become embedded in the central representation of the movement thereby necessitating the continual presence of the cue to achieve gait benefits. This does not appear to be a concern in this series of studies, as the improvements to gait performance were assessed in the absence of cues approximately 48 hours following the cessation of training. It may however, be beneficial to introduce ‘fading’ at the end of or in-between training sessions to enable participants to practice walking in uncued situations, a technique that is applied in standard RAS protocols (Thaut, 2005).

Despite indications that the training program improved gait performance through rhythmic entrainment we should also consider the likelihood that the salience of the music used in the intervention enhanced the benefits to gait performance post-intervention. It has previously been reported that when listening to self-selected,

pleasurable music brain regions, specifically the VTA and nucleus accumbens which are associated with arousal, motivation, emotion, and reward are activated (Blood & Zatorre, 2001; Menon & Levitin, 2005) increasing DA concentrations in a number of brain regions and conceivably contributing to motor facilitation. Moreover, the neural systems recruited when listening to enjoyable music are very similar to those engaged by specific biological stimuli such as sex, food, water, and drugs of abuse (Blood & Zatorre, 2001; Menon & Levitin, 2005) suggestive that music could provide psychological and physical benefits. Indeed, stimuli that are considered to be emotionally significant to the individual have dual effects. Initially the stimulus activates sensory pathways that in turn trigger autonomic and endocrine responses that alter internal states, unconsciously preparing the organism for the adaptive behaviour. Concurrently, information about the emotionally salient stimulus, in this case music is borne to the cerebral cortex. The cortical processing of the music stimulus results in the conscious perception of emotion or 'feeling' and additionally signals are sent to lower centres that augment or suppress behavioural expressions of emotion. An additional possibility for the influence of music salience on gait is through activation of the previously mentioned secondary (non-lemniscal) auditory thalamocortical pathway (Hu, 2003) which is implicated in cue-learning, temporal pattern recognition and emotion. The secondary auditory pathway has widespread connections to the motor and limbic systems and therefore is well-placed to indirectly influence motor performance through a variety of means (including modulating DA release). Lastly, the positive physiological sensations elicited by the emotional properties of the music may also enhance the dissociative effects of the music (Blood & Zatorre, 2001) narrowing the listeners attention and consequently reducing perceptions of discomfort and fatigue associated with exercise (Crust, 2004; Karageorghis & Terry, 1997; Lim,

Miller, & Fabian, 2011; Shaulov & Lufi, 2009; Yamashita et al., 2006) and thereby increasing the positivity of the exercise experience and conceivably encouraging exercise adherence (Hamburg & Clair, 2003; Huberty et al., 2008; Johnson et al., 2001; McAuley, Motl, et al., 2007; Wankel, Yardley, & Graham, 1985; Wininger & Pargman, 2003). Given the aforementioned need to potentially engage in the strategy for years or even decades to maintain therapeutic benefit the emotional and motivational qualities of the music are important with respect to maximising motor performance and increasing and maintaining therapy compliance.

6.5 Therapeutic Implications

The findings of this thesis add to the growing body of literature regarding the efficacy of using auditory rhythm, in this case unaltered, commercially available music, to influence the movements of people with PD. Previous work from our group has indicated that music may act as a cognitive distracter for people with PD when initially presented concurrent to walking (Brown et al., 2009; Brown et al., 2010). This finding is contrary to our observations amongst healthy young and older adult populations (Brown et al., 2009; Brown et al., 2010) and likely reflects differences in gait automaticity for each population. Specifically, these findings imply that whilst salient music may be effective in training and entraining more functional gait patterns amongst people with PD it may not be appropriate as an immediate entrainment stimulus unless provided in situations where adequate supervision or safety precautions are in place.

Whilst the proposed cueing strategy requires further refinement to establish the optimal parameter of the strategy prior to implementation in a clinical population, it does have the potential to be extremely versatile and inexpensive, two factors that

are critical to the widespread accessibility and implementation of any rehabilitation strategy. One major advantage of the intervention examined in this thesis is that the program is self-directed and completed in the patient's local community. Walking in the local community provides the participants with the freedom to decide when, where, and for how long they will walk, allowing patient's unparalleled autonomy in managing specific aspect of their treatment. Furthermore, given the chronic progressive nature of PD therapist-supervised interventions whilst beneficial may not be considered a cost-effective or convenient option for long-term symptom management. Whilst the gait training intervention proposed in this study is an unsupervised home-based program, it will be important that a therapist or practitioner is involved in the initial music selection and moreover that the patients walking is monitored at regular intervals to allow for the music playlist to be updated to reflect the individual's current walking abilities as necessary. In accordance with the therapeutic principles of RAS (Thaut, 2005), the tempo of the music selections should initially match the patient's inherent limit cycle as compromised gait stability and performance has been reported when the frequency of the auditory cue is set either too high or too low (del Olmo & Cudeiro, 2005; Ebersbach et al., 1999; Howe et al., 2003). New limit cycles can be entrained at a higher or lower frequency when deemed appropriate by the monitoring therapist or practitioner.

An inexpensive 'off-the-shelf' personal music player was utilised for the gait training program described in this thesis. The device is small and portable and is widely used by walkers and runners. Initial concerns that the device may not be appropriate for use by a population that can experience impaired manual dexterity (Gebhardt, Vanbellingen, Baronti, Kersten, & Bohlhalter, 2008) and may have had limited exposure to similar technology proved to be unfounded. Following the

cessation of the intervention more than 90 percent of the participants indicated that they were comfortable enough with the design and operation of the personal music player that they would consider using it again. Taken together, the novel attributes of the auditory cueing strategy proposed in this thesis could facilitate broader accessibility and application of RAS-based methodologies and strategies in the parkinsonian community, as well as other patient groups that experience disordered gait.

6.6 Future Research

In spite of finding that salient music can be effective in improving gait characteristics across a variety of walking contexts amongst people with PD a number of questions remain unanswered. In the first instance, further research will be necessary to establish the optimal parameters (i.e. frequency, intensity, duration) of the strategy and further to refine the strategy's application. We have established that music should be salient to the listener to optimise benefits to gait; however, our results regarding cue frequency have been inconclusive. Future studies will necessarily determine the potential of using salient music to incrementally increase the natural limit cycle of people with PD (in line with the SLICE protocol used in traditional RAS interventions). In addition, given the assumed relationship between motivation, emotion and arousal (Blood & Zatorre, 2001), measures that capture the perceived motivational and emotional qualities of the music should be included in future studies (i.e. Brunel Music Rating Inventory, Profile of Mood States). This information would bring us closer to resolving the complexities of which parameters contribute to the optimal music selection to accompany a gait training program for people with PD.

As the intervention study included in this thesis was a feasibility study we necessarily included strict inclusion and exclusion criterion. We were able to confirm the safety and efficacy of the music-accompanied gait training program in our target population of mild to moderate disease severity people with PD who were not freezers and did not suffer from dementia. We recognise, however, that excluding freezers potentially excludes 20 to 60 percent of people living with PD (Bloem et al., 2004; Lewis & Barker, 2009) and notably limits the clinical utility of the strategy. Prior studies (Frazzitta, Maestri, Uccellini, Bertotti, & Abelli, 2009; Nanhoe-Mahabier et al., 2012; Spildooren et al., 2012) have documented the potential of using rhythmic auditory cues set at a frequency lower than the natural limit cycle for this population to achieve positive results. This possibility deserves further investigation with salient music to increase the applicability of the cueing strategy proposed in this thesis.

Parkinson's disease is not limited to motor impairments, people living with PD also experience a diverse array of cognitive impairments that can range in severity from mild deficits in a specific domain (i.e. executive function, memory, language) to global cognitive deficits as a result of severe dementia (Muslimovic, Post, Speelman, & Schmand, 2005; Yogev-Seligmann et al., 2008). These cognitive impairments are strongly correlated to disease progression. Approximately one quarter of patients present with mild cognitive impairments at diagnosis (Aarsland et al., 2010; Litvan et al., 2011), these impairments increase in severity with disease progression with over three-quarters of people with PD developing dementia within two decades of diagnosis (Hely, Reid, Adena, Halliday, & Morris, 2008). Whilst previous research (Rochester et al., 2010) has demonstrated the feasibility and effectiveness of auditory cues in improving gait amongst people with PD and cognitive impairment, given the attentional costs assumed to be associated with music listening amongst people with

PD (Brown et al., 2009; Brown et al., 2010) it is likely that the potential benefits of this strategy will be attenuated and that safety could be compromised in those with cognitive impairments, this possibility should be excluded by careful and safe testing.

Investigating the utility of the proposed gait training strategy amongst more heterogeneous populations with PD will allow researchers to make more definitive statements regarding the findings thus increasing the ability to generalise the results to other parkinsonian and pathological populations.

6.7 Limitations

The findings in this thesis should be interpreted with consideration of a number of limitations. The first limitation of this series of studies is the small size of the study populations. Whilst the statistical power of the analyses and the generalizability of the findings are limited by the small size of the study groups the studies included in this thesis are exploratory in nature and provide a strong foundation upon which suitably powered studies can build.

A second general limitation of the studies in this thesis was that the motivational and emotional properties of the music selections were not controlled. The motivational properties of a musical piece are dependent upon the perceptual properties of the music, as well as the listeners' interpretation of the music (Crust & Clough, 2006). In the studies included in this thesis the music tracks were selected based primarily on the tempo of the track. For salient music selections the music was also chosen from a selection of the participants preferred artists, however, it is unlikely that the subjects enjoyment of and familiarity with each track would be equal. Motivation and emotion are subjective phenomena, therefore it would be difficult to control for either property entirely, however, the motivational and

emotional qualities of the music may differentially affect gait performance amongst listeners. This possibility should be investigated and subsequently controlled by implementing measures that quantify the motivational and emotional qualities of the music selections.

A number of limitations were identified that were unique to the intervention studies in this thesis. Firstly, the study populations were recruited from local support groups (Southern Alberta) and the Maritime Parkinson Physiotherapy Clinic (Nova Scotia). Though not a limitation in itself, these groups actively encourage their members to maintain a regular walking program and as such our sample of convenience was predominantly comprised of individuals who included walking in their daily activities. The studies would have benefited from the inclusion of an active control group that completed the walking intervention without music accompaniment. This would have allowed us to elucidate whether the improvements to gait performance were a consequence of the salient music accompaniment or simply the established benefits of a walking program. Despite this design constraint, the unanimously positive comments provided by the participants who had walked with music suggest that regardless of whether the improvements to gait are a outcome of the walking program and/or the music accompaniment the motivation and ‘interest’ provided by the music accompaniment contributed to the subjects enjoyment of and ultimately adherence to the intervention. Furthermore, when contacted by the researchers following the conclusion of the study the majority of the participants indicated that they were continuing to walk with music, providing additional support for the salience and perceived efficacy of the intervention.

Musical experience was not documented for the people with PD in this thesis. Music experience has been shown to differentially affect the ability to perceive the

'beat' in complex music pieces (Grahn & Rowe, 2012), with people who are frequent music listeners or musicians showing improved ability to perceive the underlying tempo of complex musical tracks, such as those used in this series of studies. It has also been reported that musicians or former musicians show different brain activation patterns during music listening when compared to non-musicians (Ono et al., 2011; Seung, Kyong, Woo, Lee, & Lee, 2005). This presents the possibility that the physical, physiological, and/or affective response of the individual may have been strongly influenced by their previous music experience; this prospect should be investigated and controlled for in future studies.

Finally, the studies would have profited from additional gait assessments to establish any detraining effects following cessation of the intervention. Previous cued gait training programs have reported the retention of gait improvements for up to six weeks after the intervention period had ceased (Rochester et al., 2010). Establishing the retention time of the improvements to gait performance and motor symptom severity would assist with identifying the optimal dosing for the strategy. Additional assessment sessions during the intervention period would also be of benefit, as the information obtained during these testing sessions would provide an indication of appropriate timing to progress the cueing protocol (i.e. provide music with a higher tempo).

6.8 Conclusion

The purpose of this thesis was to investigate the effects of music on walking performance. The findings suggest that unaltered, commercially available music may be an effective and relevant alternative to the auditory cue modalities commonly used in gait rehabilitation strategies. The salience of the music to the individual is an

important factor in mediating the physical response of the listener and therefore warrants consideration when selecting music tracks for therapeutic purposes. Indeed, it is speculated that music salience can influence dopamine levels in the brain; this provides potential to assist with movement facilitation, particularly in a population that experiences dopamine deficiencies.

The studies in this thesis also substantiate the extensive body of literature describing the positive effects of rhythmic auditory cues on parkinsonian gait that are theorised to result from direct neural coupling between the auditory and motor systems. Specifically, we found that music listening could be safely implemented amongst people with PD during home exercise and moreover an extended music-accompanied walking program resulted in objective improvements to gait performance in a variety of complex gait scenarios that are implicated in the high prevalence of falls in this population. Additional insights into the potential benefits of the novel training program were provided by subjective responses of the patients who indicated a high level of enjoyment, exceptional levels of adherence to the walking program, and increased overall activity levels. Given the progressive nature of PD, long-term engagement in the program will be critical to the maintenance of therapeutic benefits and the avoidance of the physical de-conditioning and depreciating perceptions of quality of life that typically accompany the low level of activity in this population. The music-accompaniment provided during this intervention not only provided a rhythmic cue to which the patient could synchronise their motor activity it also promoted the patients enjoyment of the activity and as a result likely reinforced their engagement in the intervention.

This thesis has not fully resolved the intricacies of establishing selection criteria for the music to be used in the proposed gait training program, nor have we

established the optimal dosing for the intervention, however, the studies included in this thesis do provide a strong foundation on which future studies can build and refine the proposed cueing strategy. This thesis represents initial steps towards a long-term goal of developing a safe, effective, sustainable, and personally relevant gait rehabilitation strategy for people living with PD that is functionally and ecologically relevant.

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