

# Swayed by Sound: Sonic Guidance as a Neurorehabilitation Strategy in the Cerebellar Ataxias

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## Declaration

I, Jon Davis Perkins, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been referenced in the thesis.

Signed.....Date.....



*“What I find most amazing is that so little information is needed to make something very practical.”*

Paul Bach-y-rita (2004)

# ABSTRACT

Cerebellar disease leads to problems in controlling movement. The most common difficulties are dysmetria and instability when standing.

Recent understanding of cerebellar function has expanded to include non-motor aspects such as emotional, cognitive and sensory processing. Deficits in the acquisition and processing of sensory information are one explanation for the movement problems observed in cerebellar ataxia. Sensory deficits result in an inability to make predictions about future events; a primary function of the cerebellum. A question therefore, is whether augmenting or replacing sensory information can improve motor performance in cerebellar disease. This question is tested in this thesis by augmenting sensory information through the provision of an auditory movement guide.

A variable described in motor control theory ( $\tau$ ) was used to develop auditory guides that were continuous and dynamic. A reaching experiment using healthy individuals showed that the timing of peak velocity, audiomotor coordination accuracy, and velocity of approach, could be altered in line with the movement parameters embedded in the auditory guides. The thesis then investigated the use of these sonic guides in a clinical population with cerebellar disease. Performance on neurorehabilitation exercises for balance control was tested in twenty people with cerebellar atrophy, with and without auditory guides. Results suggested that continuous, predictive, dynamic auditory guidance is an effective way of improving

movement smoothness in ataxia (as measured by jerk). In addition, generating and swaying with imaginary auditory guides was also found to increase movement smoothness in cerebellar disease.

Following the tests of instantaneous effects, the thesis then investigated the long-term consequences on motor behaviour of following a two-month exercise with auditory guide programme. Seven people with cerebellar atrophy were assessed pre- and post-intervention using two measures, weight-shifting and walking. The results of the weight-shifting test indicated that the sonic-guide exercise programme does not initiate long-term changes in motor behaviour. Whilst there were minor, improvements in walking, because of the weight-shifting results, these could not be attributed to the sonic guides. This finding confirms the difficulties of motor rehabilitation in people with cerebellar disease.

This thesis contributes original findings to the field of neurorehabilitation by first showing that on-going and predictive stimuli are an appropriate tool for improving motor behaviour. In addition, the thesis is the first of its kind to apply externally presented guides that convey continuous meaningful information within a clinical population. Finally, findings show that sensory augmentation using the auditory domain is an effective way of improving motor coordination in some forms of cerebellar disease.

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## LIST OF ABBREVIATIONS

SCA	spinocerebellar ataxia
FA	Friedreich's ataxia
CAG	cytosine, adenine, guanine trinucleotide repeat
GAA	guanine, adenine, adenine trinucleotide repeat
TMS	transcranial magnetic stimulation
SGEP	sonic-guide exercise programme
COM	centre of mass
COP	centre of pressure
OKR	optokinetic reflex
VOR	vestibulo-ocular reflex
ADHD	attention deficit hyperactivity disorder
PET	positron emission tomography
EMG	electromyography
MP3	MPEG-1 Layer-3 audio
$\text{m/s}^3$	jerk per metre per second
LTP	long-term potentiation
LTD	long-term depression
CIMT	constraint-induced therapy
NGF	nerve growth factor
tcDCS	transcranial cerebellar direct current stimulation

PMC	premotor cortex
vPMC	ventral premotor cortex
dPMC	dorsal premotor cortex
CD	compact disc
Hz	hertz
mm/s	millimetres per second
TBS	theta-burst stimulation

# Chapter 1 - Introduction

## 1.1 Introduction

This thesis is an investigation into improving motor behaviour in people with cerebellar ataxia. It is a multidisciplinary study that spans a number of different subjects: neuropsychology, movement science, neuroscience and neurorehabilitation. The thesis is split into two sections. The first investigates the development of auditory stimuli to convey movement information. To do so, aspects of motor control theory are used to produce auditory guides which are then tested in a healthy population. The second part of the thesis tests the efficacy of using movement-based auditory guides in a clinical population with cerebellar disease. Performance on functional neurorehabilitation exercises, both with and whilst imagining auditory guides, is assessed to investigate if movement behaviour can be instantaneously improved in this population. Following on from this study, the long-term consequences of exercising with the auditory guides are evaluated. A two-month sonic-guide exercise programme (SGEP) is implemented with changes in motor control and walking reassessed following this training period.

Over the course of these experiments, the thesis attempts to answer three central questions:

- 1) Can movement information be successfully embedded within auditory stimuli and used to influence movement behaviour in a predictable manner?
- 2) Can movement information embedded in auditory stimuli instantaneously improve motor behaviour in people with cerebellar disease? A second part to this question is whether mental rehearsal of movement-based auditory stimuli will have the same effect as listening to auditory guides?
- 3) Finally, does the use of auditory guidance over a prolonged period of time significantly alter performance on neurorehabilitation exercises and subsequently locomotion in people with cerebellar disease?

### 1.2 Stating the problem: neurorehabilitation in cerebellar disease

Neurophysiotherapy attempts to improve motor function using physiotherapeutic techniques designed to maximise neural plasticity. Neurophysiotherapy is known to be effective in improving motor behaviour following injury to the nervous system for example, following stroke (Langhorne, Coupar and Pollock, 2009). However, the evidence for motor recovery in neurological disease is much less certain. Nevertheless, positive improvements have been reported in a range of neuropathologies such as Parkinson's disease (Platz, Brown and Marsden, 1998) and cerebellar degeneration (Ilg et al., 2010).

Most neurorehabilitation techniques involve exercise programmes that engage affected limbs or body segments in repeated, controlled actions over time (Langhorne, Coupar and Pollock, 2009). Through the use of such techniques, a large body of evidence has accumulated that shows practice initiates changes at the

neuronal level (Ungerleider, Doyon, and Karni, 2002). Basic principles have been established to best initiate neural plasticity. Neurorehabilitation should be repetitive, adaptable and functional (Carr and Shepherd, 2003). Adaptability (within a rehabilitation context) is based on the fact that movement behaviour has invariant properties that are present despite different movement settings. For example, point-to-point reaches typically produce symmetrical bell-shaped velocity profiles and linear trajectories (Soechting and Lacquanti, 1981). The ability to adapt/scale movement to meet alternate task requirements (e.g. different distances or speeds) whilst maintaining invariant movement characteristics, is important in encouraging neural plasticity (Plautz, Milliken and Nudo, 2000). The concept of functional rehabilitation relates to performing exercises that are meaningful for the actor. There is evidence that functionality initiates greater neural plasticity as a consequence of increased nervous system excitation (Hunttenlocher, 2002). Interaction between neuronal groups in the brain emerges from meaningful, multimodal experience and it is important therefore that the skills trained during rehabilitation are specific to the skills used in everyday-life activities. An example might be to walk to the shop, rather than to cover the same distance using a treadmill. In addition, if an activity has purpose for the performer, it can provide a motivational factor that is less present in undirected or isolation exercises (French et al., 2010; Carr and Shepherd, 2003). The application of adaptive and functional exercises repeated over time make up the basis of many neurorehabilitation programmes.

There are however, a number of features of neurological disease that make access to such programmes difficult. Muscle weakness and fatigue or example, are common to many nervous system disorders and detrimentally affect the ability to perform

neurorehabilitative exercises. Cerebellar degeneration in particular, affects the ability to take part in the type of training programmes used within a neurorehabilitation context. Whilst not explicitly necessary for producing movement (Miall et al., 1993), damage to this sub-cortical structure leads to dysmetria and jerky, irregular, movement patterns (Manto, 2009). A classic symptom of cerebellar dysfunction is a problem scaling and adapting movements to different task situations. Topka et al. (1998) for example, have demonstrated how ataxia is more pronounced as movement speed increases. Similarly, people with cerebellar disease show high levels of intention tremor during the transport phase of reaches which increases as goals are approached (Manto, 2009). These features of ataxic movement limit people from performing neurophysiological exercises with maximum benefit (i.e. repetitively and with adaptable form). In addition, falls and unsteadiness greatly discourages engagement in functional tasks such as walking. In many cases of neurological disorder, these problems can be partially overcome through the use of assistive devices (for example, walkers and canes allow access to walking). However, the use of such devices violates one of the main principles of neurophysiotherapy discussed above, that is, movement should be performed with correct but adaptable form. A common outcome from using support aids is that compensatory actions are developed which are integrated into the nervous system as any other motor behaviour would be (Bateni et al., 2004).

A different approach to facilitating movement control is to manipulate the external environment. The practice of increasing (or substituting) sensory information is well established for a variety of neurological disorders (Feys et al., 2006). A common method is to increase sensory input through the visual domain (Griffin et al., 2011)



with classic example being to put markers (strips) on the floor to increase visual information. This technique has been shown to improve gait in people with Parkinson's disease (Azulay et al., 1999). Augmented haptic sense also improves motor skills. Gentle touch for example, using one finger, decreases postural sway in cerebellar disease (Sullivan, Rose and Pfefferbaum, 2006). Similar findings are found using the auditory system, for example, music is known to help people with Alzheimer's disease dance freely without impairment (Sacks, 2006). Slowness of movement and gait are features of this disease (Della Salla, Spinnler and Venneri, 2004). Simpler sounds such as rhythmic cues positively influence gait in Parkinson's disease or following stroke (Thaut and Abiru, 2010; Thaut et al., 1996; Rochester et al., 2011).

A developing technique for supplying sensory information for motor control is the use of motor-imagery. A number of studies have demonstrated motor-imagery excites regions of pre-motor cortex and has a facilitatory effect on movement (Yoo, Lee, and Choi, 2001; Hubbard, 2010). It has been suggested that mental rehearsal of a motor act delivers 'faux sensory information' (and in particularly faux proprioception)<sup>1</sup> to the regions of the brain concerned with motor control (Grush, 2004). However, an aspect of motor-imagery that has not been explored within a rehabilitation context is the consequences of training a motor act with sound, such as when learning an instrument. Numerous studies show that mutual coding between the auditory stimulus and motor event occurs when auditory information informs

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<sup>1</sup> As motor imagery activates responses in the whole motor system, Grush (2004) argues that the proprioception and kinesthesia that would be experienced by a real motion must be emulated (rather than just information about timing or muscle activations). This is termed faux proprioception.

motor learning. Musicians listening to a musical piece that they can play for example, exhibit motor cortex activity that reflects the playing of that piece (Kristeva et al., 2003; Meister et al., 2004). This auditory-motor association raises an intriguing possibility. Can learnt auditory-motor transformations for *rehabilitative sounds* evoke motor cortex activity through mental rehearsal of those sounds? Logically this is viable and could be a particularly useful tool in rehabilitation where, for example, the ability to produce motor imagery is impaired following basal ganglia damage (Li, 2000).

With regards to cerebellar disease, there is a paucity of studies reporting positive effects using sensory augmentation in the neurorehabilitation literature. This reality reflects the complex outcomes of cerebellar degeneration and the role of this brain structure in motor control. A number of explanations for the behavioural problems seen in cerebellar ataxia have been posited. It has been suggested for example, that the cerebellum is critical in motor learning where it operates as an error feedback monitor as a movement is executed (Houk, Buckingham and Barto, 1996). Disruption of this function would impede responses to perturbations in movement trajectory ‘online’ and would also affect the retention of functional gains following training (as motor adaption would be compromised). A different theory is that the cerebellum acts as an internal clock which regulates the timing of psychological events including movement (Ivry et al., 2002). However, a more novel proposition that this thesis embraces, is that the cerebellum acts as a prediction device for mental events. In motor control predictive theories centre around forward models which are proposed to be generated and/or stored in the cerebellum (Bastian, 2006; Wolpert, Miall and Kawato, 1998). An inability to use predictive information will cause mis-

scaling and timing errors when performing motor acts and could explain the ataxic movement that follows cerebellar dysfunction. Crucial for the ability to make fast and accurate predictions is access to clear sensory information about both the internal and external world. In this respect it has been proposed that an important cerebellar function is to acquire different forms of sensory information for use in other brain areas/tasks (Bower, 1997; Jueptner et al., 1997). All sensory pathways have circuits with, and elicit neural responses in, the cerebellum (Bastian, 2011). A lack of accurate sensory information before and during a movement would disrupt the formation of internal models, confuse error feedback (and thus motor learning) and disturb the ability to accurately time movements. It is possible therefore, that movement deficits following cerebellar disease can be attributed to impoverished sensory experience (Gao et al., 1996).

### 1.3 Augmented sensory information as a solution for movement problems in cerebellar ataxia

This study attempts to limit the problems of poor prediction and sensory acquisition/processing found in cerebellar disease, by offering increased sensory information to guide action. As sound is known to facilitate motor control in a number of neurological disorders (e.g. Thaut et al., 1996), the auditory system is a positive modality for supplying supplementary sensory information. As movement is spatio-temporal (Lee, 1998), it makes sense that augmented/substituted information should also be spatio-temporal. Is it feasible then that the form of a well-controlled action (transferable across dynamic situations) can be conveyed that also informs the

listener as to where the movement was ‘heading’ (i.e. is predictive)? The idea of prospective control is especially important due to the potential problems in predicting future states in cerebellar disease. Whilst many auditory augmentation rehabilitation studies use rhythmic stimuli (Thaut et al., 1996; Rochester., 2011), an outstanding issue with these cues is the lack of information available within the stimulus. Whilst it is clear that rhythmic cues provide goals for movement to be entrained to (i.e. they carry prospective information), there offer no information between the beats to help guide the movement to that goal (i.e. the goal is not continuously referenced). In this sense the rhythmic cues only provide one aspect of movement information.

The first task for this thesis then is to develop predictive auditory guides that also provide relevant guiding information for the duration of a desired action. If such sounds were found to successfully influence motor control, the second task would be to test the movement-based auditory guides in a target population with cerebellar ataxia. The purpose of using movement based auditory guides is to test if following predictive, continuous and meaningful auditory stimuli instantaneously reduces ataxic movement. Depending on the results of this testing, a final objective for this thesis is to measure the effects of the long-term use of the auditory stimuli on motor behaviour, or more specifically, on neurorehabilitative balance exercises. At the time of writing no external guides containing on-going, prospective movement information have been used to improve motor control within a clinical setting and this thesis is the first to do so.

## 1.4 Theoretical framework

The thesis has four main strands of theoretical consideration. Firstly, theorising around the cerebellum's function (as detailed in Chapter 4) is the starting point for this thesis. This work takes the view that a primary function of the cerebellum is to generate predictions about future events for multiple mental activities. For many of these mental tasks, the cerebellum relies on accurate sensory information to make assessments of current, as well as future, states. In this regard, this thesis adopts the opinion that sensory acquisition and processing, is a predominant aspect of cerebellar function (Bower, 1997). A further theoretical consideration is recognition of the fact that the brain is multisensory and thus, sensory information is not confined to a single domain (Meredith and Stein, 1986; Bach-y-rita, 1984). It follows therefore, that movement information extracted by the visual system could equally be used in the auditory domain. In both sections of the thesis it is assumed that multisensory processes are engaged by the delivery of movement information through sound. Thirdly, development of the auditory guides is rooted in an ecological approach to motor control (Gibson, 1966). James Gibson's ideas on invariant properties within the environment are implemented through the use of David Lee's spatio-temporal variable tau (Lee, 2005). A key aspect of tau is that sensitivity to *how* it is changing offers prospective information about the movement, as well as continuous information about the movement's progress. As a result of these features, the tau variable was an ideal way to plot movement within the sounds. A final theoretical consideration for this work is based on the ideas of Carr and Shepherd (2003), who have extensively catalogued the most appropriate neurophysiotherapy techniques to

improve motor recovery. As already highlighted, these authors have shown that to maximise neural plasticity, neurophysiotherapy should be performed with adaptable form, in a repeated manner, in functional settings. These considerations informed the development of an intervention programme to improve movement control in individuals with cerebellar ataxia.

## 1.5 Thesis plan

Chapter 2 introduces the literature regarding the relationship between movement and sound and includes relevant auditory system neurology. Identification and monitoring of auditory motion are discussed, including a review of pitch perception and why changes in pitch can be used to identify auditory motion. Motor control theory is also debated and the reasons why the tau variable was selected for use in this study. Chapter 3 is the first experiment in this work; ‘Using On-going, Dynamic Sonic-Guides to Influence Reaching’. A population of healthy individuals is used to directly test the effects of using continuous and movement-based auditory stimuli on a reaching task. Auditory guides containing different motion parameters were used and three variables recorded to measure movement behaviour: the position within the movement where the maximum velocity occurred, the lag in arrival time between the hand’s arrival at the target and the end of the sonic-guide and the average velocity of the hand during travel to the target. Chapter 4 introduces the central topics of this thesis; ataxia and the cerebellum. Literature describing recent knowledge of cerebellar ataxia and the aspects of the disease most relevant to this study are introduced. Cerebellar physiology and current thinking on cerebellar function are

included. The possibility of improvements in motor behaviour and current knowledge of how to best exploit neural plasticity for rehabilitation purposes is also reviewed. Chapter 5 is the second experimental work in this study: ‘Swaying with Sonic-Guides in an Ataxic Population’. The experiment investigates two research questions. The first is whether sonic guidance is an appropriate tool for improving motor control in people with cerebellar disease. The second is if auditory imagery of the sonic-guides can also influence motor behaviour. To investigate these hypotheses, twenty people with cerebellar ataxia were split into experimental and control groups and measured performing a lateral sway exercise. Levels of jerk were recorded to test for changes in participants’ movement smoothness at baseline, during the sonic-guide intervention and whilst mentally rehearsing the sonic-guides. Chapter 6 includes a final third experiment: ‘Applying Sonic Guides over Two Months’. This follow-up tests the outcome of the long-term use of movement-based auditory stimuli on participants’ motor-skill. A sonic-guide exercise programme (SGEP) was developed to be practiced at home. After two months, seven participants from the experimental group returned to the laboratory and were retested on levels of jerk whilst performing lateral weight-shifting exercises. Five of these participants also had their ability to walk over a short distance examined. For the walking task, placement of the feet relative to each other and step length were used to monitor changes if they occurred. Chapter 7 closes the thesis with a summary of the main findings from this research. Conclusions regarding the three questions forwarded in this chapter are addressed. In answering these questions, findings from each chapter, as well as limitations and future directions of this work are summarised.

## Chapter 2 - The Development of Sounds for Action

### 2.1 Introduction

As will be argued in this chapter, there is an intrinsic relationship between sound and motor behaviour, with movement being at the root of sound. Sound conveys properties of both the object and act from which it emanates (Gaver, 1993). For example, the ‘bang’ that follows contact between a hammer and nail, reflects the force used to move the hammer as well as the vibrational qualities of the objects (i.e. the metal of the hammer and nail). The auditory system has evolved to convey these properties to the brain from which meaning can be established. In addition to identification of sounds, the auditory system directs motion throughout daily life. For example, auditory stimuli orient vision towards movement sources so that appropriate responses can be initiated. This function is continually engaged to avoid collisions (i.e. when crossing the road) (Calvert, Spence and Stein, 2004). If an object emits a continuous sound, movement direction, speed, acceleration and arrival can be estimated.

Aspects of motor skill learning are dependent on auditory information. In the natural world, chicks deprived of auditory feedback during the early weeks of life, produce altered and disturbed bird song in adulthood (Konishi, 2004). In this example, the musculature of the vocal apparatus is not properly ‘tuned’; an effect also recognised



in humans. Speech rehabilitation is known to be more problematic in people born without hearing than for those who lose hearing later in life (Paul and Whitelaw, 2011). This finding reflects the importance of auditory feedback in establishing long-term motor learning in the vocal apparatus (and associated nervous system). Without audible vocalisations as a guide, the correct contractions and tensions of the muscles are absent, leading to altered vocal muscle control and corresponding neurology (Roder et al., 1999). Auditory information also guides larger-scale motor actions, for example, dancing. Whilst dancing in the absence of music is possible, the introduction of sound (music) likely increases the fluidity and timing of individual steps. Music is also integral to a number of sports such as ice skating and elements of gymnastics, both of which use the rhythms of music to guide complex motor acts (Effenberg, 2007). But it is not only in specialist sports where auditory information guides motor behaviour. When jogging for example, the rhythms created by the feet contacting the ground, interspersed with the rhythms of inhalation and expiration create a ‘sonic map’ of the runner’s ‘beat’ (McDermott et al., 2003). Disruption to this map causes misplaced feet and the necessity of adjustments in breathing for a few steps following perturbation. A corresponding effect is found in tennis where auditory delays in the sound of the ball contacting the racket, causes mistiming of strokes (Takeuchi, 1993; Mead and Drowatzky, 1997). In team sports requiring group coordination, auditory cues guide collective motor behaviour. When rowing, the rhythm produced by the oars entering and exiting the water, aids synchronisation of motor activity between oarspersons (Schaffert, Mattes and Effenberg, 2010). In the examples cited above, the dominant property of the sound that guides movement is either rhythm within music or an emergent rhythm from the act engaged in. That

the brain picks-up and uses this information to guide movement so effortlessly, has not gone unnoticed by movement scientists and those involved in motor rehabilitation (see Thaut, McIntosh, and Rice 1997, for example). It is worth considering therefore, how it is that auditory information processing has evolved such that sensorimotor transformations occur so regularly.

## 2.2 Auditory system evolution

Despite the auditory system being anatomically the best preserved sensory organ in the fossil record, little is understood about the evolution of this complex set of organs (Clack and Allin, 2004). However, efficiency in identifying auditory cues from predators, food sources and mates would provide a significant evolutionary advantage, leaving adaption of the auditory apparatus a subject of natural selection (Yost, 2008; Stebbins, 1983). This is particularly true in situations where internal and/or external visual information would be impoverished (i.e. where eyesight was poor or during the night) (Stebbins, 1983). This hypothesis is supported by Nilsson (2009) who has suggested that evolution of the sensory systems is driven by sensory tasks. It is unsurprising therefore, that the auditory systems of specific species have evolved to identify sounds relevant to the animal's environs. In some instances, recognition of an auditory event is coupled with recognition of the underlying movement, or more specifically, the animal moving. For example, desert snakes move in unique ways which produce low frequency sound. The primary food source for these animals is the desert rodent. In desert rodents, the auditory system has evolved to decipher the low frequencies sounds made by snakes to avoid predation

(Webster and Webster, 1977).<sup>2</sup> This example is a demonstration of how movement and its resultant auditory output, is an object of natural selection.

The evolutionary link between hearing and movement is further emphasised by the anatomical and physiological similarities between vertebrate auditory and vestibular systems. These systems share anatomical correlates within the inner ear, have analogous mechanical systems for information transfer, and share the VIII cranial nerve within which, efferent neurons of each system bundle together (Nikolletseas, 2010). In addition to physiological similarities, both systems predominantly interpret information that results from motion. Movement of the head is registered in the vestibular apparatus through a change in the flow of aqueous/gel-like solutions in the semi-circular canals and otolith organs. Hair cells suspended in the aqueous solution when disturbed, initiate neural responses in the vestibular fibres (Baloh and Honrubia, 2001). Self-motion and position with reference to gravity, are sensed through this mechanism (Day and Fitzpatrick, 2005). Motion monitored by the vestibular apparatus is often self-generated and its importance in stabilising posture can be identified by the debilitating effects of vestibular disorders. Meniere's disease for example, is a little understood vestibular pathology that results in the loss of vestibular hair cells along the sensory epithelia of the vestibular apparatus (Tsuji et al., 2000). The primary symptoms of the disease are vertigo and the sensation of falling, even when prone on the floor (Andersson, Hagnebo and Yardley, 1997).

The auditory system also ultimately processes movement information. Hair cells suspended in an aqueous solution within the inner ear, transform incoming stimuli

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<sup>2</sup> The desert rat has an enlarged middle ear which allows hearing at frequencies below 0.1 kHz (see Ravicz et al., 1992).

into neural discharges. However, in this instance hairs are disturbed in response to sound waves (displaced air) from the vibration (movement) of a source object (Pickles, 2012). In this regard the auditory system is sensitive to ‘movement’ at a much finer frequency than the vestibular apparatus and is also predominantly concerned with monitoring external information (Lysakowski and Goldberg, 2004).<sup>3</sup> The similarities between auditory and vestibular apparatus have led to postulations that one system evolved from the other. In keeping with the evolutionary theory that organisms evolve from simple to more complex forms, it is likely that the auditory system emerged from the vestibular apparatus (if external auditory information is considered more complex than self-generated motion information). As Lysakowski and Goldberg (2004) note:

*‘The presumed original function of the inner ear was to monitor rotational and linear movements of the head as well as the orientation of the head relative to the Earth vertical gravitational vector. As such, the inner ear functions as a proprioceptor. At several points during the ear’s evolutionary history, one or another organ has taken on an exteroceptive function, the detection of sound/or substrate-borne vibrations.’*

(p. 59)

It is possible then that sensitivity to motion is the driver of adaptive change within the inner ear. If this hypothesis is correct it would make sense that aspects of motion are represented within the auditory system.

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<sup>3</sup> Whilst monitoring of language is a primary function of the auditory system in humans, this is an exception in the animal kingdom.

## 2.3 Identifying sound in the environment

The ability to locate the source of a sound is a primary function of the auditory system in mammals, birds and insects. As mentioned, this skill is essential for predation, feeding and mating. To pinpoint a sound, the brain has to be skilled in extracting meaningful information from the multitude of oscillating sound waves hitting the auditory apparatus (Johnsrude et al., 2013). A sound wave is created through the vibration of an object whether that is a hammer and nail or the vocal chords. This vibration displaces (through compression or expansion) surrounding air molecules resulting in a 'wave' which has a number of characteristics. One is that the form of the wave consists of peaks and troughs repeating cyclically (Pickles, 2012). That the brain effortlessly isolates a single sound wave from many, indicates that the inner ear is adapted to detect specific features of information within the auditory array. In a similar manner, auditory mechanisms for isolating and extracting information from moving sound sources must also exist. Auditory motion is identified in several ways.

### *2.3.1 Localising a sound source*

A sound source's position is identified through two physical phenomena when surveying the horizontal plane. The first is through the 'interaural time difference' (ITD) and the second, the 'interaural intensity difference' (IID) (Fitzpatrick and Kuwada, 2001, Jones et al., 2013). Both the ITD and IID occur as a result of the natural physiology of the animal, and more specifically, due to the distance that exists between the animal's ears. As a result of this distance, a sound wave from a

single source reaches each ear at slightly different times (i.e. the time between peaks of the sound wave are more dispersed as a function of distance). This time difference registers in micro seconds but the brain is readily able to detect and discriminate such margins. The IID is a similar phenomenon; it refers to differences in sound intensity at the two ears that are also detected by the brain. Sound intensity can be thought of as the amount of energy carried within a sound wave per unit area. Sound intensity reflects the amplitude of the original vibration and the amount of energy used to initiate that vibration. Sound intensity decays as it reaches the ear furthest from the sound source, causing a discrepancy which is perceived at each ear (Wambacq et al., 2007). It is from these small time and intensity differences that the brain is able to locate sound. Early experimentation provided evidence that ITDs and IIDs are independent mechanisms, with ITDs detected at frequencies below 1000 Hz and IIDs identified at frequencies above.<sup>4</sup> This model is known as Duplex theory (Macpherson and Middlebrooks, 2002). A tenet of this theory is that, with reference to the head, angles and positions in the environment are calculated from patterns of neural response to ITDs and IIDs. An important aspect of how this is achieved is the distance between the ears which, as it remains constant, calibrates the ITD and IID, so that changes in the auditory signal can be registered (Grantham, 1995).

### *2.3.2 Doppler Shift*

ITDs and IIDs are not the only ways in which an object's position can be derived from the auditory array. The Doppler Effect is a well-known phenomenon where

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<sup>4</sup> Research suggests there is considerable overlap between ITD and IID in sound localisation. It has been suggested that both use frequencies lower or higher (respectively) than previously assumed (see Jones et al., 2013 for review).

direction and rate of movement can be calculated through sound. The Doppler Effect is perhaps best known from hearing passing ambulances or ice-cream vans. From changes in the pitch of the vehicle's siren, a listener can determine whether the ambulance or ice-cream, is heading towards or away from him or her. The Doppler Effect occurs as a function of distance and the properties within a sound wave. The number of peaks within the sound wave, that pass a specific point over a period of time, is known as the frequency. The further away from an observer the source of the sound, the greater the energy that is lost in the sound wave. As a result, the distance between peaks becomes more dispersed (i.e. the wavelength is increased) meaning fewer peaks hit the listener per second. As a result of this phenomenon, a change in how the frequency is heard occurs (McBeath and Neuhoff, 2002). From the direction of this change (i.e. does the frequency increase or decrease), the observer can perceive if the sound source is approaching or receding. It is important to note however, that the actual frequency emitted from the source object remains the same but is nevertheless heard as a shift. In this regard it is more accurate to talk of the Doppler illusion rather than effect (Ghazanfar and Maier, 2009). Despite this, in addition to directional information, the Doppler Effect gives a listener approximate estimates of, speed and arrival of an object (Jenison, 1997). Parallels can be drawn with the concept of optic flow, a key property of which is that spatio-temporal relationships can be extracted from changing patterns in the optic array (Lee, 1998). That the Doppler Effect also reveals spatio-temporal relationships, suggests that (as in the visual field) there are invariant characteristics of the auditory scene (Gaver, 1993). Invariance in auditory spatio-temporal relationships is exploited to guide movement in the natural world for example, through echolocation. One aspect of

echolocation is to ‘set up’ Doppler shift detection through the emission of high frequency sounds which in turn, reflect from objects in the environment. Studies using bats (and other echolocating mammals) have shown that there is a fixed relationship between the delay of the returning signal and the velocity of approach/contact of an object (Simmons et al., 1995; Lee et al., 1992). Humans without vision are also known to use echolocation by producing a series of clicks with the tongue (Teng, Puri and Whitney, 2012). Of interest to this study is that non-blind humans are also capable of quickly learning to use echolocation to identify room size and target distances (Schörnich, Nagy and Wiegrebe, 2012). What these and other echolocation studies demonstrate, is how readily sonic stimuli can be used by mammals to create precise auditory maps of the environs within which to move and of the objects within that space.

### 2.3.3 Auditory looming

A spatio-temporal feature of auditory processing is ‘time-to-contact’ (TTC) information.<sup>5</sup> TTC can be extracted from sound intensity and is known as auditory looming (Neuhoff, 1998, 2001; Seifritz et al., 2002). A number of interesting findings stem from auditory looming research, the foremost of which is that auditory system responses are greater in the presence of approaching, as opposed to receding, looming sounds (Neuhoff, 2001; Ghazanfar, Neuhoff, and Logothetis, 2002). This observation is in keeping with an evolutionary history where an object’s approach is

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<sup>5</sup> TTC in this thesis does not refer to the host of studies that suggest metric time or velocity is used to understand arrival (see Tresilian, 2004, for example). Throughout this work TTC refers to an object’s arrival being perceived as specified by the changing variable tau (described by Lee, 1980) where velocity and distance information are redundant.



more likely to herald danger than a receding one (i.e. predation). A further interesting aspect of auditory looming research is that time-to-arrival estimations are often premature (Neuhoff, 2001; Maier and Ghazanfar, 2007). This finding is also explained in evolutionary terms. If a primary function of auditory looming is collision avoidance, arriving early would be an important mechanism to ensure aversive action is taken in time (Neuhoff, 2001; Bach et al., 2009).

Looming signals are known to be multisensory with visual and auditory signals prominent in initiating evasive responses (multisensory processing is discussed in section 2.5) (Maier et al., 2004). Information in alternate sensory domains act collaboratively to enhance perception accuracy. For example Calabro, Soto-Faraco, and Vaina (2011), showed that directionally congruent auditory stimuli, increases motion identification when a moving object is camouflaged with the same texture as its background. This study highlights how the brain readily uses all sensory information available for perception. The facilitatory effect of auditory looming on visual movement recognition has been evidenced at the neural level. Using transcranial magnetic stimulation (TMS), Romei, Gross and Thut, (2010) showed that the visual cortex is directly activated following exposure to auditory looming signals. That such activation occurs, suggests neural mechanisms for looming-type stimuli in auditory or visual domains have co-evolved to maximise motion recognition within the environment.

#### *2.3.4 The what and where of sound*

Brain imaging studies have also revealed that, analogous to the visual system (see Goodale and Milner, 1992), there are separate auditory pathways for the ‘what’ and

‘where’ of auditory information (Lomber and Malhotka, 2008). Perception of what an object is has been shown to activate an anterior-ventral pathway whereas responses to location occur in a posterior-dorsal pathway (for both static and dynamic location) (Rauschecker, 2011). In macaque monkeys, Romanski et al. (1999) showed that the different auditory streams terminate in dissimilar areas of prefrontal cortex. fMRI investigations in humans support the findings of ventral and dorsal stream function, however, target areas for these auditory pathways differ to other primates as a consequence of language processing (Arnott et al. 2004). Behavioural studies suggest that distinct auditory processes for identification and location are present from birth. Infants for example, recognise and locate their mother’s voice (from many), hours after being born (DeCasper and Fifer 1980; Fleming et al. 1999). This skill reflects the importance of auditory acuity as a survival mechanism in infancy.

## 2.4 Temporal representation in the auditory system

Time is an important factor to consider when describing perceptual experience. Senses such as taste and smell, do not need a temporal component to give meaning (value) to incoming stimuli. This is also true of some qualia of vision, such as colour, depth or an object’s features (presented as a static image). However, depending on what one is doing, more useful information is gleaned as a stimulus changes over time and this is particularly true of auditory information. A split second of sound gives minimal information regarding location, identification or motion. This reality reveals the fundamental purposes of the auditory system which are to identify

direction, to detect movement and to communicate. The latter two functions are wholly dependent on time (Møller, 2006). It is unsurprising therefore that behavioural studies indicate that the auditory system encodes temporal information with greater accuracy than other modalities (McAuley and Henry, 2010; Repp and Penel, 2004). McAuley and Henry (2010) showed that participants are more sensitive when making tempo judgements of auditory rather than visual rhythms. In addition they demonstrated that pre-exposure to auditory rhythms influences tempo judgements in the visual domain (participants made judgements that were more similar to the auditory rhythm). These findings are supported by imaging research which has shown that attending visual rhythms activates the putamen following pre-exposure to auditory rhythm but not without (Grahn, Henry and McAuley, 2011). A similar bias in auditory processing can be found when synchronising movement to auditory or visual rhythms (Repp and Penel, 2004) or when learning rhythmic sequences presented through either touch or vision (Conway and Christiansen, 2005). A number of explanations have been posited for the predisposition to temporal acuity in the auditory domain. Hove, Spivey and Krumhansl (2010) for example, showed that the type of stimuli used to create visual rhythms effects how well they are perceived. A different explanation relates to the specific features of auditory rhythms. Even when identical, different beats within a sequence are known to have an ‘accent’ and are not heard in the same way. An example would be that the first beat in a bar is often experienced as being louder (Phillips-Silver and Trainor, 2007). It has been argued that the brain attunes to auditory accents periodically, aiding in the perception of rhythm (Grahn, 2012). As there are no known equivalents in other sensory domains, the perception of accents may be one reason for increased temporal

accuracy in the aural system. Regardless of the reasons behind greater temporal accuracy in the auditory system, it is clear that aspects of time are incorporated into the auditory nervous system as discussed below.

#### *2.4.1 Processing a sound wave and its frequency*

A soundwave begins its journey at the outer ear which picks up and reflects the wave through the ear canal towards the eardrum. The vibrational signal of the drum is then transferred via the ossicles (three small bones of the inner ear) to the cochlear, the sensory organ of the ear in mammals (see Dallos, Popper and Fay, 1996 for review). The cochlear, is a small snail shaped organ which contains three fluid filled cavities (the scala vestibule, the scala tympani and the scala media). These cavities are separated by Reissner's membrane and basilar membrane respectively (Plack, 2013). A normally functioning cochlear filters broadband sound into channels (frequency tuned bands) for further processing later in the auditory apparatus. Changes in frequency tuning are known to be a cause of hearing loss and it has been argued that this is a result of the spectral and temporal structure of sound being perceived differently (i.e. the 'edges' of the frequency bands mentioned above are less defined) (Henry, Kale and Heinz, 2014). The basilar membrane is the part of the cochlear where frequency is 'sorted'. This is due to its vibrational properties where incoming stimuli are transformed into temporal firing patterns in the auditory nerve (Møller, 2006, Pickles, 2012). The basilar membrane contains frequency-sensitive areas meaning that it is tonotopically arranged as a property of its diverse stiffness and morphology (Oxenham, 2012). High frequencies are mapped towards the top of the structure, with low frequencies represented towards the base. In this respect the

basilar membrane acts as a band-pass filter (Plack, 2013). Adjacent to the basilar membrane, sits the organ of Corti which supports a multitude of sensory hairs that synapse with independent auditory nerve fibres. Each one of the sensory hairs individually codes for a specific frequency. Research on the neural firing rate of auditory nerve fibres shows phase-locking to the sound's frequency (Köppl, 2012; Avissar, 2007). Phase-locking indicates that the auditory system is sensitive to temporal information at the neural level, and also provides a mechanism through which temporal resolution is preserved in the auditory nerve until it reaches downstream targets such as the inferior colliculus in the brainstem (Plack, 2013; Oxenham, 2012). Auditory nerve fibres are of different (frequency-specific) diameters and, as the propagation rate of the action potential relates to nerve thickness, information regarding different frequencies arrives at sub-cortical brain regions with the timing aspects of the stimulus intact (Møller, 2006). Phase-locking also occurs in ensembles of neurons in the auditory cortex. Time-varying patterns of neural activity are found that correspond with the temporal envelope of speech sounds (Ghitza, 2012). Within these patterns of neural activity, oscillatory behaviour (i.e. bursts of theta, beta, or gamma frequency bands) adapt in line with the incoming stimulus (Doelling et al., 2014; Peelle, Gross and Davis, 2013). Temporal resolution in the auditory apparatus is also coupled to spatial resolution. Spatial resolution is another outcome of the (tono)topical arrangement of the basilar membrane. As each area of the membrane codes for a specific frequency, the 'distance' between frequencies is 'mapped' and transferred to the patterns of neural activity in the auditory nerve. Thus temporal representation has a corresponding spatial representation. As Langner (1992) notes:

*“...temporal information about periodic signals is represented in auditory nerve fibers by synchronized spikes and transformed in the central auditory system by neuronal correlation mechanisms into spatial information— represented in neuronal maps.”*

(p.118)

The conclusion from this observation is that auditory processing is spatio-temporal and that shifts in frequency can be understood as shifts in space-time.

#### *2.4.2 Neural correlates of pitch processing*

The previous discussion indicated that the frequency of a sound has special meaning in auditory perception. Perceptual awareness of the frequency of a sound wave is known as pitch (Bendor and Wang, 2006). Pitch can be a combination of several different harmonics but the brain is able to interpret them as a single tone (tone generally relates to the fundamental frequency of the sound) (Langner, 1992). Studies have shown that in humans cortical areas in general respond to harmonic pitch cues more than noise of a similar frequency (Norman-Haignere, Kanwisher and McDermott, 2012). Pitch processing is essential in communication and for enjoying music. It is unsurprising therefore, that humans are skilled at recognising pitch. Infants as young as six months old for instance, demonstrate the ability to distinguish between relative pitch<sup>6</sup> (Plantinga and Trainor, 2005). In adults, fMRI studies show unique areas of the brain are activated in response to pitch stimuli (Hall and Plack, 2009; Griffiths et al., 2010). Of particular relevance to the present study, is the ability to understand relative pitch (as opposed to absolute pitch) a feature of which is pitch *contour* (i.e. whether a pitch tone increases or decreases). In longer, continuous

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<sup>6</sup> Relative pitch refers to the relationship between different pitch tones (a melody). The melody remains recognisably the same even if played in a different key.

sounds this is known as; frequency-modulation, frequency sweep or, with particular reference to music, a pitch glide (Rauschecker, 2013). The majority of expressive auditory information involves pitch modulation (i.e. speech and music). The basis for music and vocal communication is melody which consists of contiguous individual tones. However, using pitch glides to modulate from one tone to the next is a ubiquitous feature of complex sounds and suggests that understanding pitch contour is a fundamental human skill (McDermott and Oxenham, 2008). It is unsurprising therefore, that pitch contour is represented in the nervous system. fMRI experiments in humans, have identified unique neural correlates that are activated in response to either upward or downward frequency sweeps (Hsieh et al., 2012).<sup>7</sup> Sensitivity to pitch glides in humans can also be honed. For example musicians have been shown to display greater sensitivity to changes in pitch structure than non-musicians (Fujioka et al., 2004). This is also true of tonal languages (e.g. Cantonese) where speakers are found to be more attuned to changes in pitch (Bidelman, Hutka and Moreno, 2013)

## 2.5 Multisensory processes

Historically research considered the senses individually. There was good reason for approaching the study of the sensory systems in this way, as each sensory organ has its own unique sensory epithelia (e.g. mechanoreceptors in the skin) and extracts specific forms of energy from the environment. However, it has long been known

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<sup>7</sup> These regions are the supratemporal plane (in the right auditory cortex) and the superior temporal gyrus (in the left anterior region).

that the senses interact and influence one another (Calvert, Spence and Stein, 2004). In the last twenty years, as a consequence of improved brain imaging techniques, understanding of how deeply interrelated sensory processing is has rapidly expanded (Molholm and Foxe, 2010). Generally, multisensory processes contribute to perception in two ways. When information in one modality (representing a single perceptual event), is presented with congruent information from another modality, it is called *cross-modal matching* (Calvert, 2001). Cross-modal matching is described as a ‘complex of two or more modality-specific stimuli’ (Stein et al., 2010, p. 1719) where sensory information is integrated late in the experience, and in specific areas of the brain (Calvert and Thesen, 2004). Typically, in experiments investigating cross-modal matching, reaction times and consistency of object/event perception are greatly improved when two or more sensory inputs are available (Wallace, Meredith and Stein, 1993). A different multisensory mechanism, integrates perceptual streams early in an event and results in two or more sensory signals merging to form a new unitary percept (Stein et al., 2010). This phenomenon is known as *multisensory integration*. A characteristic of multisensory integration is an increased neuronal response known as superadditivity. For example, if the tactile and auditory stimulation are understood as contiguous the same neurons respond with a greater neural spike rate and amplitude (Holmes and Spence, 2005). Recordings of superadditive responses show that they are larger than the sum of sensory responses presented individually (Stanford and Stein, 2007). That superadditive neurons exist has been taken to suggest an evolutionary bias for integrated sensory streams, without which the perceptual world would be greatly impoverished (Stanford and Stein, 2007; Nagy et al., 2006).



Greater understanding of multisensory experience has challenged traditional views of the senses and a new model has emerged with multisensory processing as the norm in perception. As Foxe and Molholm (2009) identify:

*“... the job of a neuron is not to remain completely faithful to a given sensory system but to calculate as best it can, a specific functional outcome [...] if there is useful information to be had from a second sensory system regarding the computational goal, then it seems a fair bet that multisensory information would be integrated into that neuron’s computation.”*

(p. 150)

Integration of visual and auditory streams occurs on a daily basis with interaction effects between these two information sources well documented (Vroomen and de Gelder, 2000; Chen and Yeh, 2009). An effect familiar to most people occurs when attending a film at the local cinema, where the actors’ voice is readily attributed to the lips moving on screen. Whilst the moving lips and sound source are separate information streams (in different locales), the brain effortlessly merges the two to form a coherent unitary experience (Bonath et al., 2007). Other than redirecting sound, visual information can influence what is heard. McGurk and MacDonald (1976) for example, showed that the sound ‘da’ is heard if the lip movements ‘ga’ are seen at the same time as the sound ‘ba’ is played. This effect demonstrates the brain’s unconscious ability to assimilate or make use of perceptual experience from the sensory information available.

Of interest to this study is how multisensory integration might influence movement. The primary senses involved in awareness of motion are visual and somatosensory/proprioceptive (Sober and Sabes, 2003). However, auditory information has been shown to influence tactile sensation (Jousmaki and Hari, 1998),

grasping (Sedda et al., 2011), movement judgement (Lagarde and Kelso, 2006) and motion detection (Sanabria et al., 2004). Such findings suggest that sound can be manipulated to effect motor behaviour for rehabilitation and a number of heuristics have been established for how this can best be achieved. One observation is that different sensory streams should be presented congruently so that information is understood to represent the same object/event. For example in auditory-visual interactions, the stimulus must have spatial and temporal coincidence to ensure cross-modal matching or multisensory integration (Calvert, Spence and Stein, 2004; Driver and Spence, 2000). However, for many patients receiving neurorehabilitation, actual movements and sensory stimuli will not have spatial and temporal coincidence (due to deficits in motor ability). Nevertheless, if stimuli are understood to represent movement (through instruction), other multisensory process can still be engaged (as in the McGurk Effect) until such a time as congruence can be achieved (through practice). A second observation, that can be used to initiate multisensory processes, is that available sensory streams are used in order of reliability. Sensory input is weighted with relevance to perceived experience, such that sensory input with low variability will be relied upon more than a stream that is less consistent (Ernst and Banks, 2002). This finding suggests that the introduction of a new but more reliable stream of sensory information can quickly become the primary source of sensory input.

### *2.5.1 Neurological underpinnings of multisensory processes*

Single cell recordings have been used to investigate multisensory processes. Studies have revealed neurons throughout the brain that fire *only* in the presence of cross-

modal stimulation (this finding has been expanded to include bi- and tri- sensory sensitive neurons) (Calvert, Spence and Stein, 2004). Multisensory neurons are identified throughout the sensory processing areas of the cortex. In a recent study, fMRI revealed that unitary sensory stimuli elicit distinct spatial patterns of neuronal activity, in both the related primary sensory cortex and other non-related sensory cortical areas (Liang et al., 2013). Multisensory neurons are known to aggregate in other brain regions including those recognised as important in motor control. For example Nagy et al. (2006), showed that multisensory neurons converge in the basal ganglia. A related area that has undergone intensive study is the superior colliculus (SC) (Perrault et al., 2005; Meredith and Stein, 1986). The SC has deep connections to the basal ganglia (Shires, Joshi and Basso, 2010) and up to 60% of its neurons display either additive or superadditive effects in response to multisensory input. The SC is located within the brainstem and has direct input from visual, auditory and somatosensory streams (Wallace, Meredith and Stein, 1993). The SC also projects to the cerebellum (via the pons) where its signal is modified and returned in a multisensory feedback loop (Matsuzaki and Kyuhou, 1997; Wallace, Meredith and Stein, 1993).

A specialised type of multisensory neuron has also been identified - the multisensory mirror-neuron. Mirror neurons discharge both when an action is performed and when that action is observed in others (Ferrari et al., 2003; Rizzolatti et al., 1996). In an experiment using macaque monkeys, it was shown that multisensory mirror cells in the F5 region of the premotor cortex, became active in response to both the visual and auditory aspects of the same action (Kohler et al., 2002). By tearing pieces of paper and dropping sticks, it was demonstrated how these neurons are activated by

hearing the sound of the action in isolation, seeing the action in isolation and both together. The significance of this finding is that it represents an ‘action recognition’ system in the brain that includes auditory and visual streams in an unsegregated form. Importantly for this thesis, these studies show that multisensory neurons converge in brain regions involved in the initiation, monitoring and prospective control of action. This reality reflects how movement control requires integration of proprioceptive, vestibular and visual streams. The presence of multisensory neurons in prospective-motor control areas of the brain (Forsythe, 2011), advocates that understanding multisensory processes is important for neurologic rehabilitation of movement disorders. The basis for this understanding should be that, as Paul Bach-y-Rita (1975, 2004) points out, all sensory input, once entered into the nervous system, takes the same form; patterns of pulses through neurons. It is reasonable to hypothesise therefore, that if a person has a sensory deficit leading to a specific behavioural outcome, relevant sensory information (i.e. that initiates the same patterns of pulses) in an alternate sensory modality could be used to re-learn and/or improve that condition.

### *2.5.2 Movement Sonification*

A question that emerges from the previous discussion is how to transform movement into sound? It is clear that all actions unfold through time and space so how can the spatio-temporal aspects of movement be represented within an auditory guide? One method is to use sonified movement (Effenberg, 2007; Berger and Kleiman-Weiner 2006; for a review see Hermann, Hunt and Neuhoff, 2011). Although a relatively new area of research, movement sonification takes the parameters of a particular

action, for example the increasing/decreasing spatial displacement of a person jumping, and transforms this into (for example) a rising/falling pitch tone. Through this process, an auditory 'mirroring' of the movement is created. Sonification has many disparate applications, for example it can be used to display data sets (Chemseddine and Noirhomme-Fraiture, 2008) but of particular interest to this study, is its use as biofeedback for helping athletes improve motor performance (Chollet, Madani and Micallef, 1992). These authors used pressure sensors to record forces acting on the hands, and accelerometers attached to the body to record speed. These parameters were transformed into an auditory signal to guide swimmers in the water. What is particularly useful about sonified movement is that the changing parameters of an action are mapped as it unfolds. In this respect, sonification includes the dynamics of a real-world action and represents temporal and spatial relationships (Effenberg, 2007). Sonified movement therefore, differs significantly from the rhythmic auditory cues discussed in the introduction to this chapter. Rhythmic sounds present sequential goals to entrain and couple actions to but contain no information about how to get there (or how the movement is proceeding). What sonification delivers is both a method of prospective guidance (i.e. goals) but also on-going information about movement progress. These dual types of auditory movement information mirror more closely the information normally available to the nervous system as an action is performed. Incorporated into sonified movement are an individual's own physical constraints. However, this is problematic where movement pathology is present as actions that are for example, jerky or poorly formed, would produce irregular sonification that would provide poor guidance. To

develop sonified movement guides for people with neurological disease then, would require guides that reflect how a person *should ideally* be moving.

## 2.6 Interim summary

So far this introduction has highlighted the relationship between auditory stimuli and movement. It has described a number of ways in which movement and sound are interrelated. It has been argued that the auditory system has evolved to integrate and decipher spatio-temporal information and is therefore an appropriate target for delivering additional sensory information to improve motor control. Aspects of sound that are relevant to understanding motion (i.e. modulating pitch) and are potentially, the most useful for using in rehabilitation have also been discussed. A remaining question is how to plot motion within sound? To answer this question motor control theory is discussed to explore what information is used to control action.

## 2.7 Motor control

The basis of controlling all movements is to first, select the correct sequence of muscle activation, and secondly to generate the correct levels of stimulation to bring the effector to the desired spatial position (Morris et al., 1994). There are several complex questions as to how animals achieve this and at present, there is no unified theory of motor-control. Movement requires that muscle activity is sequenced so that smooth coordination occurs between different component parts. Timing then is

essential to sequenced and coordinated action. However, neural conduction speeds are inherently slow in the nervous system<sup>8</sup> (Desmurget and Grafton, 2000) meaning that the possibility of using feedback information is limited. To move successfully then requires the motor system to produce a signal that includes a prediction of where the hand, foot etc. will be in the future. This also applies to control of movements that require interception of external moving objects (e.g. predation or ball catching). To be successful at these activities requires the mover to make predictions about arrival of both themselves and the object at a future point in space-time (i.e. the point of interception). It is a question therefore, how the nervous system anticipates and controls for future position, when sensory information regarding current position is already outdated by the time it reaches the brain. Of further interest to motor-control theorists is what exactly is being controlled? There are multiple sources of information available to the nervous system that could be used (for example, velocity or distance). It is a matter of debate however, whether the nervous system uses position and its derivatives to control movement (Lee, 2005). A further persistent topic for motor-control theorists is known as the ‘degrees of freedom problem’ (Bernstein, 1967) which is the recognition that due to the abundant joints, muscles, forces etc. involved in motor control, there are multiple ways a motor problem can be solved. So how does the nervous system select the appropriate movement pattern from the options available particularly as much of the information available will be redundant (Todorov and Jordan, 2002)? Given that muscles, tendons, joints, limbs etc. all have their own individual behavioural properties, this is

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<sup>8</sup> For example, it takes a minimum of 100 milliseconds for a visual stimulus to reach the motor regions of the brain and an appropriate response to be initiated (Schmolsky, 1998). In larger peripheral neurons, delays can be upwards of several hundred milliseconds (Lim and Choe, 2006).

a nontrivial task. A good place to start when trying to answer these questions is to introduce the work of the eminent neurophysiologist Nikolai Bernstein. Of primary importance, was Bernstein's recognition that organisms are active and goal seeking rather than passive receivers of information (that is then responded too) (Veresov, 2006). This observation extends beyond understanding movement and is important to psychology as a whole. A number of subsequent factors follow when activeness is introduced. To actively seek means the activity must be intended. Moving with intention requires a plan which can only be conceived before the action is initiated (i.e. it must be prospective) (Bernstein, 1967; Lee, 2005). Enacting movement plans requires monitoring of the action as it proceeds as well as perception (either internally or externally) of the intended goal. In other words movement is dependent on sensory information and is therefore fixed within an action-perception framework (action-perception is discussed further in 2.7.5) (Noë 2004). Bernstein (1967) argued that the brain must produce a 'motor image' which conveys all of the necessary information for the action (muscle contractions, force etc.) to the periphery *before* the movement is initiated. Through careful observation of people in motion Bernstein (1967) noted that;

*'There exist in the central nervous system exact formulae of movements or their engrams ...[that] contain in some form of brain trace the whole process of the movement in its entire course in time.'*

(p. 37)

Bernstein further understood that the 'exact formulae of movements' would necessarily include 'whole body' representation, as movement of an effector has consequences for how forces are experienced in remote parts of the body. To take a



step forward for example, has a profound effect core balance, so the person moving must know the *sensory consequences* of that step before it is taken. Bernstein proposed that the ‘motor image’ is organised around the movement goal (which must also be perceived) and inevitably be spatiotemporal (as *all movement* unfolds through space and time). To successfully complete a simple motor act then, requires intentional, anticipatory, goal-oriented, sensorimotor information (Bernstein 1967; Lee, 2005) meaning that movement is a complex of processes that are fundamental to psychic life. The importance of these factors is best explicated in the infant development literature. Theorists argue that, as motoricity precedes cognition, it is motor activity (or the predictive aspects of motor control) that develops a sense of agency and feelings of being ‘in’ the world that also extend to understanding the intentions of others thus laying the foundations of communication and socialization (Solms and Panksepp, 2012; Trevarthen, 2005; Llinás, 2002). This proposition is confirmed by the growing body of evidence that suggests prediction deficits in early infancy are a cause of learning problems such as autism (Sinha, 2014).

Bernstein’s ideas have greatly influenced the field of motor control and in the last forty years two prominent strands of theory have emerged: the ‘motor’ approach and the ‘action’ approach (Petrynski, 2007). The motor approach is a top-down theory, which suggests that movement is controlled through motor commands (motor programs) initiated in a sequential manner. The action approach on the other hand, proposes that movement is bottom-up and organises itself through coordinative self-assembled structures (dynamics) (Abernethy and Sparrow, 1992).

### 2.7.1 *Motor programs*

In 1951 Karl Lashley released a seminal paper that addressed the topic of serial ordering. This paper arrived at a time when behaviourism was dominant and the prevailing view was that movement occurs through a 'reflex chain'. This view, as the name suggests, postulates that movements are organised as a series of reflex actions where one component stimulates an adjacent component in an on-going cascade until a particular objective is achieved (Clower, 1998). However, Lashley observed a number of problems with this idea. One was the nerve conduction problem described earlier which disqualifies the idea that feedback can be used for the next part of a sequence in fast actions. Another issue was that movement is possible when sensory feedback is disrupted so how could the sequence continue when the chain is in effect broken? These problems led Lashley to conclude that movements must be hierarchically organised and that the nervous system must contain plans for action (Lashley, 1951). He put forward the idea that for any given motor problem, general plans are internally generated from which a specific plan (or motor program) could be selected.

With the advent of cognitivism in psychology, the idea of motor programs became part of information processing theory of brain function (i.e. information enters the nervous system, is processed and an appropriate response initiated). A motor program refers to a set of instructions stored in the brain that is selected and executed in response to a specific motor task (Morris et al., 1994). Within the set of instructions, it is proposed that all of the necessary information (i.e. timing, muscle torques, force etc.) for initiation and control of the action are stored. Motor programs solve a number of motor control related issues, such as how movements are timed

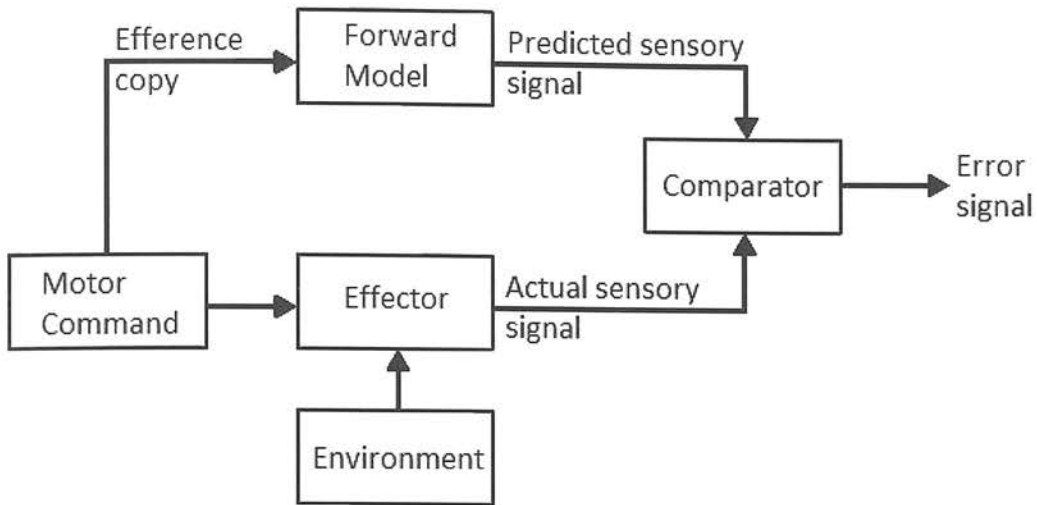
and sequenced. However, the concept of a motor program also introduces new problems, the most prominent of which is storage (Morris et al., 1994). The storage problem stems from the fact that in daily life there are so many situations requiring a motor solution, that it is implausible that an equivalent number of commands could be stored centrally. To tackle this problem, Schmidt (1975) proposed a hierarchical model that suggests two different classes of movement; one in which movements have invariant properties and another in which movements are modifiable (Schmidt, 1975; Schmidt and Lee, 2011). For example, if the word 'Schmidt' was written with the preferred hand, and then with the non-preferred hand, the letters in each word would appear different (have been modified) but would still spell 'Schmidt' (has invariant properties). Schmidt's theory proposes that there is a 'generalised motor program' (GMP) that remembers the forces, muscle synergies and timing properties of each letter (Schmidt and Lee, 2011; Phillips, Ogeil and Best, 2009). An actor therefore, need only modify amplitude to complete the task. Schmidt's model accounts for a large class of movement and drastically limits the number of motor programs needed to be stored in the brain. Evidence for GMPs (and motor programs in general) comes from experiments using animals and humans. Carter and Shapiro (1984) got participants to learn a sequence of wrist rotations and then once learnt, asked participants to perform the sequence as fast as possible. They found that individual wrist movement timings, stayed in ratio to the overall movement sequence at both speeds. They interpreted this result as evidence of an invariant set of instructions prescribing movement duration regardless of external conditions. Physiological experiments in cats and monkeys provide further support for GMPs. In both species, experimenters have severed the afferent nerves in the spinal cord so

that sensory information to the body is absent (Grillner, 1981; Taube and Berman, 1968). In these experiments, controlled motor behaviour in the animals was still observed suggesting movement is under central control and is not reliant on external information. However, this finding is debated and there are clear examples where movement uses input from the environment. For example, the same activation pattern (motor signal) to the muscles of the elbow, results in different behavioural outcomes if the elbow's initial position is varied. If the arm is at the side of the body, elbow flexion causes the forearm to move upwards, if the arm is held out to the front, the forearm moves in a planar motion (Shumway-Cook and Woollacott, 2007). In this example, it is clear that external factors influence the control of the movement as much as the motor signal.

### *2.7.2 Internal models*

A common problem in motor control is how the nervous system distinguishes between self-generated and external information. An example of why this may be problematic is to think of movements of the eyeball. When the eye moves, the visual image moves across the retina in much the same way as an object within the visual image would if it were moving. It can be seen how an inability to distinguish between these two sources of sensory information would cause major problems for perception and movement. To solve this issue, early motor theorists proposed that a copy of the motor commands (called the efference copy) is created which can then be used to compare the sensory signals generated from self-actions. This is known as refference (von Holst 1954). A related idea is that of corollary discharge proposed by Sperry (1950). This was the suggestion that the efference copy is inhibitive and

integrated into the nervous system to cancel out the effects of reafference. The concepts of efference and corollary discharge have been used to explain why people cannot tickle themselves (Blakemore, Wolpert and Frith, 1998), can understand their own speech acts in noisy rooms (Hickok et al., 2011) and it has also been implicated in schizophrenia (Ford et al., 2012). Efference and corollary discharge are also integral to motor control and the concept of internal models (Kawato, 1999; Desmurget and Grafton, 2000; Wolpert and Kawato, 1998; Morton and Bastian, 2006). Internal models are described as ‘a system which mimics the behaviour of a natural process’ (Wolpert and Kawato, 1998, p.1318). A natural process when performing a motor act would have to recognise that the dynamics of an effector (e.g. the arm), and the conditions within which it is acting, differ depending on context. Motor commands therefore, need to account for both internal and external constraints. To achieve this, two variants of the internal model have been proposed; forward and inverse models (Desmurget and Grafton, 2000; Wolpert, Miall and Kawato, 1998). As the name suggests, forward models make predictions about where a particular effector (the hand for example) will be at a future moment (i.e. its position and velocity) from the current state of the system and the motor command. In doing so, the forward model encapsulates the input and output of the system (Desmurget and Grafton, 2000). The efference copy of the motor commands is a prediction of the sensory consequences of the planned movement. Using the efference copy, actual and predicted movement can be compared and an error signal established from which adjustments in trajectory or subsequent movement can be made (see Figure 1.1).



**Figure 1.1** Schematic diagram of a forward model showing error signal generation from comparison between actual and predicted sensory signals.

It has been argued that motor commands take the form of an inverse model (Wolpert, and Kawato, 1998). Here the concept of a forward model is reversed and instead of the motor command being formed in an exploratory (predictive) fashion, the inverse model generates commands based on the desired final state of the effector. Wolpert and Kawato (1998), suggest that forward and inverse models act collaboratively and become paired through learning. In this model, the predictive aspects of the forward model, directly contribute to the inverse model's motor command output. A feature of internal models is that they emphasise the importance of predictive information in controlling action. However, it is still not clear what information is used to inform these predictions (Bastian, 2006).

### *2.7.3 Dynamical systems theory*

Movement is the product of actor-environment interaction (Lee, 2005). In recognition of this reality, a different way of looking at how the motor system

controls movement was developed within the context of actor-environment coupling (Kelso, 1997). Dynamical systems theory was traditionally used to describe patterns in a range of phenomena in the natural world, from cloud formations to river flows (Thelen and Smith, 2006). The theory argues that action is constrained by three factors: the task (what is to be achieved), internal physical properties (i.e. the musculoskeletal system) and external (environmental) factors (Newell, 1986). From the interaction of these factors it is proposed that the system self-organises into ‘attractor states’. Attractor states remain stable until perturbed through motion, and a new resting state configuration is needed (Haken, Kelso and Bunz, 1985). Self-organisation of attractor states is a central tenet of the dynamical systems approach to motor control which *ipso facto* abrogates the need for motor programs (Kugler and Turvey 1987; Kelso, 1997). As Shumway-Cook and Woollacott (2007) note:

*“...when a system of individual parts comes together its elements behave collectively in an ordered way. There is no need for a “higher” center issuing instructions or commands in order to achieve coordinated action.”*

(p. 14)

An example of how ‘individual parts behave collectively’ can be seen in the transition from walking to running in horses. At a certain speed, the horse begins to trot (from a walk) and a corresponding change in the pattern of its leg movements is seen (i.e. the horse always has two feet on the ground (diagonal pair) when trotting and always three feet on the ground when walking). What is important here is that it is the reaching of a critical speed that acts as the control parameter that causes the change from walk to trot, not an instruction from the brain. Physiological experiments support dynamical systems theory. In an experiment using monkeys,

Polit and Bizzi (1979) trained the animals to point towards different cues after which their arms were completely deafferented. It was found that following the surgery, the monkeys still managed to point towards the cues indicating that the musculature stabilises the arm trajectory without afferent control. In humans, a series of experiments by Feldman et al. (1998) identified attractor states in operation. By sudden loading or unloading a weight on the hand, they showed that the arm naturally finds an ‘equilibrium point’ that reflects the ideal torque and joint angle for each load. They proposed that the nervous system does this by setting a threshold level (or length) for each muscle. If that threshold is exceeded by the constraints placed upon it, the nervous system needs to recruit further motor units for that muscle. This became known as the ‘equilibrium point hypothesis’ (Feldman and Levin, 2009). Since these experiments, it has been shown that due to their spring like and elastic properties, muscles organise themselves to a preferred length (Lehart, Pincivero and Rozzi, 1998). This organisation can be thought of as a resting state for the musculature that underpins the ‘natural’ configuration of the body.

Dynamical systems theory has been very influential in describing how actions are controlled. In doing so, the approach uses two equations: the next-state equation and the output equation (Jordan, 1996). The next-state equation describes how state changes as a function of the current state  $x[n]$  and the input  $u[n]$ :

$$x[n + 1] = f(x[n], u[n]) \quad (\text{Equation 2.1})$$

where  $n$  is the time period.

The output equation specifies how the output  $y[n]$  is obtained from the current state:



$$y[n] = g(x[n]) \quad (\text{Equation 2.2})$$

Equation 2.1 is dependent on input to the system which will typically consist of multiple variables. For instance, to understand the dynamics of the leg in the horse example, knowledge of joint angles, muscle torques, inertia, velocity etc. of the leg and other body parts would be necessary. Whilst this is a powerful way to describe the movement of a system, in terms of plotting sounds to guide action it is not obvious how dynamic equations may be of use.

#### *2.7.4 Information for motor control*

The basis for discussing motor control theory here is to identify a way to plot movement as sound. However, in the two theories presented thus far, both use measures such as position and its time derivatives as control variables in their computation. As mentioned however, it is still debated whether or not these measures are sensed by the nervous system (Lee, 2005). Nevertheless there is evidence that these kinematics are represented at the neural level. For example, imaging studies have demonstrated there are neurons that become active in response to acceleration, speed and distance cues (Cao, Gu and Wang, 2004, Tan et al., 2009, Ebner, 2009). Similarly, linear and angular accelerations initiate responses in the neural pathways of the vestibular system (Day and Fitzpatrick, 2005). However, it is still not clear if these responses are indicative of identification or signify that these variables are being used in a control strategy. A further issue with using kinematic variables for control is that it seems unlikely that the nervous system operates in miles per hour or millimetres (Lee, 2005; Gibson, 1979/86). An obvious problem for such a hypothesis

is that values could potentially be limitless, for example, how fast should a hand be extended to pick up a cup? Using position, force etc., also introduces the necessity of mental calculation (Gibson, 1979/86). Given that many movements are rapid and that there are small time windows available for adjustments, further processing would be a hindrance in controlling action.

### *2.7.5 Ecological perception*

The previous discussion raises the question of what other information could be used to control movement. One possibility is that in many instances, information available within the environment is satisfactory for motor control.

In the 1960s, James Gibson presented a new way of thinking about perception based mainly on observations of light and vision (Gibson, 1966). Gibson argued that perceiving and acting constrain one another, or in other words, that perceptual information becomes available through action, and action is controlled through perception (Gibson, 1979/86; Rookes and Willson, 2000). This hypothesis challenged standard theories of perception at the time, which assumed the external world was constructed through mental representation. The mental representation view of the world, posited that perceptual information is meaningless until given significance through cognition (Fajen, Riley and Turvey, 2008; Rookes and Willson, 2000). In opposition to this idea, Gibson proposed that many properties of the environment could be understood without cognitive processing or rather, could be directly perceived. Direct perception implies a world perceived as it is, rather than constructed from memories and/or experience, and frames the perceiver within an

action-perception interaction. This affords new possibilities for knowledge of the world as Gibson (1979/86) noted:

*"If what we perceived were the entities of physics and mathematics, meanings would have to be imposed on them. But if what we perceive are the entities of environmental science, their meanings can be discovered."*

(p.33)

However, direct perception remains a controversial topic. It has been argued that if the world is directly perceived, visual illusions, such as Mach's well-known motion perception illusion, should not occur (Ullman, 1980). It has also been suggested that direct perception is contradicted by the incontrovertible fact that in many cases, tool use is learnt within a social context (Neisser, 1994). However, it is also incontrovertible that there are invariant features within the perceiver-environment interaction. Examples are characteristics like the horizon ratio (i.e. objects are intersected by the horizon at eye-height above the ground), directly stipulating object size relative to the observer, and texture gradients specifying depth (Rookes and Willson, 2000). When walking or sprinting towards an object for example, to the observer the expansion rate of the object's size remains proportional to the rate at which the actor is moving. In this example, the relative movement between the observer and environment causes objects to appear to move. This phenomenon has been termed 'optic flow' (Gibson, 1979/86; Lee, 1980) and is one way in which the relationship between an organism and the environment is specified. Invariance within optic flow scales an observer's action possibilities in the external world. For example, the distance to the other side of the road might be understood in terms of stride lengths (Warren, 2007). That flow patterns in the visual stimulus denote

possibilities for action is known as *affordance* and the concept extends to the properties of objects. Affordances can be thought of as structural information within the environment that influences how motor behaviour is performed (Warren, 2007) so for example, when reaching for an object, initiation, travel and the end-goal of the reach are influenced by the ‘fit’ between the actor and the task environment (Ishak, Adolph and Lin, 2008; Smith and Pepping, 2010; Sartori, Straulino and Castiello, 2011). Gravitational effects are also incorporated into action possibilities in the environment. As gravity on Earth is constant, it has been suggested that animals sense this and plan actions accordingly (McIntyre et al., 2001).

So far this discussion mostly relates to invariant properties within the visual stimulus, but as has already been mentioned, there are also invariant characteristics of the auditory scene (Gaver 1983). Given the multisensory nature of perceptual information, this is perhaps unsurprising. However, as vision is known to influence how many movements are executed, and is central to interceptive actions, invariant guiding information within the optic flow field would be a useful component to guide actions in the auditory domain. The question remains, what is the invariant guiding information in the visual domain that can be transformed into sound? To explore this possibility further, tau theory (Lee, 2005) is discussed.

## 2.8 Tau theory

### 2.8.1 Tau introduction

In experimental work on the optic control of braking, Lee (1976) showed how the inverse of the rate of dilation of any two points on the surface of the object in front

(e.g., a car or a wall), specifies the time-to-contact (at a constant travelling speed) of that object. Lee named this variable *tau* ( $\tau$ ) and it is defined as *time-to-contact at current closure rate*. Through sensing the rate of change, it has been argued that this single variable is all that is needed to adequately control movement (i.e. the tau-dot hypothesis) (Lee, 1976; 2005; 2009; Yilmaz and Warren, 1995). Tau is the ratio of the current distance-to-goal over the current instantaneous speed and can be expressed symbolically as:

$$\tau(x,t) = x(t)/\dot{x}(t) \quad (\text{Equation 2.3})$$

where  $x(t)$  is the distance to the goal at time  $(t)$  and  $\dot{x}(t)$  is the rate of change of  $x$ .

Sensing action goals are central to tau theory. Once a goal is identified a ‘gap’ between effector and goal can be defined. Lee argues that successful, well-ordered movement involves controlling the closure of these gaps (termed ‘action gaps’) (Lee, 2005; 2009). An example of an action gap is found in braking manoeuvres. The gap is clearly specified, and a number of studies have shown that keeping the  $\tau$  of the gap constant is a successful strategy for controlling the closure of the gap (Hopkins et al., 2004; Yilmaz and Warren, 1995; Lee, 1976).

Tau has several important characteristics. One is that tau is a temporal measure meaning that it can be sensed in any modality. This has been demonstrated experimentally in reaching movements, where the use of the tau-dot strategy has been evidenced in the proprioceptive domain following visual manipulations of the target (Hopkins et al., 2004). Similarly it is suggested that humans are sensitive to the tau of a pitch modulating between two notes (Schogler, Pepping and Lee, 2008). A

further characteristic of the tau variable is that, in line with its ecological underpinnings, it is a first order estimate that can be directly perceived. In this respect, if tau is used to guide movement, measures of speed, acceleration and distance, become unnecessary for control. Tau has proven to be a remarkably robust concept. Its use has been supported experimentally in many different species and situations. Spatio-temporal analyses of bats and pigeons landing on perches, hummingbirds docking at a flower, and landings in flight simulators, all suggest the use of the optic variable tau (Lee, 2005; Lee, Reddish and Rand, 1991; Padfield, Lu and Jump, 2012). However, some doubts have been raised as to what degree tau is used to control actions (e.g. Rock, Harris and Yates, 2006; DeLucia, 2005). These studies suggest that other information both internally (i.e. knowledge) and within the environment is used to control movement. DeLucia (2005) for example, showed that previous knowledge of the size of an approaching ball, affects time-to-contact judgements. Nevertheless, these investigations do not suggest that tau information is not also available and/or used in motor control. Imaging studies support the hypothesis that tau is a well understood property of the environment. Magnetoencephalography (MEG) in humans demonstrated that twenty two percent of neurons in the right parietal cortex (and associated regions) respond directly to tau information (Tan et al., 2009). Looming sensitive neurons have also been identified in non-humans. Single cell recordings in the nucleus rotundus of the pigeon (Wang and Frost, 1992) and more recently in cats (Liu et al., 2011), identified neurons that respond to looming stimuli. These findings imply that looming (or tau-sensitive) neurons are common across species. However, like other brain imaging studies it is still not clear if tau sensitive neurons are active in response to identification of tau

information or used in a control strategy. Further investigations suggest the latter hypothesis is more likely. Wu et al. (2005) demonstrated that a percentage of tau-neurons are sensitive only to time-to-collision information, whereas others are involved in initiating avoidance behaviour. The existence of neurons that instigate evasive responses is physiological evidence for Lee's earlier proposition that there are critical values within the optic array that once reached illicit a behavioural response (Lee and Reddish, 1981). Similarly, the finding provides evidence for the observation that expanding visual objects elicit avoidance behaviour in babies as young as two to four months (Kay and van der Meer, 2000).

The discussion of tau so far has related only to how single gaps are sensed and controlled. Of course a large class of actions require sensing and monitoring of multiple gaps (for example interceptive actions). To explore how this might be achieved, tau theory was expanded to include how movement might be controlled when two gaps need to be coordinated.

### *2.8.2 External tau-coupling*

External tau-coupling describes how coordination is achieved when intercepting an object that is in motion. Lee proposed that to do so entails sensing the taus of two gaps (Lee, 1998). For example, when kicking a moving football, the space between where the ball is at the present moment, and the point where the actor intends to intercept it, is one gap (a motion-gap). The peak of the kicking leg's backswing, to the same intended point of interception, is a second gap. The external (ball) motion-gap and the self-generated (foot) gap, both need to be perceived and monitored by the nervous system. Predictive information must also be extracted from the ball and

supplied to the foot (i.e. an estimate of where the ball will be at a future point in time). To successfully make contact with the ball requires that the taus of both gaps remain in constant ratio, so that both close and reach zero simultaneously thus resulting in a successful interception (Lee et al., 2001). The equation for tau-coupling is;

$$\tau_y = k\tau_x \quad (\text{Equation 2.4})$$

where  $\tau_y$  and  $\tau_x$  equal the time to closure of each gap (x and y respectively) and k is the coupling constant.

### 2.8.3 *TauG*

The idea of tau-coupling was expanded further to include movements where there is little external information available for coupling. When reaching for a stationary cup for example, there is no motion gap provided by the cup to couple the tau of the hand to. Despite this, in the absence of pathology, movements are still well formed and controlled. Lee proposed that the nervous system achieves this by generating an internal tau guide ( $\tau_G$ ). To complete a movement, the actor couples their action onto the internal guide (i.e. they  $\tau$ -guide the movement) (Lee, 2005). The internal guide has been characterised as ‘a patterned energy flow’ in the nervous system. In endeavouring to mathematically formulate the intrinsic guide, Lee (2005) speculated that any intrinsic guide would include recognition of the Earth’s gravitational influence as an evolutionary constant (and thus be an internalised factor). The guide was therefore derived from the movement pattern of a bouncing ball travelling from



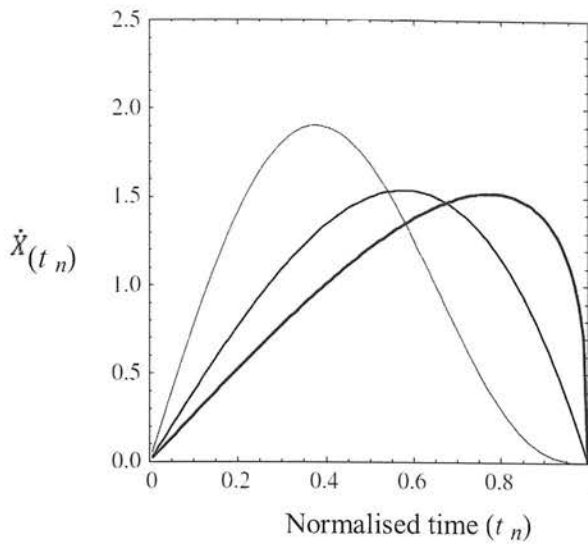
the ground to its zenith and back again to the ground. Basing the guide on Newton's equations for motion the  $\tau_G$ -guide follows the formula:

$$\tau_G = \frac{1}{2}(t - T_G^2 / t) \quad (\text{Equation 2.5})$$

where  $T_G$  is the duration of the movement and time,  $t$ , equals zero at movement start and  $T_G$  at movement end. In this special case of tau-coupling, the closure of the self-generated action and tau-guide are kept in constant ratio so that both close simultaneously and reach zero at the same time. This is expressed symbolically as:

$$\tau_x = k\tau_G \quad (\text{Equation 2.6})$$

Where  $\tau_x$  is the tau of the movement,  $k$  is the coupling constant and  $\tau_G$  is the intrinsic guide. The coupling constant  $k$  is important in tau theory. The value denotes the acceleration and deceleration profile of an effector as it moves from start to goal. Low values of  $k$  ( $0 < k < 0.5$ ) result in longer periods of deceleration and a gentle arrival. High values of  $k$  ( $0.5 < k < 1$ ) indicate shorter periods of deceleration and greater velocity at arrival (Lee, 2005). If  $k$  values equal or exceed 1 it means that the effector is still accelerating at the goal (i.e. a collision has taken place). If  $k$  values equal or exceed 1, it means that the effector is still accelerating at the goal (i.e. a collision takes place) (see Figure 2.2).



**Figure 2.2** The effect of varying  $k$  on the speed of closure of gap  $X$ . Different  $k$ -values are denoted by the thickness of the lines.  $k=0.25$  thin,  $k=0.5$  medium,  $k=0.7$  thick. Adapted from Schogler, Pepping and Lee, 2008.

Experiments have shown that human movements appear  $\tau_G$ -coupled under a number of different conditions. New-born babies suckling and musicians performing are both examples (Craig and Lee, 1999; Schogler, Pepping and Lee, 2008). With regards to motor control theory, the internal  $\tau_G$ -guide appears to be very similar to an internal forward-model. However, the  $\tau_G$ -guide differs in a few crucial respects. Firstly, the  $\tau_G$ -guide does not use position or its derivatives as a control variable and secondly, the  $\tau_G$ -guide is not a set of instructions, executed sequentially *per se* (i.e. a mental representation) but rather an ecological construct that interfaces between the intrinsic and extrinsic world.

There are a number of outstanding questions regarding the veracity of the  $\tau_G$ -hypothesis (Lee, 2009). For example, that there is a one-to-one relationship between patterns of neural firing and movement form is contentious. As the physiologist Nicolai Bernstein pointed out ‘an unequivocal relationship between impulses and movement does not and cannot exist’ (in Whiting, 1984, p.82). There are also questions regarding what form the tau-guide would take in the nervous system (i.e.

the ‘ $\tau_G$ -pattern’ is loosely defined and appears to include any entity moving under the influence of gravity). The suitability of using the  $\tau_G$ -equation to assess complex movement behaviour is also questionable (this topic is discussed further in Chapter 5). However, these concerns are not the focus of this thesis. The aim of this discussion is to identify a variable that could be used for developing sounds for movement guidance and it is here where one aspect of  $\tau_G$  is useful. As the  $\tau_G$ -equation models a hypothesised internal tau-guide, by default it also models how the tau of an effector moving towards its goal would change (the theory predicts that there is a one to one relationship between internal guide and movement pattern). It is possible therefore, to create an instruction within a guide of how to ‘ideally move’ by modifying the  $k$  value (as desired) and specifying movement duration using this equation.

#### *2.8.4 Why auditory guides were based on tau*

There are many ways in which movement can be transformed into sound (e.g. the sonification described above). However, tau is used in this study for a number of reasons. Tau is an invariant property of perceiving and acting and its use to guide movement has been demonstrated in many real-world situations. This implies that sounds based on this variable will be more ecologically valid than other measures. In addition, as tau appears to be an evolved property of organism-environment interactions, exposure to tau information will not be novel. This increases the possibility of understanding sonic-guides as movement. As argued earlier, it is likely that listeners will have already been exposed to auditory-tau information in some capacity (e.g. auditory looming). This fact makes understanding the concept of

auditory-tau for self-generated movement less challenging. That tau denotes spatio-temporal relationships also makes auditory guides more ecologically meaningful as all actions unfold in time and space. Importantly, the way in which tau modulates within the sounds will clearly define goals (i.e. sound termination). By sensing the goal through the rate of change, tau also affords opportunities for the perceiver to move (i.e. in time and space). In addition, at any given moment, guides reference the goal meaning information about how the movement is proceeding can be extracted. A final important reason why tau is used in this study is its potential for increasing multisensory processes. As has been mentioned above, the ecological validity and spatio-temporal properties of the guides suggest tau-based sonic information will quickly be recognised as task relevant and activate the multisensory brain areas involved in motor control.

## 2.9 Motor control summary

This section has given a summary of the major approaches and issues in motor control theory. In doing so, the discussion has identified the most appropriate variable (tau) to be used to transform movement into sound. To do so, a pitch sound will be modulated using the  $\tau_G$ -equation. The next stage of this thesis is to test whether the tau information embedded in these pitch glides can be sensed and used to guide movement.

# Chapter 3 - Experiment 1: Using On-going, Dynamic Sonic Guides to Influence Reaching

## 3.1 Introduction

In the last chapter, ideas regarding the relationship between sound and movement were introduced. Mechanisms through which the auditory system understands motion, and how these might be exploited to deliver additional sensory information were discussed. Notions around which aspects of the auditory array are ideal for conveying movement, as well as which motor control variable could best be used to plot sounds for guidance, were put forward. It was argued that tau (as described by Lee and Reddish, 1981), due to its availability to the nervous system and simple computation, is an ideal way of developing rehabilitative sounds. In addition, as a consequence of its distinctive neural processing in the brain, pitch was identified as an effectual way to convey tau information for movement simulation. The aim of the first experiment is to implement this discussion to produce sonic guides that can influence how movement is executed. To do this, auditory guides conveying motion will be created to augment sensory information for motor coordination. An open question in establishing the sonic guides is whether or not sounds can be developed that deliver guiding information over the course of a complete action (i.e. provide continuous online feedback). By making on-going information available, guides

attempt to replicate the dynamics of a well-executed movement within the sound. An additional question is whether sounds can inform listeners as to when guides will terminate ahead of time (i.e. can they also contain prospective information?). As previously mentioned, theories of direct perception suggest the rate at which invariant information changes specifies time-to-contact. It is the dynamics of the auditory stimuli therefore, that offer perspective guidance. The experiment then explores the feasibility of on-going and prospective sonic guides. This topic is important as, whilst there are plenty of studies using prospective auditory stimuli (for example rhythmic cues), the literature is sparse when it comes to coordinating movement to on-going and dynamic, external auditory stimuli.<sup>9</sup> Further still, almost nothing is known about synchronising movements to sounds based on a variable used in guiding motor acts in everyday situations. To the knowledge of the author there are no studies that use external auditory stimuli based on biological motion for rehabilitation purposes.

To test the possibility of on-going and dynamic auditory guides, rising pitch sounds were manipulated to simulate the changing tau margin for the gap of a simple reaching action. Reaching was used due to its relative simplicity (i.e. an action well practiced in daily life and with fewer degrees of freedom than whole body movements). To explore if tau information embedded in the guides is picked up and used by listeners, differing values of the tau constant  $k$  were embedded within each

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<sup>9</sup> External auditory cues are as opposed to self-generated cues such as biofeedback studies (see Dozza et al., 2007) or auditory imagery cues explored in other psychological experiments (for example, see Keller, Dalla Bella and Koch, 2010). The topic of auditory imagery is returned to in section 5.3.

sound. Changing the value of  $k$  alters the steepness of how the pitch rises (see previous chapter). The manipulation of  $k$  is intended to affect changes in the position of the peak velocity of the reach as well as affect arrival times and movement velocities. To this end, responses to  $k$  are an indicator of to what degree movement behaviour is influenced by the sonic guides.

### 3.1.1 *Reaching*

Reaching is an essential skill central to many different tasks from making tea to boxing. There are a number of invariant characteristics to reaching behaviour that remain stable across individuals and a range of alternate situations (for an excellent review of reaching behaviour, see Shadmehr and Wise, 2005). When reaching for different objects or objects at alternate distances, relative timing of movement execution remains consistent, i.e. the unfolding of shoulder, elbow, and wrist, follows a scaled but distinct pattern (Soechting and Lacquaniti, 1981, Georgopoulos, Kalaska and Massey, 1981). Furthermore, in point-to-point reaches, the end effector (the hand) typically displays a linear pathway between initial and target position<sup>10</sup> (Bizzi, 1981) and a smooth symmetrical bell-shaped velocity profile (Abend, Bizzi, and Morasso, 1982). In addition, similar peak velocities are also recorded (Prasad et al., 2006). These factors are considered invariant characteristics of reaching actions independent of speed, duration and range of motion and are known as the scaling effect (Zhang and Chaffin, 1999). Underlying reaching invariance are stereotyped patterns of agonist and antagonist muscle activity (Gottlieb, 1998). Studies using electromyographic (EMG) recordings show initial bursts of agonist muscle (assumed

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<sup>10</sup> In three dimensional Cartesian coordinates.

to accelerate the limb), followed by bursts of antagonist muscle (thought to be responsible for controlling approach). A final burst of agonist muscle is expressed as the limb is brought to rest. Christou et al. (2007) suggest this final activity controls oscillations of the hand as the movement terminates.

Movement can be described as either ballistic or non-ballistic with ballistic actions typically being very rapid. Due to delays in neural transmission speeds,<sup>11</sup> feedback information cannot be relayed to the brain in time for appropriate adaptations to be made during movement execution. For this reason, it has been argued that ballistic actions cannot be under (closed-loop) sensory control (Gan and Hoffman, 1988). However, there is no velocity threshold that deems one movement ballistic and another non-ballistic with some questioning the notion altogether. Saccadic eye movements for instance, are very rapid and have been held up as the classic example of a ballistic motion. Nevertheless, it has been amply demonstrated that saccades undergo sensory adjustment even after initiation of ocular muscle contraction (Pélisson et al., 2010). Rapid movements in larger parts of the body can also be adapted after an action has started. Professional table-tennis players for example, have been shown to correct forehand drives after movement initiation (Bootsma and van Wieringen, 1990). The average duration for forehand drives in the study was less than 200 milliseconds. That such ‘ballistic’ actions are alterable supports the idea all movement is under some form of sensory control (Lee, 2005), although the idea remains controversial. What is clear however, is that movements of longer duration

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<sup>11</sup> For example, conduction speed through the nervous system from onset of a visual stimulus to a motor response is in the range of 100 to upwards of 500 milliseconds. Lim and Choe (2006) highlight the problem of these conduction speeds by calculating an object travelling at 40 mph would pass nine meters in the 500 milliseconds it would take for the neural signal to result in an appropriate response.



are open to adjustment through feedback mechanisms (neuronal delay is not an issue at greater durations). An interesting aspect of longer duration movements is that typically similar patterns of kinematic invariance are found (Shadmehr and Wise, 2005).

Despite the seemingly similar behaviour across all reaches, kinematics can be altered in a number of situations. Direction for example, is known to influence reaching trajectory. Desmurget et al. 1999 showed trajectories are significantly curved in unrestrained movements. Similarly, reach kinematics are altered when reaching in the vertical plane, either up or down (Atkeson and Hollerbach, 1985). In grasping reaches, bell-shaped velocity profiles are skewed with increased periods of deceleration (Marteniuk et al., 1987). The amount of skew is a function of both the size and fragility of the object being grasped meaning that a longer deceleration phase reflects the degree of complexity involved in the task. Related to this phenomenon is Fitt's law (or the speed/accuracy trade off) (Shumway-Cook and Woolacott, 2007). When reaching for a target, movement time variability is dependent on the distance and/or size of the object (Plamondon and Alimi 1997; Medina, Jax and Coslett, 2009). As task complexity increases, movement speed decreases. Similarly, arrival times at a target become more variable with increased task difficulty (Dean, Wu and Maloney, 2007). However, despite the fact that aspects of reaching are variable under certain conditions, invariant characteristics remain when reaching repeatedly for the same object in the same position. Additionally, with practice reach kinematics become increasingly stereotyped as the action is progressively automatised (Darling, Cole and Abbs, 1988). In the present study, start and target position remain stable for each reach and target size does not change. The

task is also well practiced and is relatively uncomplicated (participants reach for the target forty times and are not asked to grasp the target, which is neither small nor fragile).<sup>12</sup> Under normal conditions (i.e. if participants reached for a target without auditory guidance), it would be expected that a symmetrical bell-shaped velocity profile and straight-line trajectory would be recorded across reaches. The object of this experiment is to influence these stereotyped actions in a manner dictated by the auditory guides. Durations of the reaching actions (as specified by sonic guides) were such that reaching could be executed at a moderate velocity (the slowest guide was 0.8 seconds and the fastest 1.2 seconds). These durations should allow for the possibility of sensory feedback to influence reaches and for adjustments to be made.

## 3.2 Using auditory stimuli to guide action

As mentioned earlier, exactly how motor acts are synchronised with auditory information is not fully understood (Lagarde and Kelso, 2006). However, where auditory feedback is made available to guide movement, it is clear the task becomes easier. There are a number of ways in which auditory stimuli can be presented.

### 3.2.1 *Closed-loop auditory bio-feedback*

One of the best-known ways auditory information is used in rehabilitation is through closed-loop feedback scenarios where a person's movement produces a monitorable auditory output. Research into (auditory) sensorimotor integration is most commonly

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<sup>12</sup> The target is a water bottle top approximately 2.5w x 1.5h centimetres glued to the table. A full description of the experimental design is in section 3.2.5.

explored using vocalisations. Error correction has been studied based on feedback models that rely on the nervous system being able to predict sensory outcomes (by comparing output with an internal model of the expected) (Wolpert and Kawato, 1998). Support for feedback/internal models being used in auditory-motor transformations, comes from studies using delayed auditory feedback (DAF) which show that if self-generated vocalisations reach the ears with delay, speech is disrupted (Hickok et al., 2011; Finney and Warren, 2002). In such examples, articulations are slow, lack fluidity and often the rate of vowel pronunciation is variable. The conclusion from these studies is that a discrepancy between the internal model and expected sensory outcome (what is heard) causes confusion and leads to disturbed vocal output. Vocalisation experiments reveal the potential for auditory information to guide movement (in this instance, movement of the vocal cords). However, vocalisation control requires small, precise motor actions and the vocal apparatus is located internally. How then does sensorimotor integration occur in closed loop situations with gross motor actions and external objects?

The most revealing line of enquiry in this regard comes from the literature on learning and playing musical instruments which has shown the centrality of auditory feedback in developing a musician's motor skill (Pfordresher, 2006). If auditory feedback is blocked from skilled pianists (whilst playing ability is unimpaired), elements of the expressive features of performance are missing or disturbed (Repp, 1999; Pfordresher and Kulpa, 2011). Moreover, if auditory feedback is manipulated in a similar way to the DAF studies mentioned above, significant changes in motor response occur. Motor initiation delays are the most prominent of these leading to

profound effects on timing within musical performance (Pfordresher and Palmer, 2002).

That auditory information affects motor behaviour in closed loop scenarios has not gone unnoticed in efforts to rehabilitate people with motor problems. Various methods are used such as transforming a patient's electromyographic (EMG) or electroencephalogram (EEG) output into auditory cues (Wolf, 1983) for closed loop guidance. In these examples the muscle or brain activity underlying a person's motion can be directly 'heard' and movement behaviour adjusted in response (Dursun et al., 2004). An issue with this type of approach is that the necessary equipment is expensive and highly specialised. It is not generally available at home, or indeed in many rehabilitation settings, meaning many potential beneficiaries are excluded through lack of access. Various research teams have addressed this concern with a focus on less cumbersome methods of closed-loop auditory feedback for guidance. Dozza et al. (2007) for example, developed devices containing accelerometers which produce auditory feedback in the form of a tone. After being attached to the body, the generated biofeedback devices significantly reduced postural sway in quiet stance for people with vestibular disorders. In a similar manner, pressure sensors placed on the heel of the foot, improve walking posture in people with spastic diplegia (Kassover et al., 2005).<sup>13</sup> Such studies demonstrate the potential of closed-loop auditory feedback techniques for rehabilitation and the benefits to ataxia are a possibility that also deserves attention. However, self-generated auditory stimuli techniques have crucial limitations in neurological

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<sup>13</sup> The pressure sensors triggered a constant auditory cue in response to the correct foot placement on the floor.

rehabilitation. Some of the muscle activity or aberrant movement trajectories created from self-generated actions would cause the resultant auditory stimuli to be noisy and/or confusing. Beyond this issue, the focus of self-generated stimuli is directed towards how participants *are* performing rather than how they *should be* performing. A problem with this approach is that it is not clear if the comparator (what should ideally be happening) is available to participants<sup>14</sup>. In this regard, self-generated bio-feedback mechanisms may actually create more difficulties when following auditory cues than not. As Ying et al. (2011) note with regards to using EEG signals for ataxic movement;

*“EEG mapping may be distorted in the setting of neurologic disease, which may affect the ability of ataxia patients to use EEG-based BCI (brain computer interfaces)”*

(p.192)

An answer to this problem would be to not use self-generated sounds but instead, use external sounds containing instruction for the listener about how to ideally move.

### 3.2.2 Open-looped auditory guidance.

The studies discussed so far, all relate to self-generated auditory feedback requiring the actor's motion to produce the sound for action guidance (i.e., closed-loop feedback models). What is less understood, are the fundamentals of sensorimotor synchronisation with external auditory stimuli such as in dancing. Here movement is coupled to rhythm but the music gives no feedback as to how well a movement is

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<sup>14</sup> Unavailability could occur for numerous reasons. Damage to the sensory systems, muscular dystrophy or congenital disorders of the motor system are examples.

being performed. To couple to external sounds in this way is an example of open-looped auditory guidance.

Most of the research on coordination with external auditory events comes from the literature on finger tapping. This research has repeatedly demonstrated humans are very skilled at coordinating finger placements with rhythmic stimuli (Repp, 2005; Repp and Doggett, 2007). Coordination of finger taps relies on predictive information about ‘what is coming next’. It has been demonstrated that the predictive aspect of rhythmic cues is generated by the specifics of the interval ratio (Sakai, Hikosaka and Nakamura, 2004). Evidence of predictive behaviour is that taps consistently arrive early in relation to the beat. This is known as negative asynchrony, where arrival times can be as much as 80 milliseconds before the beat (Aschersleben, 2002). It has been argued that early arrival of the tap is a consequence of attempts by the nervous system to overcome the neural delays inherent in the motor system. Many finger tapping studies use the error between the beat and the tap as a way of exploring synchronisation (Repp, 2005). The ability to sense and adjust to error rate has been put forward as a method by which beat matching is achieved (Repp, 2005) although this theory has been challenged (Launay, Dean and Bailes, 2013). There are limitations to the tap literature however. Corrective adjustments are applied to subsequent taps meaning that adjustments during the flight part of the movement are ignored. A further issue is that finger taps are a relatively small and peripheral motion (albeit an important one) much like the vocalisations discussed earlier. It is still a matter of debate therefore, how much finger tapping reveals about larger scale actions (Rodger and Craig, 2011) (or indeed actions that are not rhythmic such as discrete movements like reaching). Knowledge of synchronisation between

large scale movement and external auditory stimuli comes from rehabilitation studies into cued walking with Parkinson's diseased individuals.

Parkinson's disease is characterised by a number of motor symptoms. Bradykinesia is almost always present, with tremor and rigidity also being significant factors (Tugwell, 2008). People with the disease are known to have difficulties in producing internally generated movements as opposed to movements initiated in response to external cues (Fellows, Noth and Schwarz, 1998). The problem leads to an over-reliance on external information being used to guide action. Building on this finding, sensory cueing in different modalities has been used as a way to externally generate additional information for people with Parkinson's disease to move to (see Rubenstein, Giladi and Hausdorf, 2002, for a review). One example is the use of Rhythmic Auditory Stimuli (RAS) (Miller et al., 1996, Thaut et al., 1996) which are embedded within music.<sup>15</sup> RAS set goals for coupling (each pulse of the rhythm) and due to their nature (i.e. set interval ratios), prospective information can be extracted. After entraining to RAS, a sense of where a particular effector should be can be perceived before the goal (the beat) arrives. Thaut et al. (1996), asked individual's with Parkinson's disease to practice walking in conjunction with RAS over a three week programme. Results showed gait was improved as measured by stride length, velocity and cadence (Thaut et al., 1996). The mechanisms through which such improvements occur are not fully understood. It has been proposed that external guides allow Parkinsonian movement control to 'jump' between different parts of a motor sequence (McIntosh et al., 1997; Cunnington et al., 1995). This hints at a

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<sup>15</sup> RAS are just one method of using auditory stimuli for rehabilitative purposes. Other explorations have used metronomes, clicks and tones amongst other sounds.

problem of integration between sensory input and motor output (Abbruzzese and Berardelli, 2003). Such an explanation agrees with the well documented deficits in proprioception and internal sequencing found in the disease (Seiss et al., 2002; Klockgether et al., 1995). Other speculations are that RAS organise (at least partially) internal information by preparation/excitation of the muscles (Safranek, Koshland and Raymond, 1982; Miller et al., 1997) or help to direct attention towards internal signals (Rochester et al., 2005).

An issue that comes to light in both the finger tapping and RAS studies discussed is an overwhelming use of rhythm-based stimuli. These types of auditory cues can be described as ‘empty’ (in terms of sensory information) as between beats there is no information to guide acts (Effenberg, Fehse and Weber, 2011). An open question therefore, is whether filling in the gaps between beats with relevant movement information would be of similar or greater benefit in guiding motion. In addition, as rhythmic cues require a succession of beats to provide prediction, can individual movements be prospectively guided by on-going, dynamic auditory cues? Exploring these questions is central to this first experiment.

### *3.2.3 Theoretical underpinnings of on-going, dynamic sonic guides*

Before discussing how on-going sounds might benefit neurological rehabilitation, it is worthwhile considering how continuous guiding information is involved in controlling an unfolding movement in a healthy individual. In the real world successful movement depends on two critical features. First, a clear understanding where the effector is heading (the goal) and secondly, if the movement is under sensory control, monitoring of how the effector is proceeding at any given moment



(Gosselin-Kessiby, Messier and Kalaska, 2008; Lee, 2005; Sarlegna and Blouin, 2010). So, rather than auditory guides containing only one element significant for motor control (the goal), it is reasonable to hypothesise that including information on *how to reach that goal* would greatly enhance sensory experience.

The influence of on-going information in motor control is evident from ‘time to contact’ (TTC) research into braking and interception tasks. A number of studies have established that time to contact information coordinates motor behaviour (see Hecht and Savelsbergh, (2004) for an in-depth review of TTC literature). Sensing when an object will arrive at target location affords the opportunity of continual adjustment in relation to the approaching/approached object (Lee, 1976; Lee and Reddish, 1981). An example is braking as a car speeds towards a wall. To avoid collision, the driver has to know when to start applying the brakes well in advance (Lee, 1976). In this regard, perceiving the wall is only half the problem in successfully avoiding impact. Without understanding the ‘time to’ aspect of the wall, it is likely application of brake forces will be too late for the car to be brought under control before collision. This example highlights the necessity of having access to continual sensory feedback about the target rather than just perception of it. The idea can be extrapolated to movement in general including reaching actions. In the example above, changes in ‘optic flow’ are being used to control the car (Lee, 1976; 2005), but as discussed in the auditory looming studies (see section 2.3.3), there is no reason why analogous changes in auditory stimuli could not also be used to convey guiding information.

It makes sense then, that continuous sensory information could also be valuable when attempting to relearn motor behaviour after neurological injury. This is

particularly true given that, for a number of neurological disorders or following brain insult in specific brain areas, the ability to integrate rhythmic information is impaired. Di Pietro et al. (2004) for example, describe the case of a musician with lesion to the left temporal-parietal cortex who could not follow or produce auditory rhythms despite melodic and metric competencies being preserved. This finding indicates separate neural networks for auditory rhythm and melody processing as has been confirmed by numerous behavioural (Piccirilli, Sciarma, and Luzzi, 2000; Peretz and Kolinsky, 1993) and imaging studies (Bengtsson and Ullén, 2006; Overly et al., 2004). It is clear then that ‘empty’ rhythmic cues are not suitable for sensory augmentation in all situations. It is possible however, that on-going guidance could overcome this problem by offering information for the duration of discrete actions. Discrete actions are defined as having a single goal clearly bounded by a beginning and end with no transitory forms (reaching and throwing fall under this classification) (Cordo et al., 1995). People with cerebellar degeneration are impaired in the production of discontinuous (discrete) movements (Spencer et al., 2003; Spencer, Ivry and Zelaznik, 2005). These authors argue that this deficit is due to a lack of goal representation in discrete actions as compared to on-going continuous<sup>16</sup> motion, from which goals emerge. This would suggest that finding a way to include goals in discrete action guides would benefit this neurologic population. The question is then, can the changing dynamics of an action (that indicates a goal) be made available in external (open-looped) auditory stimuli? The reality of such sounds would open access to a new set of intervention possibilities and benefit

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<sup>16</sup> ‘Continuous’ in this instance refers to a cyclical movement without a clear beginning or end in line with traditional skill classification. Circle drawing and handwriting are two well-investigated examples.

neurorehabilitation practice in general. For one, such stimuli would make it feasible to target specific features of the motor behaviour deficit. If a person was regularly under-reaching for example, it would be possible for the dynamics of the sound to account for this and guide the mover to accelerate for a longer period at the start of the action. Additionally, if the temporal structure of the stimulus was continuously informing participants as to ‘where it was heading’ (in terms of time to contact), goals could be inferred from the changing dynamics within the sound. A secondary outcome of ‘goal generation’ is that the travel part of an action is likely to become more constrained. Unlike moving to ‘target stimuli’ (such as empty rhythmic cues) where movement adjustments might be left until the end of an action, continual guidance would likely result in continual adjustment as the movement proceeds.

### 3.3 Creating and testing dynamic sonic guides

As discussed in Chapter 2, to create the sonic guides it was decided to modulate the pitch glides to simulate the changing tau margin of a reaching action as described by Lee, (1976). The reasons for this choice were threefold. Firstly, tau by nature is a sensory variable (i.e. it is hypothesised to be sensed rather than computed) meaning it is appropriate for augmenting sensory awareness. Secondly, tau carries the two types of information important in the control of action discussed above. On-going and dynamic information from the beginning of the action until the target is reached and prospective information that constantly references the target ahead of time. Thirdly, by using the closing tau margin to plot guides, an existing way to adapt movement trajectories within the sounds is already established (i.e. by manipulating k-values).

### 3.3.1 *Experiment one: Testing sonic guides for reaching*

The main question of this experiment is; can dynamic sounds be used to affect the way a motor task is performed in a predictable way? To answer this, healthy individuals will be asked to perform a reaching task whilst following on-going, dynamic, externally generated cues. Auditory cues containing differing ‘trajectory patterns’ (i.e. different tau guides) will be played to participants to guide reaches.

Participants will reach for a target and coordinate arrival of the hand with the sonic-guide termination. In doing so, the experiment tests the efficacy of continuous dynamic sounds in guiding movement. Efficacy is established through confirmation of a number of secondary questions. First of all, is the tau information contained within each guide being used or do participants rely on other available cues (such as the visual stimulus or estimates of duration)? If information within the sounds is being used, it is expected that corresponding movement kinematics will be found in participants’ reaching behaviour. Secondly, if participants are using guiding information, are there guides that ‘make more sense’ or give a ‘clearer instruction’, than another? Coordination times between the hand’s arrival and sonic-guide termination are used to explore this question, with greater precision (arrival time) considered to reflect clearer guiding information. Finally, as differing tau parameters alter the steepness of the rise in pitch, it is reasoned that these will be heard as faster or slower and effect movement accordingly.

### 3.4 Methods

#### 3.4.1 Participants

Seventeen participants aged 18-58 years (mean  $23.88 \pm \text{SD } 10.34$ , median 19 years) were recruited from The University of Edinburgh, eight female, nine male. One male and one female were left handed; all others were right handed. No participants reported any hearing difficulties.

#### 3.4.2 Sonic Guides

The independent variable in the experiment is the sonic-guide (rising pitch glide) played to subjects. Two types of sound were developed. One type (tau sounds) mimicked how the tau of a reaching movement action gap changes when being closed. The second (linear) mirrored the closure of the same gap but in this case in a non-ecological way where pitch rose linearly. All sonic guides started at 215 Hz and rose over one octave to 430 Hz ( $A_3$  to  $A_4$  on a piano keyboard). The sound with a linear increase in pitch was computed using NCH software using a sample of the tone used for the tau sounds. Tau-based sounds were created using a tone generator. The pure tone produced was modulated following the formula;

$$f = f_{\text{range}} T_G^{-k/2} (T_G^2 - t^2)^{1/k} \quad (\text{Equation 3.1})$$

Where  $t$  is time at a given point,  $f_{range}$  = end frequency – start frequency,  $T_G$  is the duration of the sound and  $k$  is a constant representing the slope.<sup>17</sup>

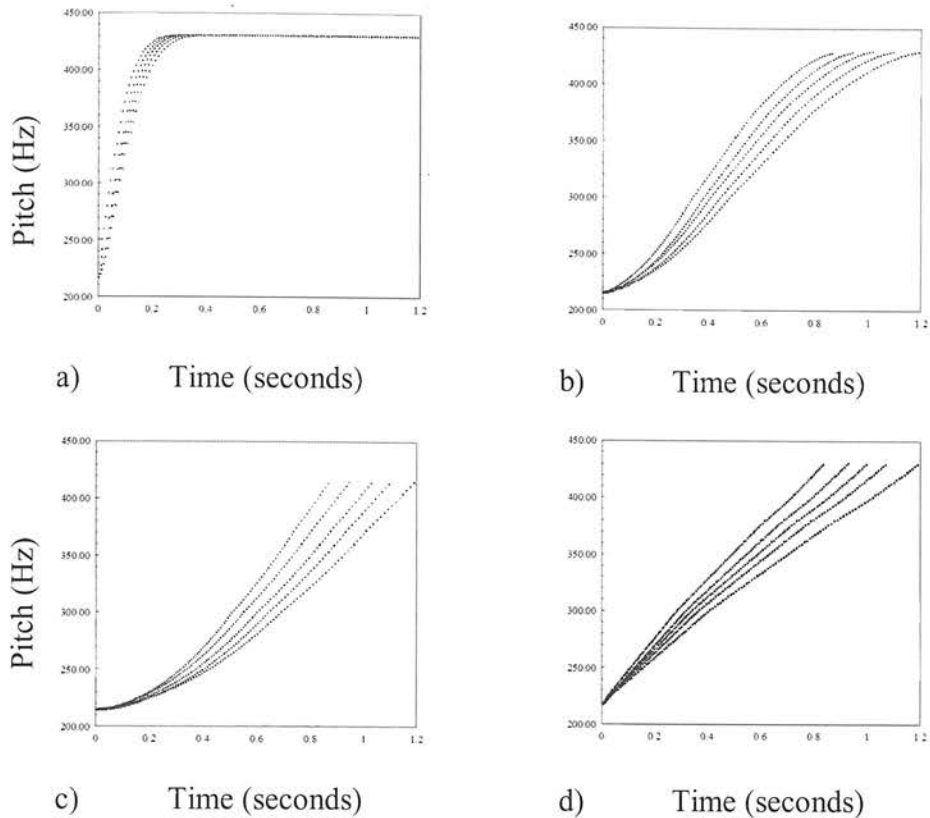
Equation 3.1 is a combination of the equations for  $\tau_G$  guidance discussed in section 2.8.3 (Lee, 1998). It models how a gap would ideally be closed given that duration and value of  $k$  are known. In this respect the equation simulates an aspect of biological motion. Duration was found through averaging ten control reaches and  $k$  was set at the experimenter's discretion depending on the type of motion desired. The slope ( $k$ -value) and duration ( $T$ ) are the only parameters manipulated in the experiment (see section 2.8 for discussion of the  $k$ -value). Low  $k$ -values produced sharp early pitch rises with longer slow rises produced for higher  $k$ -values. For tau-based sonic guides, three different  $k$ -values were used,  $k=0.2$ ,  $k=0.5$  and  $k=1.0$ . Profiles of how sounds rise over time are plotted in Figure 3.1 (a-d). Sounds  $k=0.2$  (Figure 3.1a) and  $k=0.5$  (Figure 3.1b) are sigmoidal and contain two components representing acceleration and deceleration phases. Figure 3.1a, shows how acceleration is steep and early in the guide after which there is a long deceleration phase. For  $k=0.5$ , acceleration is slightly longer than deceleration representing a slightly skewed bell-shaped velocity curve. It is important to note that despite having 'deceleration' components, pitch continually rises in both guides and is heard as such.<sup>18</sup>  $k=1.0$  (Figure 3.1c) does not have a deceleration phase and 'collides' as the sound ends (i.e. is still accelerating) and contains an exponential rise in pitch

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<sup>17</sup> The  $\tau_G$  formula was programmed in Labview™ by G.J. Pepping (1998) to be used in conjunction with a pitch generator to create sonic guides.

<sup>18</sup> The rising pitch is in keeping with the earlier discussion (see section 2.3.3) that the human auditory system is more sensitive to 'approaching' auditory information than receding (Neuhoff, 1998; Seifritz et al., 2002).

representative of a real-world action where arrival with force is required (e.g. a punch).



**Figure 3.1** Profiles of the rising sonic guides. Pitch modulates between 215Hz to 430Hz. Clockwise from top left: the three tau-derived sounds (a)  $k=0.2$ , (b)  $k=0.5$ , (c)  $k=1.0$  and a single non-tau derived sound (d) linear.

The linear sound (3.1d) is not based on biological motion and although still accelerating as the sonic-guide finishes, pitch rises linearly in an artificial manner. For each of the four categories of sound, five sonic guides of different time duration were created (0.8, 0.9, 1.0 1.1 and 1.2 seconds), making a total of 20 sonic guides. Each guide was administered twice with order of presentation randomised. To establish durations, a healthy control was used to find a mean (rounded to the nearest tenth of a second) by reaching to a button ten times without any instruction relating to accuracy or speed. Once the mean had been established, four additional durations

were calculated (two either side), by the addition or subtraction of 0.1 second intervals. Different length sonic guides were employed to eliminate the possibility of participants using duration to guide reaches as well as interfere with the formation auditory memory cues (Chen, Penhune and Zatorre 2008a).<sup>19</sup> Between slowest and fastest sounds there was a 0.4 second time difference. The forty sonic guides were ordered into an MP3 file using online random generator software ([www.random.org](http://www.random.org)). Each sonic-guide was separated by a silence of 1 second plus the duration of the preceding sonic-guide (see Appendix A). Silences and sonic guides were deliberately of different durations so that rhythm was obscured. The intention was to force participants to follow the instruction within the sound rather than attempt to predict 'what was coming next'. The MP3 containing the forty guides lasted for approximately two minutes.

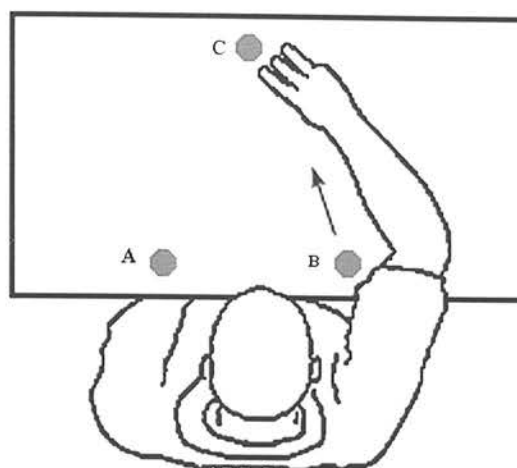
### 3.4.3 *Experimental design*

Participants sat with the preferred hand placed on the table placed in front of them. The middle finger rested on a starting marker (a sticker) placed near the table edge (see Figure 3.2). Instructions were given to reach out to a button placed an arm's length away (approximately 45 cm) directly in front of the participant. The 'button' was a bottle top 2.5 centimetres wide and 1.5 centimetres that was high glued to the

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<sup>19</sup> The time difference of 0.1 seconds was chosen to keep the sonic-guide duration within the range of movement times recorded by the control (and thus assumed to be ecologically valid). Additionally, research has demonstrated this time window is distinguishable in the human auditory system (Grondin, 2010).





**Figure 3.2** The experimental set up. Participants reached for the target C from start point B if right handed and start point A if left handed (see text for details).

table. Start markers for the left and right hand were placed equidistance either side of the button. Subjects were asked to begin reaching as the sonic-guide started and to coordinate arrival at the target with the end of the sound. Four beeps were included in the MP3 file which acted as a countdown for participants and experimenter. Exactly on the fourth beep the experimenter started the recoding of the motion capture which meant that the playing of the auditory guides and the motion capture were perfectly synced. This allowed for the coordination of the hand's arrival at the button and the end of sound to be recorded. Arrival consisted of placing the middle finger on the button. One sonic-guide represented one reach with silences in between guides giving participants time to return the hand to start position ready for the next guide. Each participant practiced the task using randomly selected sounds before trials began. Sonic guides were presented sequentially with the experiment lasting approximately two minutes.

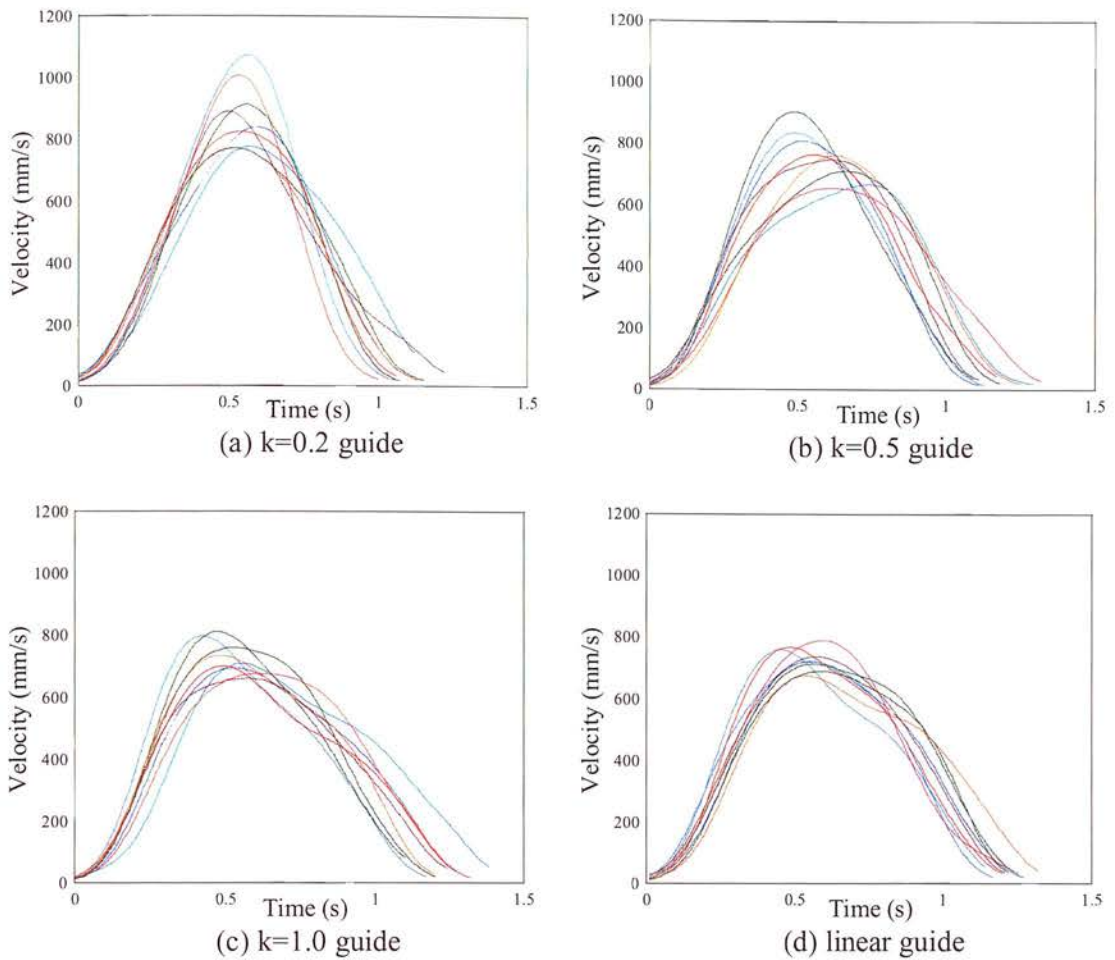
### 3.4.4 Equipment

Sounds were played using a Dell™ PC with standard stereo speakers placed in front of participants on the table. Each subject had a 10mm reflective marker on the metacarpophalangeal joint (i.e. the knuckle) of the middle finger of the reaching hand. Three ProReflex MCU500 Qualisys™ motion capture cameras recorded hand movements in Cartesian coordinates at 500 Hz. Each session was video recorded using a Toshiba H-10 HD.

## 3.5 Analysis and results

Participants completed the forty sways (ten per condition). An example of the velocity profiles of a single participant's reaches are displayed in Figure 3.3 which highlights some interesting points. First it can be seen that for both of the guides with deceleration phases (a and b), the majority of velocity curves are smooth and bell-shaped. This is as opposed to (c) and (d) where there is a distinct 'kink' in the curve between 0.5 and 0.8 seconds. This kink reflects the lack of information in these guides and implies a change in the intended motor commands. It is also clear that reaches are under sensory control as movements are being adapted in response to the sounds. Of interest is the fact that reaches in the  $k=0.2$  category are of shorter duration. This suggests that the rising steepness of the pitch, is making this participant hear these sounds as shorter than they actually are. A final observation from these data is that in guides where a deceleration phase is present, there is more variability in peak velocities, for example, in (a)  $k=0.2$ , peak velocity ranges between

approximately 700 to 1100 mm/s whereas in (d) linear, this drops to between 630 to 800 mm/s. This is evidence that this participant is using endpoint information within



**Figure 3.3** Velocity profiles (mm/s) for the ten reaches in each category of sound.

the guides to plan the motor action (as higher velocity is a consequence of sensing the faster arrival of the end of the sound).

To explore the group three variables were calculated: peak velocity position, arrival lag time (coordination between arrival of the hand and the end of the sonic-guide at the target) and peak velocity. Position of the peak velocity (PPV) represents the maximum in the bell-shaped velocity curve, where acceleration is zero. As such,

periods of acceleration and deceleration can be calculated from this point. PPV therefore relates to an estimate of the k-value denoted by tau. As the PPV reflects k, it is predicted that the PPV will appear earlier in the reach across conditions from  $k=0.2$  to linear. It was also decided to compare the PPV with the value of k derived from analysing the data using the  $\tau_G$ -equation. As PPV and  $\tau_G$ -k denote the same value it is expected that scores will be similar. Arrival lag time at the sonic-guide endpoint (i.e. how delayed/early the hand is in coordinating with the end of the sound) was calculated to test if sounds with specific k-values were easier to couple to than others. More accurate coordination and less variability is expected where guides contain information more closely related to the task (multisensory theory tells us task relevance increases saliency). Finally, peak velocity was analysed to investigate the rate at which reaches were executed between initiation and target arrival. It was reasoned that participants will hear and adjust movements in relation to how steep the pitch glide rises. As acceleration in the guide (pitch steepness) is lower with higher k-values, it is predicted that peak velocity will be fastest for  $k=0.2$  and slowest for  $k=1.0$  and linear conditions.

Overall participants were expected to perform (i.e., coordinate) better with guides containing deceleration phases ( $k=0.2$  and  $k=0.5$ ) than with guides without deceleration phases. This expectation is based on the fact that under ordinary circumstances, participants would use both acceleration and deceleration to accomplish the experimental task. In this regard,  $k=0.5$  and  $k=0.2$  represent a 'natural' reach more than the other two guides. For the same reasons, sonic guides  $k=1.0$  and linear are expected to be more difficult to coordinate with as there is little meaningful task related information to guide reaches. However, as  $k=1.0$  is based on



biological motion (albeit a continually accelerating biological motion) it is assumed that this guide will be easier to follow than the linear guide.

### 3.5.1. Analysis one: peak velocity position in the movement

Using KaleidaGraph software the R-trajectory was calculated from the X, Y, Z coordinates exported from the motion tracking.<sup>20</sup> Data was smoothed using a Gaussian  $\sigma$  8 before start and end points were identified for each reach as demarcated by zero to zero velocity crossings. To take account of noise (drift at the start/end of the motion), movements were considered to begin and terminate after a threshold of three percent of the peak velocity had been crossed. The time of the peak velocity position for each movement was noted and then a simple calculation created a ratio of where within each reach the PPV appeared.

$$PPV = (t_{pvR} - t_{ms}) / D \quad (\text{Equation 3.2})$$

Movement start times ( $t_{ms}$ ) were subtracted from peak velocity times ( $t_{pvR}$ ) before being divided by movement duration (D). This time-normalised reach durations and produced a scale from zero to one, with zero equalling movement initiation and one representing reach termination. Mean PPV was then calculated in each sonic-guide category for the cohort (160 reaches per condition).<sup>21</sup> Results are displayed in Table 3.1 and plotted in Figure 3.4. A  $\tau_G$ -analysis was then performed on the same data (using Formula 2.8 in Chapter 2). The intrinsic tau of each movement was plotted on

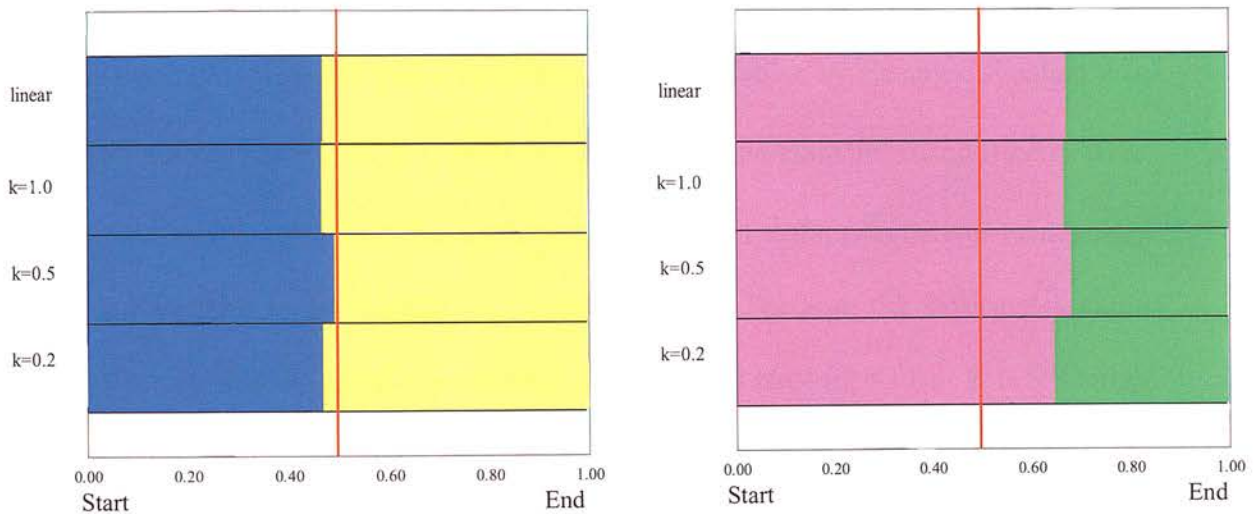
<sup>20</sup> The equation used was  $R = \sqrt{X^2 + Y^2 + Z^2}$

<sup>21</sup> One participant was excluded as their reaches exited the recording space.

the x-axis against the tau of the movement on the y-axis. The slope of this regression gives estimates of  $k$ . Mean and standard deviation  $k$ -values were calculated for each sound condition and are also presented in Table 3.1. Percentage coupling and  $R^2$  ranged across conditions from 95.31-97.06% and 0.971-0.973 respectively (see Appendix B).

**Table 3.1** Mean and standard deviation of peak velocity position (PPV) and  $k$ -value (derived from the  $\tau_G$ -equation) for the different sound conditions  $k=0.2$ ,  $k=0.5$ ,  $k=1.0$  and linear.

Sonic Guide	$k=0.2$	$k=0.5$	$k=1.0$	linear
Mean PPV	0.469	0.493	0.473	0.471
SD PPV	0.060	0.0635	0.062	0.061
Mean $k$	0.646	0.680	0.668	0.671
SD $k$	0.143	0.149	0.174	0.179



**Figure 3.4** Graphs for the PPV and  $k$ -value data. Periods of acceleration (blue for PPV, purple for  $k$ -value) and deceleration (yellow for PPV, green for  $k$ -value) for each category of sonic guide. The red line at 0.5 indicates the halfway point of the reach.

The first noticeable aspect of Figure 3.4 is the large difference between the PPV and the  $k$ -values. The  $\tau_G$ -analysis suggests that reaches contain long periods of

acceleration and short deceleration whereas PPV scores are more evenly distributed. Despite this, Figure 3.4 suggests that the changes between conditions are proportionately similar for both PPV and k-value (i.e. k=0.2 is the smallest and k=0.5 is the largest number in both data sets). Similarly there is clustering for both results with the PPVs all close to the mid-point (0.5) and the k-values close to 0.65. It was decided therefore to explore these data further. Nonparametric tests were used as both data sets were found to be skewed. For the PPV data, Friedman's ANOVA revealed a significant effect of PPV for category of sound ( $\chi^2(3) = 15.58, p < .001$ ). Wilcoxon tests were used for post hoc comparisons using Bonferroni adjustments to correct for the number of tests used. All effects are thus shown at the 0.0125 significance level. Significant differences were found between conditions k=0.2 vs. k=0.5 ( $Z = -4.113, p = 0.0001, r = -0.32$ ), k=0.5 vs. k=1.0 ( $Z = -3.188, p = 0.001, r = -0.24$ ) and k=0.5 vs. linear ( $Z = -3.366, p = 0.001, r = -0.26$ ). Friedman's ANOVA was run on the k-value data and a significant effect of k-value by category of sound was also found ( $\chi^2(3) = 7.96, p < .047$ ). Wilcoxon tests and Bonferroni adjustments were applied and it was found that there was a significant difference between categories k=0.2 vs. k=0.5 ( $Z = -2.628, p = 0.009, r = -0.2$ ). For both the PPV and k-value analysis, k=0.2 appeared significantly earlier in the movement than k=0.5. During the k=0.2 reach, participants decelerated earlier in the action and for a longer period. This suggests that between these conditions, reaches were being influenced in the manner specified by the experimenters. For the category k=0.5 in the PPV analysis, participants not only produced scores significantly later than k=0.2 but also scores that mirrored the k-value embedded in the sonic-guide (the PPV score was 0.493). This finding reflects the moderately skewed bell-shaped velocity profile programmed

for this category. This mirroring was not found in the  $\tau_G$   $k=0.5$  analysis where mean  $k$  equalled 0.68; a much greater skew representing a long acceleration phase that was not present in the sound.

A conflicting result was that the PPV for  $k=1.0$  and linear guides, appeared significantly earlier in the reach for these conditions than  $k=0.5$ . As neither  $k=1.0$  or linear contain deceleration periods, PPVs were forecast to appear late in the action (or not at all if being followed exactly). However, for the  $\tau_G$ -analysis this was not the case with scores of 0.668 and 0.671 for  $k=1.0$  and linear respectively. Whilst this initially appeared to be a positive finding compared to the PPV analysis, we know that the PPV analysis is *the actual position of the peak velocity* (as it was simply recorded by looking at where it fell between the start and end) indicating that the  $\tau_G$ -equation does not produce data that is representative of what the mover is actually doing. For the PPV analysis, no significance was found between  $k=0.2$ ,  $k=1.0$  and linear, and all scores appeared on the same side of the midpoint (i.e. the red line at 0.5). Similarly, for the  $\tau_G$ -analysis, no significant effects were found between  $k=0.2$ ,  $k=1.0$  and linear and all scores appeared on the same side of the midpoint (this time around 0.65). This suggests that for these categories of sound, sonic guides initiated the same reaching behaviour. For both the PPV and  $k$ -value analysis, there was also little difference between  $k=1.0$  and linear sonic guides (PPVs were 0.469 and 0.473 and  $k$ -values 0.668 and 0.671 respectively). It had been expected that whilst both sounds would be coordinated with poorly, linear would produce inferior scores as it was based on non-biological motion. However, this was not found.

A different exploration of the PPV and  $\tau_G$ -analysis used standard deviation (SD). It is argued that as the SD records the amount variability in PPV and  $k$  scores, this



reflects the clarity of the movement instruction provided by the guide. Again a clear difference in SD score between the PPV and  $\tau_G$ -k was recorded. For the PPV analysis, SD is quite uniform across all conditions suggesting that participants found the instructions within the guides easy to understand. In contrast the  $\tau_G$ -analysis produced SDs twice that of the PPV, with  $k=1.0$  and linear conditions producing the greatest amounts (0.174 and 0.179 respectively). This was expected as these two conditions had no deceleration phase and therefore limited predictive value with regards the endpoint. However, it does not make sense that one analysis shows limited variability whereas the other shows more. Again this reflects confusing scores produced by the  $\tau_G$ -analysis for example, in the  $k=0.5$  category,  $k$ -values ranged between 0.3 and 1.5. That  $k$  values above one were recorded makes little sense in this experiment, as it is certain that no participant was still accelerating as they reached the target.

### *3.5.2 Analysis two: coordinating arrival with the sonic-guide endpoint*

For this analysis, the Y-axis was selected to identify when the hand arrived at the target in coordination with the end of the sound. Positional data was differentiated once with respect to time to produce velocity and then plotted against one another. Endpoints were identified using zero velocity crossings in KaleidaGraph software, with times rounded to the nearest 1/100 seconds. Next the sonic-guide MP3 was plotted in music editing software Audacity (see Appendix A). Endpoint times were noted to give the position (in time) of each of the forty guides. Sonic-guide endpoint times were then subtracted from participant arrival times to produce an arrival lag

score for each reach. The percentage of reaches that arrived early or late was then calculated for each sound category and sound duration (summarised in Table 3.2).

**Table 3.2** Descriptive data showing the percentage of reaches that arrived at the target after the sound had ended. Each sound duration and category is shown.

Sound duration	0.8	0.9	1.0	1.1	1.2
% late	90%	90%	64%	49%	42%

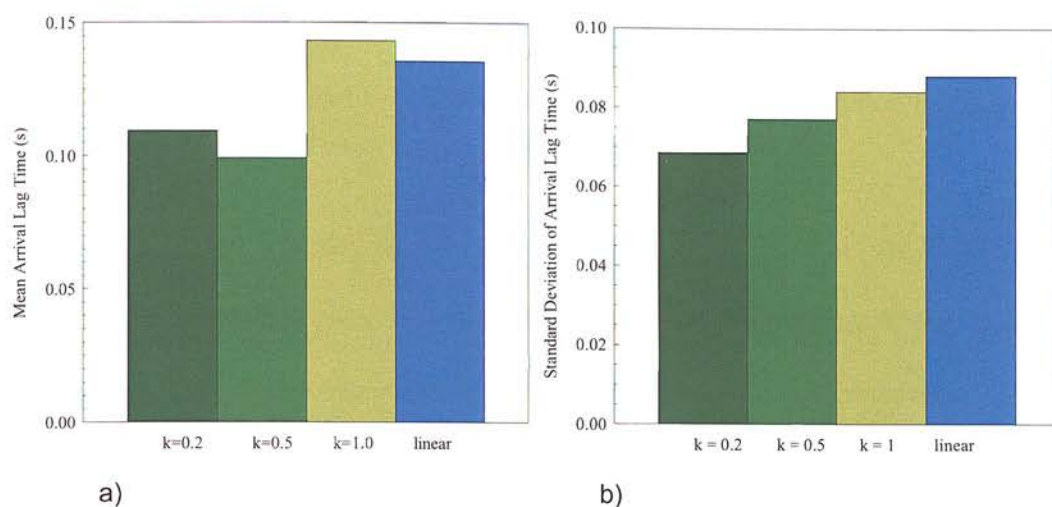
  

Sound category	k=0.2	k=0.5	k=1.0	Linear	Overall
% late	66%	65%	55%	74%	69%

These data show that the shorter the sound duration the later the arrival as is expected. The data for the sound category are more mixed. Participants performed roughly the same when a deceleration phase was included (e.g.  $k=0.2$  and  $k=0.5$ ). For continually accelerating sounds, whilst  $k=1.0$  was fairly evenly split between early and late arrival, the linear condition produced the largest percentage of reaches arriving late of any condition. This was expected as there was no anticipatory information available in these guides. It is suggested that  $k=1.0$  produced a different result to linear here as it is based on biological motion. To explore arrival time further absolute values were calculated so that arrival lag times measured how far from the endpoint (in seconds) the hand appeared regardless of being early or late. Mean and standard deviation arrival lag time were then calculated for each condition. Results are in Table 3.3 and plotted in Figure 3.5a and b.

**Table 3.3** Mean and standard deviation arrival lag scores (seconds) for the four conditions.

Sound condition	k=0.2	k=0.5	k=1.0	linear
Mean	0.109	0.099	0.143	0.136
SD	0.069	0.077	0.084	0.088

**Figure 3.5 a and b** a) Mean of arrival lag times. b) Standard deviation of arrival lag times. Scores are reported in seconds.

Both k=0.2 and k=0.5 conditions produced low mean arrival lag time scores (Figure 3.5a). k=0.5 was the lowest suggesting participants found this sonic-guide the easiest to coordinate with. This implies information within the k=0.5 sound is more readily available than the information within other guides. A one-way repeated measures ANOVA was performed after a Mauchly's test of sphericity was conducted and the sphericity assumption was found to be violated ( $\chi^2(5) = 18.56, p < 0.05$ ). Due to the violation, a Greenhouse-Geisser estimate ( $\epsilon = 0.53$ ) was accepted instead of the normal F-ratio. A significant effect of sonic-guide on arrival lag time was found ( $F(1.63, 26.8) = 5.88, p > 0.05$ ). Post hoc tests using Bonferroni corrections were carried out which revealed significant differences between k=0.5 vs. k=1.0 ( $p < 0.044$ ) and k=0.5 vs. linear ( $p < 0.036$ ). These results confirm findings from analysis

one that  $k=0.5$  'makes the most sense' with regards to coupling information. When following  $k=0.5$  participants increased accuracy by 0.044 seconds compared to  $k=1.0$  and 0.037 seconds in relation to linear. A small improvement in accuracy was also recorded against the  $k=0.2$  condition (0.010) but this was not significant. When coupling to  $k=0.2$ , although non-significant, participants showed better accuracy than for  $k=1.0$  and linear. This likely reflects the presence of a deceleration period within these guides.

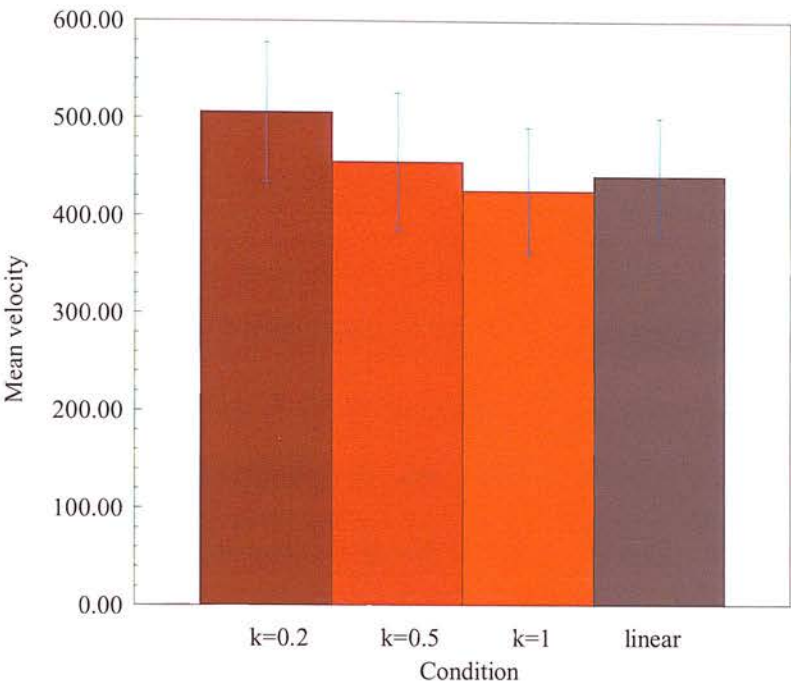
Standard deviation was also used to test for consistency of arrival (see Figure 3.5b). Figure 3.5b shows SD rises incrementally across conditions from  $k=0.2$  to linear. The graph suggests participants found following guides increasingly difficult depending on how far to the 'left' within the sound  $k$ -values appeared. However, an F-ratio variance analysis to test for significance between SD values did not reveal any significant differences at the  $p < 0.05$  level.

### 3.5.3 Analysis three: peak velocity

The Z-axis was used to calculate peak velocity. The Z-axis runs perpendicular to the table and captures the up and down component of participants' reaches. After data were smoothed, positional data was differentiated once with respect to time to give velocity (see previous analyses). Peak velocity values were identified for each movement using KaleidaGraph software. Mean and standard deviation peak velocity was then calculated for each of the four sonic-guide conditions. Scores are listed in Table 3.4 and plotted in Figure 3.6.

**Table 3.4** Mean and standard deviation for peak velocities in each condition (mm/s).

Sound condition	k=0.2	k=0.5	k=1.0	linear
Mean	506.09	455.34	426.00	441.10
SD	71.33	70.64	64.87	59.74



**Figure 3.6** Graph of mean peak velocity (mm/s) with standard deviation bars across conditions.

Figure 3.6 shows that for tau based sounds, peak velocity decreased sequentially from condition k=0.2 to condition k=1.0 with linear marginally faster than k=1.0. This trend agrees with the prediction that sounds would be heard as faster in relation to increased steepness of the pitch glide (as seen in the velocity profiles displayed in Figure 3.3). Increased steepness is clearly mimicked by amplified peak velocities in corresponding reaches. After an initial exploration data was found to be skewed so non-parametric tests were used to test for significance. A Friedman’s ANOVA was carried out and a highly significant result for peak velocity was found ( $\chi^2(3) = 28.98$ ,  $p < 0.001$  two-tailed). For post-hoc testing, Wilcoxon matched pairs were run after a

Bonferroni correction was applied. All effects are thus presented at the 0.008 significance level. Significant differences in velocity were recorded between  $k=0.2$  vs.  $k=0.5$  ( $T = 12$ ,  $r = -0.74$ ),  $k=0.5$  vs.  $k=1.0$  ( $T = 4$ ,  $r = -0.83$ )<sup>22</sup>. These results show participants respond to the steepness of the rising pitch glides by accelerating the hand towards the target with increasing speed as specified by the  $k$ -value of the guide. Effect sizes are large suggesting that the influence of the different guides on peak velocity was robust. The average speed in each category specified by the sonic guides is 45.72 cm/s.<sup>23</sup> As can be seen, participants peak velocity when following guides in the  $k=0.5$  category nearly matched this average with  $k=0.2$  faster and  $k=1.0$  and linear lower as predicted. A result not expected was that the linear condition produced a result close to significance in comparison to  $k=1.0$  ( $p > 0.009$ ). The likely explanation for this is that, as  $k=1.0$  is based on biological motion there is a bend in the pitch rise which may be perceived as rising more slowly (compared to linear). Standard deviation was also analysed to test whether or not participants were producing consistent peak velocities. A variance ratio test revealed there were no statistical differences between SDs at the  $p < 0.05$  level.

### 3.5.5 Summary of results

Peak velocity positions were as predicted for guides containing deceleration phases ( $k=0.2$  and  $k=0.5$ ), but not for those without ( $k=1.0$  and linear).  $k=0.5$  was mirrored

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<sup>22</sup> Significance was found between multiple conditions (for example  $k=0.2$  vs.  $k=1.0$ ). However, only incremental comparisons across conditions from  $k=0.2$  to linear are of interest to this study and are reported here.

<sup>23</sup> The mean was calculated by finding the speed for each guide and then averaging for each category. Distance to the target (45cm) was divided by the duration of each guide (0.8 to 1.2 seconds). From this the mean of 45.72 cm/s was calculated.



almost exactly with  $k=0.2$  appearing significantly earlier in the reach than  $k=0.5$ . However, results for both  $k=1.0$  and linear guide showed no evidence that the instruction in the guide was influencing PPV. Participants timed arrival better when using guides with deceleration phases compared to those without. Significant differences in arrival accuracy was recorded for  $k=0.5$  than for both  $k=1.0$  and linear conditions. Peak velocity was adapted in line with the change in steepness of the pitch glides. Significant decreases in peak velocity were recorded in line with increasing values of  $k$  within the guide.

### 3.6 Discussion

#### 3.6.1 General discussion

The present study tested the hypotheses that on-going and dynamic auditory guides would alter the movement characteristics of a reaching action in a predictable way. The effects of auditory stimuli on movement behaviours are well documented (Thaut et al., 1996; Repp, 2005; Dozza, Horak, and Chiari, 2007). However, there are few reports in the literature that present on-going information for the duration of the action. Movement dynamics were conveyed in auditory form and the degree to which these were mirrored was an indication of the influence of the sonic guides. This is the first time reaching dynamics have been embedded in auditory stimuli based on an aspect of motor control theory (i.e. Lee, 1980). As the kinematics and arrival accuracy of participants' reaching were adapted, results provide evidence for the use of on-going, dynamic information to guide motion. This is in agreement with the limited research that shows continuous stimuli alter reach trajectories (Rodgers and

Craig, 2011). The study adds to the auditory cuing literature but also expands it by demonstrating the efficacy of both on-going and dynamic sounds. Results confirm information reflecting the changing tau of an ‘auditory action-gap’ can be sensed and used to guide movement with predictable effects. An unrelated finding was that using the  $\tau_G$ -equation to analyse data produces confusing results. High percentage coupling and  $r^2$  values were reported (see Appendix B) showing that peoples’ reaches fitted the predictions of the  $\tau_G$ -equation. Tau theorists argue that these scores provide evidence of an internal guide. However, as  $k$ -values did not reflect the *real* peaks of velocity found through the PPV analysis, doubts are raised about this proposition. These doubts are explored in greater detail in Chapter 5 but for this experiment, the  $\tau_G$ -analysis was a hindrance to understanding the questions asked in this work. However, this experiment was not set up to test the  $\tau_G$ -hypothesis. The sole purpose was to get an estimate of how well participants were mirroring the changing dynamics of the sounds. The PPV analysis was more than adequate for this task.

In a number of studies, error correction has been suggested as a control mechanism for sensorimotor synchronisation (Repp, 2005; Takano and Miyake, 2007). In this experiment the use of error correction was made difficult by limiting the amount of information available. Guide and silence durations were different and were also presented randomly. This meant that the MP3 sequence was non-rhythmic and that estimates of interval length or guide duration from the previous display could not guide the current reach. The effects of auditory memory, which can guide movement under certain conditions, were also limited by presenting sounds in this way (Chen, Penhune and Zatorre, 2008a). PPV results showed that the kinematics of the reach were affected by the different sound conditions. Given the presentation of guides



described above, it is reasonable to attribute these changes in the timing/execution of reaches to the presence of guiding information within the sounds. This finding compliments the literature highlighting that movement is adapted by sensory feedback after initiation (Bootsma and van Wieringen, 1990; Gosselin-Kessiby, Messier and Kalaska, 2008) and that relevant sensory information is amodal (i.e. here the auditory system is used). It is suggested this is achieved in much the same way as optic flow is used in visual-motor transformations. In large scale actions (such as walking), optic flow instigates rapid adaptations in movement trajectory if the intended target moves. When optic flow is unavailable, the same target movement does not instigate adjustment at the same rate or amplitude (Bruggeman, Zosh and Warren, 2007). It is proposed that similar adjustments are made in auditory-motor transformations. It is argued that ‘auditory-flow’ (the sound’s modulation), contributes to the formation of motor commands for the reach. As described in Chapter 2, these will be predictive (i.e. Bernstein, 1967; Lee, 2005; Linas, 2009) as proscribed by the rate at which the sound is modulating. This motor plan can then be continuously updated as the movement proceeds by comparison with the on-going guide and the sensory input produced by the reaching action (reafference) (von Holst, 1954; Wolpert and Kawato, 1998). The kinks found in  $k=1.0$  and linear (Figure 3.3) can be explained in this way. That the kinks appear in the deceleration phase suggests a motor plan is initially formed (from hearing the initial rise in pitch) but then its execution is disrupted as the anticipated deceleration phase (which is absent in the sounds) does not match the internal guide. This is not the case in  $k=0.2$  or  $k=0.5$ , where the smoothness of trajectories suggests formation and activation of the anticipatory internal guides is based on clear information. An interesting feature of

adapted trajectories in  $k=0.2$  and  $k=0.5$ , is that participants must be scaling reaches to preserve the ratio of acceleration/deceleration determined by the sound. Movements have to incorporate movement initiation delays inherent at the start of each motion (Hanes and Schall, 1996). Initiation delays are reflected in the fact that a large proportion of these data produced late arrival. That participants are able to incorporate initiation delays into movement behaviour further suggests that prospective information is extracted from the initial steepness of the rise in pitch. This proposal supports the idea that tau information is available in the sounds and can be used to adapt movement patterns ahead of time (Lee, 2005).

A number of studies show a neurally based preference for biological motion when extracting movement from the optic array (Simion, Regolin and Bulf, 2008; Pelphrey et al., 2003). This phenomenon is also found in the auditory domain where identification of sounds from real-world actions, as opposed to artificial ones, is represented neurally (Baumgart et al., 1999). Additionally, auditory biological motion evokes neural responses in the same brain regions as visual biological stimuli (Bidet-Caulet et al., 2005). In this investigation, an attempt was made to simulate biological motion by basing sounds on the changing tau-margin, with linear guides representing artificial motion as a comparator. Whilst a difference was found between early and late arrival, all other results were similar meaning this study failed to show a preference for biological motion when guides contained the same instruction (i.e.  $k=1.0$  and linear both delineated constant acceleration to the target).

This experiment revealed a strong, unconscious association between auditory and movement systems (see Chapter 2 for a discussion of this topic). Of the four sounds only  $k=0.2$  was distinctive in its auditory representation due to the early pitch rise

and long deceleration. The other three guides sounded comparable and at first listen could easily be mistaken for the same sound being played at manipulated speeds. That results were so clearly influenced by guide information, particularly in arrival accuracy and peak velocity, reveals a pronounced ability to integrate sound and movement. This sensitivity is further highlighted by the fact that the only direct instruction given to participants was to coordinate the arrival of the hand at the target as the sound ended, *not to explicitly follow the guide*. As a consequence, scores reflect how movement was influenced without any conscious expectation of changing dynamics within the sound. That movement was influenced in this way further supports the idea that auditory stimuli can define the characteristics of the motion (Lewis, Beauchamp and DeYoe, 2000; Neuhoff, 2001) and moreover, influence movement kinematics.

### 3.6.1 Multisensory processes

An explanation of how guides may be influencing reaching commands is to frame the results within a multisensory context. As discussed in Chapter 2 (see section 2.5), a key driver of multisensory integration is stimuli from different perceptual domains being presented congruently (Shams and Seitz, 2008; Powers, Hillock, and Wallace, 2009). Congruent streams of sensory information are perceived as emanating from the same source and promote activity in multisensory neurons and regions of the brain (Meredith and Stein, 1986). The outcome is increased facilitation in identification (and performance) of a behaviour. In this experiment three sensory streams are used to complete the action. Visual information is always present (the target and hand are always in the field of view), proprioceptive information is

available (particularly after reach initiation) and auditory information is added. It is likely then, that multisensory processes would occur where auditory guides convey motion relevant to the task. In this experiment, multisensory theory posits that a congruent auditory stream would be integrated to form a unitary precept of the hands motion (Driver and Spence, 2000). Of the guides used in this investigation, there is a strong argument to say that only guides containing deceleration information ( $k=0.2$  and  $k=0.5$ ) would suit the reaching task presented (as reasoned earlier, the task would typically require acceleration and deceleration phases [Soechting and Lacquaniti, 1981]). Furthermore, due to the atypical arrangement of the acceleration period in  $k=0.2$ , it is likely  $k=0.5$  would make the most 'movement sense'. Data support these propositions in all three analyses and especially in arrival accuracy. That participants coordinated better with the sonic-guide when following  $k=0.5$ , agrees with research which shows that congruent auditory and visual information improve reaction times (Chen and Yeh, 2008; Sinnett, Soto-Faraco and Spence, 2008).

Results for the other guides could also be explained within the context of multisensory processes or lack thereof. If sonic guides did not convey meaningful task relevant instruction, it is hard to argue they could be congruent. In this scenario multisensory activity would not be engaged or greatly reduced. A lack of congruent multisensory activity could potentially explain the scores of  $k=1.0$  and linear in both the PPV and arrival accuracy analysis. Confirmation of the influence of the type of sounds used in this experiment on multisensory neural activity would need another level of analysis beyond the scope of the current study. However, given the set-up of the experiment and what is known about integration of multiple streams of sensory information, it is improbable that multisensory processes would not occur.

### 3.6.3 *Dual tasks*

It is also worthwhile considering the effect of dual tasks on this experiment. The effects on performance and outcomes have been widely studied (Johnston and McCann, 2006; Gazes et al., 2010) and a common consequence is degraded performance when two or more competing psychological processes take place simultaneously. In this investigation, it is plausible that incongruous information within the guides made following sounds a distinct task separate from the act of reaching. There are a number of consequences from such a conflict. Significant attentional resources would be redirected towards resolving ambiguity between the inconsistent streams of information (resulting in slower reaction times) (Jonikaitis, Schubert and Deubel, 2010). Linear and  $k=1.0$  results can be explained by this model which also accounts for the robust differences in peak velocity. The need to resolve task ambiguity between sound and vision may have caused participants be hesitant and is another explanation for the kink seen in  $k=1.0$  and linear (Figure 3.3). A further consequence of conflicting information streams is that the brain may attend to a single source and abandon the other (Welch and Warren, 1980). In such circumstances the more ambiguous stream(s) tend to be ignored. Scores hint at the possibility then, that in some instances auditory guides were abandoned and vision and/or proprioception relied upon instead.

### 3.6.4 *The influence of vision*

Whilst strong evidence was shown for both peak velocity and arrival accuracy there was ambiguity in the results of the PPV analysis. The ambiguity could be related to the role of vision as an influencing factor in the experiment. Vision monitored the

hand as it reached towards the target giving information regarding progress. Visual memories were also being established based on past experience (Schenka and McIntosh, 2009). These could be used to guide movement and provide accurate target and hand information for up to five seconds after presentation of the goal/target (Westwood, Heath, and Roy, 2003; Miall, Haggard and Cole, 1995). Given the time frame used in this experiment visual memory could successfully guide reaches even if vision was suddenly withdrawn. Both vision (as the target is seen) and visual memory will be contributing to the motor system's reach action plan (Sober and Sabes, 2003) suggesting that acceleration and deceleration phases would already be incorporated into a strategy for completing the reach before initiation (Schlerf and Ivry, 2011, Satori et al., 2011). It is possible therefore that sounds interfere with visual knowledge causing the same conflict problem as discussed before.<sup>24</sup>

The power of visual cues is further revealed by the PPV analysis. Despite a statistical difference found for some guides, participants initiated deceleration within a small time window with PPV scores being closer together compared to the k-values in the guides. For example in the  $k=0.2$  condition, mirroring would produce PPV values close to 0.2 rather than the 0.469 recorded. Whilst it is recognised that small differences in timing can have large effects on movement accuracy, and that the difference between  $k=0.2$  and  $k=0.5$  was significant, results suggest that despite the availability of additional sensory information, the nervous system still produced

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<sup>24</sup> Proprioception also plays a key role in planning and executing movement. Sober and Sabes (2003), have shown how joint angle velocity, muscle contraction etc. are controlled through afferent sensory information from the Golgi bodies, muscle spindles, cutaneous receptors etc. Proprioceptive invariants could also limit the effectiveness of auditory information.

movement with invariant kinematics. This is in agreement with the literature on reaching (Georgopoulos, Kalaska and Massey, 1981; Dounskaia, 2007) and implies vision and visual memory influence aspects of the reach (mechano-proprioception undoubtedly also plays a role here).

Within any motor plan for a reaching action, there are critical values (i.e. a perceived distance) that trigger the deceleration phase (Lee and Reddish, 1981; Kayed and van der Meer, 2000). This is another way in which vision/visual memory may influence movement kinematics. In this study, sounds with deceleration components contained critical values (i.e. the k-value) whereas the  $k=1.0$  and linear sounds did not. In this respect it is unsurprising that guides with ‘heard’ critical thresholds that matched vision/proprioception, outperformed guides where there was none.

A final thought on the role of vision reflects research showing vision dominates auditory information particularly where the auditory stream is ambiguous or of poor quality (Calvert et al., 2004, Sinnet et al., 2007). As using sound to guide self-generated reaches is unusual, and reaching with vision (and proprioception) is heavily practiced, it may be difficult to influence the dominance of these sensory streams. Given this reality, it is all the more notable that two guides influenced the PPV and that strong significance was found for arrival accuracy and peak velocity.

### *3.6.5 Implications, limitations and further directions*

The main implications from this study are directed toward neurological rehabilitation. Augmenting sensory information to improve movement is well-established and auditory stimuli, due to their temporal acuity and close association with the motor system, are particularly useful. The focus of the literature on sensory



augmentation/substitution however, is dedicated to the *outcomes* of rehabilitation programmes. This focus means scant attention has been paid to the qualities or appropriateness of the auditory cues used. The findings from this investigation address this issue and demonstrate how the properties of auditory cues could be used to influence movement kinematics by a clinician. In this respect, guides have the potential to be a low-cost and effective tool for use in conjunction with recognised neurorehabilitation strategies. Not only could on-going, dynamic cues be used in the treatment of neurological disease where goal identification or rhythm comprehension is impaired, but the specifics of a motion could be targeted in movement rehabilitation. For example, speed and periods of acceleration and deceleration could all be adjusted under the guidance of on-going, dynamic sounds for action.

There are a number of unanswered questions that stem from this research. One is that only one method of conveying movement information within the sounds ( $\tau$ ) was tested.<sup>25</sup> It is yet to be established whether other aspects of motor control theory would be equally useful. However, as the sonic guides were effective and because of their simplicity there is no reason, to not use  $\tau$  to plot sounds. Nevertheless, a number of variables can be used to control of movement (for example the vestibular system is sensitive to linear acceleration in forward motion [Day and Fitzpatrick, 2005]). It might be appropriate therefore, to use different variables to encode movement dynamics depending on the patient/motor deficit.

It is well understood dissimilar duration movements engage different control mechanisms (and neural pathways) (Spencer, Ivry and Zelaznik, 2005). In this study all movements are of relatively long duration and clearly have the potential to be

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<sup>25</sup> The linear guide was an alternative type of sound but it was not based on motor control theory.



adapted under sensory feedback. What is not known is how and if alterations are made with continuous auditory feedback in faster actions. For dynamic sounds to be used in a clinical setting this would be important as many functional movements (including reaches) are very rapid. An investigation of this sort may also add to an understanding of the fundamentals and limits of sensorimotor integration.

Whilst tau-guided sounds attempt to mimic an aspect of biological motion, the quality and clarity of this proposition is not known. It would be of interest to test tau sounds against other biologically derived auditory cues (such as sonified movement) for comparison. Similarly, the tone used in the research was artificial (pitch glides were electronically generated). As the human auditory system shows a preference for natural sounds (Moerel, De Martino and Formisano, 2010) a useful line of enquiry would be to test if natural sounds could convey the dynamics of biological motion with greater resolution than artificial sound.

While the reasoning for using pitch makes sense, this experiment did not examine if other sound properties may be superior in conveying motion. An obvious candidate would be sound intensity due to its involvement in looming and environmental motion detection (Neuhoff, 2001).

As discussed, a limitation of the study is the influence vision/visual memory may have exerted over auditory information where guides were ambiguous. To lessen this effect, the experiment would have greatly benefited from a task not requiring accuracy (and thus vision). By excluding vision, the extent to which continuous and dynamic sonic guides influence motion could be advanced. Beyond being a topic of interest in its own right, sound influencing movement without vision is important as in many neurological conditions, visual information is impoverished or absent. The

same arguments also apply to proprioceptive information as peripheral neuropathy is common feature of neurological disease.

The study failed to show that sonic guides influenced the PPV to appear late in the reach (or in other words; to instigate a longer acceleration period than deceleration). This may have been a design flaw as a more ‘meaningful’ late PPV guide may have produced clearer results (for example  $k=0.7$  might be more appropriate than constant acceleration). Manipulating movement trajectories late in the action is important if guides are to be effective for different types of movement rehabilitation. Without this ability, the opportunity to affect a class of movements is lost and the usefulness of continuous dynamic sounds reduced.

### 3.6.6 Conclusions

This study provides evidence that movement kinematics and arrival accuracy can be influenced by auditory cues. Results show improved performance when auditory information is task relevant (congruent). The study reveals task relevancy can be communicated by making the dynamics of a typical motion continually available throughout the sonic guide. In this respect, on-going, dynamic sonic guidance improves motor coordination. The study is the first of its kind to successfully incorporate motor control theory into guides for action. Using the tau margin was found to be an effective way of conveying motion dynamics in sound. With refinement, a precedent has been set for the use of on-going, dynamic stimuli for movement guidance within a neurorehabilitation context.

## Chapter 4 – The Ataxias, Cerebellum and Neural Plasticity

### 4.1 Introduction

In the last chapter the efficacy of using on-going, predictive sounds to influence movement behaviour was demonstrated. The next stage of this research is to address which types of motor problem are most likely to benefit from continuous sonic guides and how these guides are best applied. Due to the cerebellum's role in motor control and sensory processing, cerebellar pathology is a prime candidate for explorations into movement rehabilitation using augmented sensory information. This chapter first describes cerebellar disease (cerebellar ataxia) and the cerebellum, after which ways to improve motor performance through neurophysiotherapy are introduced.

### 4.2 Ataxia

Ataxia, meaning 'lack of order' (Burke and Hammans, 2008) or 'irregularity, confusion and disorderliness' (Berciano et al., 2005), was originally a generic term for the inability to produce well-formed movement. Increasingly it is used to describe

a range of non-specific neurological disorders where the primary aetiology is damage to the cerebellum or sensory systems (Bastian, 1997). At the time of writing there are no known cures and no pharmaceutical interventions, leaving physiotherapy as the sole recourse to alleviate symptoms (Morton and Bastian, 2009). The ataxias are subdivided into two main groups; those that are acquired and those with a genetic aetiology.<sup>26</sup> Due to the lack of rehabilitation options and disease prevalence, this research aims to work predominantly with hereditary ataxia. It is recognised however, that finding cohorts of cerebellar patients presenting with brain injury confined exclusively to the cerebellum is unlikely.

#### *4.2.1 Acquired ataxia*

Acquired ataxias are defined as ataxia in the absence of genetic factors (Klockgether, 2007). The main symptom is usually neuronal damage or degeneration confined to the cerebellum. Three important subgroups have been identified, namely, damage as a result of toxicity (especially alcohol [Sullivan et al., 2000; Manto, 2010]), vitamin deficiency (particularly b<sub>1</sub>/thiamine [Harper, 2006]) and immune response (for example gluten ataxia [Hadjivassiliou, Grünewald and Davies-Jones, 2002]). It is likely that there is considerable overlap between these subgroups as for example, vitamin deficiency often accompanies alcoholism. Other subgroups of acquired ataxia are cerebellar damage following infarction/insult (Jensen and St. Louis, 2005) or ablation (following astrocytoma for example) (Sgouros, Fineron and Hockley 1995).

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<sup>26</sup> A third group of ataxias has recently been identified; mitochondrial ataxia (Lax et al., 2012). The outcome of disruption to mitochondrial DNA strands is similar to that of the nucleic hereditary ataxias.

#### 4.2.2 Hereditary ataxias

The largest group of ataxias are those with a genetic basis. Nosology is difficult as symptoms are often complicated through other parts of the nervous system being involved (Klockgether, 2007). Alongside cerebellar atrophy, common areas additionally affected are the brainstem and spinal cord (Eichler et al., 2011; Lukas et al., 2006). Heritable ataxias are split into two categories, autosomal recessive (for example Friedreich's ataxia [FA]) [Pandolfo, 2012]) or autosomal dominant (i.e. the spinocerebellar ataxias [SCAs]) (Klockgether, 2007; Pandolfo, 2004).

For both recessive and dominant ataxias, genotypic manifestation is trinucleotide repeats (usually CAG for the SCAs and GAA for Friedreich's ataxia) causing dysfunction or absence of important proteins (for example, Ataxin) (Orr, 2012). There are multiple outcomes of disrupted protein synthesis such as cellular demyelination, cell dysfunction or death. At the time of writing, 43 subtypes of SCA have been identified by their molecular aetiologies, each presenting with unique clinical manifestations (Matilla-Dueñas, 2012). This figure will undoubtedly continue to rise as research into the cerebellar ataxias expands. Despite the disparate diagnoses presented above, the main neurological sign for all genetically based ataxias is cerebellar atrophy.

#### 4.2.3 Ataxia symptoms

Cerebellar atrophy manifests in a number of recognised clinical symptoms. The most prominent of these are; ataxic gait/stance, dysmetria (a mis-scaling of action magnitude), dysarthria (slurred speech), oculomotor disturbance and action tremor. Further signs include dystonia (sustained muscle contraction) and muscle spasticity

(Diener and Dichgans, 1992; Manto, 2010). Early signs of the disease are instability when walking and dysarthria. Disease onset and progression differ from diagnosis to diagnosis but in general, symptoms steadily increase overtime. In some cases pathology stabilises but this is rare. Problems of mobility are a particular frustration. This feature of cerebellar ataxia relates to increased postural instability with many affected individuals increasingly relying on walking aides as the disease progresses. In many instances, progression leads to the use of wheelchairs prematurely as a result of falls related to instability. The reality of walking difficulties in ataxia highlights the cerebellum's role in balance maintenance (Horak and Diener, 1994; Van de Warrenburg, 2005). A number of critical processes central to walking ability are relayed through the cerebellar apparatus. These are discussed later in the cerebellar function section.

## 4.3 The cerebellum

### 4.3.1 *Cerebellar anatomy*

The cerebellum develops from the metencephalon along with the pons. Cerebella primordia emerge at 6 weeks as two thickenings from the alar plate (Ten Donkelaar et al., 2003). These thickening form anatomically distinct compartments and give rise to the proliferation of two types of specialist cell, the Purkinje and granule cells (discussed below) (Ten Donkelaar et al., 2003). Purkinje cells originate from the cerebellar ventricular zone whereas granule cells migrate from the caudal part of the rhombic lip (Mizuhara et al., 2010; Wingate, 2001). The two cerebellar primordia later fuse to form the midline known as the vermis. However, vermal fusion is

debated and it has been suggested that the cells of the vermis arise from separate primordia (Louvi et al., 2003). This view is supported by the fact that the vermis differentiates later than the hemispheres and that developmental disease can cause complete absence of the vermis whilst the hemispheres remain intact (Cho et al., 2011).

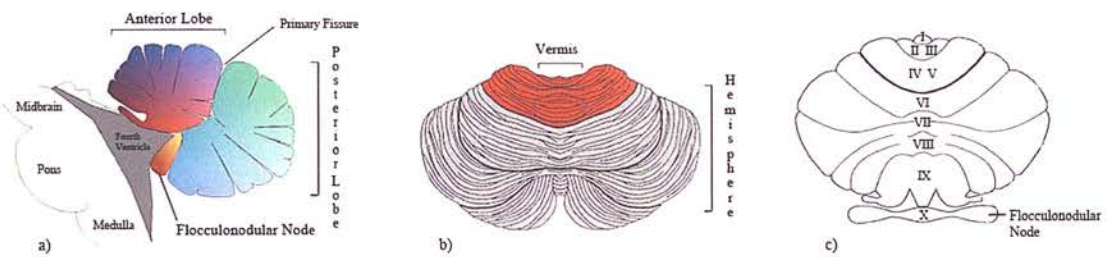
Once formed, the cerebellum sits rostrally to the occipital lobes, above the brain stem. It has changed little throughout its evolution and is unique in having the densest number of cells found anywhere in the brain. The cerebellum is heavily folded onto itself to form a large surface area. If unrolled it would cover approximately the same space as an unravelled neocortex even though only one seventh the size (by volume) (Sultan and Glickstein, 2007). Of particular interest to motor control theorists and neuroscientists is the cellular circuitry of the cerebellum (see Ito, 2011 for review). Cerebellar cells are found nowhere else in the nervous system and have distinct properties and function (Ito, 2002; Boyden, Katoh and Raymond, 2004). The five predominant cell types are; mossy fibres, granule cells (whose long axons are known as the parallel fibres), Purkinje cells, basket cells and climbing fibres.<sup>27</sup> Purkinje cells represent the only efferent pathways of the cerebellum to other brain structures (Voogd and Glickstein, 1998). Afferent, excitatory, mossy fibres connect to granule cells which in turn synapse with inhibitory Purkinje cells (at the parallel fibres of granule cells). This configuration is uniform throughout the structure and gives the cerebellum a unique cytoarchitecture.

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<sup>27</sup> Other cells (for example, Lugaro and unipolar brush cells) are also present in the cerebellum (Colin, Ris and Godux, 2001). For the purposes of this review however, only the most prominent and well-studied cells are presented.



This discovery has led to postulations that the cerebellum performs the same operational function, regardless of sensory input (Wolpert, Miall and Kawato, 1998). The cerebellum is divided into three lobes (anterior, posterior and flocculonodular; see Figure 4.1a) and connects with other brain areas at only three junctures. These are the cerebellar peduncles that relay incoming and outgoing cerebellar pathways to the spinal cord, brainstem and cerebral hemispheres respectively (Granziera et al., 2009). A posterior view of the cerebellum shows the distinct ridge structure of the vermis surrounded on either side by the two hemispheres (see Figure 4.1b).



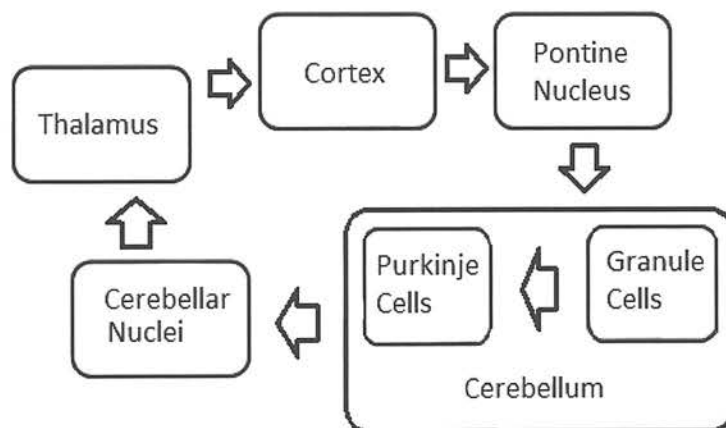
**Figure 4.1 a-c** a) Sagittal view of the brainstem and cerebellum with major anatomical divisions highlighted. b) Posterior view of the cerebellum showing anterior (red) and posterior (grey) lobes and central vermis ridge. c) An unfolded cerebellum showing subdivisions I-X based on Larsell nomenclature (Figures adapted from Grimaldi and Manto, 2012).

The vermis is composed of lobules (labelled I-X), that run rostrally-caudally. Extending from each lobule (anteroposteriorly), are folds of cerebellar tissue (folia) which make up each of the cerebellar hemispheres (see Figure 4.1c) (Haines and Dietrichs, 2012; Musolino, Stoodley and Schmahmann, 2012).

Cerebellar output is relayed to other brain structures via the fastigial, interposed and dentate nuclei deep within the cerebellum, with further efference from the extra-cerebellar vestibular nucleus (Colin, Ris and Godux, 2002). Targets for cerebellar nuclei are the spinal cord and especially the thalamus. The thalamus has many functions but a large amount of input is from the globus pallidus (part of the basal



ganglia), an area crucial in the initiation of voluntary movement (Augustine, 2008). Input to the cerebellum is mediated through two main precerebellar structures, the inferior olive and pontine nuclei. The inferior olive receives afferents from a number of sources such as the spinal cord, reticular formation and from the motor cortex via the red nucleus (Augustine, 2008). The output cells of the inferior olive are the climbing fibres that synapse directly with Purkinje cells (Llinás, 2009). The pontine nuclei are a prominent source of mossy fibres in the cerebellum reflecting the close developmental history between these two structures. The largest amount of input to the cerebellum comes from the pontine nuclei which receives afferents from most of the cerebral cortex and striatum, the primary input of the basal ganglia (Augustine, 2008). Corticospinal tracts also include the pontine nuclei meaning that motor signals being conveyed to the cranial and spinal nerves are also sent to the cerebellum. Reviewing the input-output features of the cerebellum, it can be seen that all primary relay sites are in the brainstem and are involved in reciprocal engagement with proprioceptive centres from the body. Cerebellar connection with motor cortex is



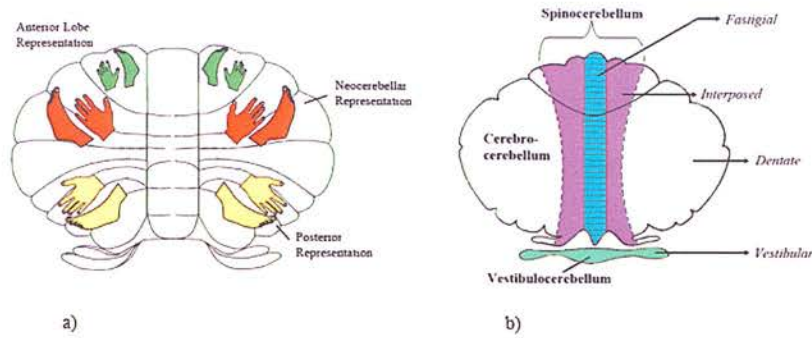
**Figure 4.2** Schematic of the cerebellothalamocortical circuit showing the direction of flow of neural impulses from the cortex back to cortex, via the cerebellum. Adapted from Kelly and Strick, 2003.

well evidenced (see Kelly and Strick, 2003) but it is now clear that the cerebellum connects with prefrontal brain regions not typically associated with motor control (Middleton and Strick, 2001). The input/output described above forms ‘cerebellar loops’ from which cortical signals return to the same areas of cortex (see Figure 4.2). These loops are known to be ‘closed’ making them an ideal mechanism for adaptive control (Strick, Dum and Fiez, 2009; Kelly and Strick, 2003).

#### *4.3.2 Functional anatomy of the cerebellum*

The cerebellum is somatotopically organised with bodily segments represented ipsilaterally (Grodd et al., 2001; Stoodley and Schmahmann, 2008). In some cases, this means that lesion sites can be identified through dysfunction of a particular limb etc. Two topical maps are widely recognised (see Figure 4.3a). However, a full understanding of cerebellar somatotopic organisation is far from complete. Indeed some authors have pointed out that body representation is not contiguous and that body parts are represented in multiple areas (Manni and Petrosini, 2004). These authors propose that a ‘fractured somatotopy’ is a more accurate reflection of cerebellar arrangement. Regardless of this finding it is clear that body parts are mapped to specific areas of the cerebellum and that through time a complete (fractured) somatotopy will be revealed (Schlerf et al., 2010).

The cerebellum is divided functionally in relation to mossy fibre projections to three areas; the spinocerebellum, cerebrocerebellum and vestibulocerebellum (Barlow, 2002). The first two functional zones project to the cerebellar nuclei with the vestibulocerebellum projecting to the vestibular nuclei in the brainstem (see Figure 4.3b).



**Figure 4.3 a and b** a) A schematic of somatotopic representation in the unfolded cerebellum (adapted from Schlerf et al., 2010). b) Functional divisions based on mossy fibre input showing the spinocerebellum (including interposed region), cerebrocerebellum and vestibulocerebellum. Output to cerebellar nuclei is also shown.

#### 4.3.3 Localization from cerebellar injury

Lesions in specific cerebellar zones or cerebellar efferent/afferent pathways, result in predictable behavioural outcomes. The spinocerebellum for example is concerned with maintenance of muscle tone and coordination of muscle activation in response to perturbations of posture. Damage to this area often leads to problems of gait (Fredericks, 1996). The consequences of injury to the cerebrocerebellum are difficulties in learning new sensorimotor skills as well as cognitive and affective problems. Vestibulocerebellar damage leads to nystagmus and instability reflecting this regions input from the vestibular apparatus (Pothier, Ranalli and Rutka, 2011). Global cerebellar degeneration results in bilateral dysfunction affecting limbs and trunk as well as potentially all of the above (Brazis et al., 2012).

There are also sensory consequences from cerebellar injury. Vestibulo-ocular and optokinetic reflex eye movements (VOR and OKR) are disturbed in cerebellar patients, leading to nystagmus and problematic saccadic and smooth pursuit of visual information (Voogd et al., 2012). Vestibular information (other than the VOR) is also degraded following cerebellar damage. This can lead to symptoms similar to those

found in vestibular disease (e.g. vertigo) (Lee et al., 2006). Traditionally cerebellar damage was thought not to impair proprioceptive information. However, research shows cerebellar patients have problems monitoring kinaesthesia (Grill et al., 1994) and deficits in somatosensory input (Restuccia et al., 2007). Given the large amount of sensory pathways returning from the body that terminate in the cerebellum (Frings et al., 2004) these findings are perhaps not unexpected.

## 4.4 Theories of cerebellar function

### 4.4.1 History and development

Due to its distinct appearance and clearly defined limits, the cerebellum has always been considered to perform a specialist function. Study of cerebellar function has a rich history<sup>28</sup> however; the work of Pierre Flourens (1794–1867) is a good place to begin as his observations greatly advanced our understanding of this subcortical structure. Flourens noted that animals with cerebellar ablation and humans with cerebellar lesions are able to generate movement but that it is uncoordinated and equilibrium is affected (Flourens, 1842, in Yildirim and Sarikcioglu, 2007). These observations confirmed the idea that the cerebellum is involved in the *coordination* of the motor system. Gordon Holmes (1876 –1965) built upon this research in a landmark paper of 1917, where he carefully described numerous symptoms observed in First World War soldiers with gunshot wounds to the cerebellum. Looking through Holmes (1917) list of symptoms such as; disturbances of muscle tone, speech, gait,

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<sup>28</sup> Space constraints have led to many important researchers being omitted from this brief history of cerebellar research. Notably missing in no particular order are; Rolando, Golgi, Jackson, Purkinje, Lugaro, Rademaker, Larsell, Babinski, Sherrington, Bolk, and Luciani amongst others.

voluntary movement and tremor, is like reading a modern day textbook of cerebellar function. Holmes also organised cerebellar symptoms following lesion into specific categories raising the possibility of cerebellar localization. Exploration of the structure by Ramon Y Cajal (1852-1934) revealed cellular organisation including descriptions of the Mossy fibres, granule and Purkinje cells (Sotelo, 2008). The impact of Cajal's careful examinations are still relevant today and have inspired a number of further discoveries such as the finding by Mario Ito, that Purkinje cell circuitry produces inhibition in the cerebellar nuclei (Ito, 2012). The theoretical implications of Ito's work motivated prominent models of cerebellar function such as Marr's (1969) computational ideas, and later, Kawato and Wolpert's (1999) forward models (see below).

The anatomical discoveries of the previous two centuries, have led to a degree of certainty about much of the cerebellum's organization and function and a role in movement coordination has been established. Despite this, the mechanisms through which this is achieved are far from understood and a unified theory of cerebellar function is yet to be resolved. Much of the confusion stems from the myriad brain activities that the cerebellum seems to influence suggesting multiple functions. An argument against this reasoning is the uniformity of the cerebellar cytoarchitecture, which is therefore assumed to perform the same operation. However, if the cerebellum does perform a single operation, it would have to account for the cerebellum's role in non-motor functions, the study of which has become prominent over the last few decades (see Strick, Dum and Fiez 2009, for review). The idea of a non-motor cerebellum is not new. Watson (1978) for example, suggested the cerebellum is involved in; emotion, motivation and visual and auditory

discrimination. Nevertheless, a role for the cerebellum in cognitive functioning is still debated. Glickstein and Doron (2008) for example, argue that there are only weak connections between the cerebellum and prefrontal areas and suggest cerebellar activation during cognitive tasks is a result of eye movement planning/execution or damage in other brain structures. Evidence in support of this view is that many of the pathways between prefrontal cortex and cerebellum are involved in motor control (Glickstein and Doron, 2008). However, the behavioural, anatomical and neuroimaging evidence has become so overwhelming that Glickstein and Doron's concerns can be discounted. An early leap forward was the discovery that the cerebellum is connected via the thalamus to prefrontal regions (Middleton and Strick, 1994) (see Cerebellar anatomy above). A surprise finding was the reality of separate output channels serving motor and cognitive functions (Middleton and Strick, 2001). These discoveries were complemented by a plethora of studies reporting cognitive deficits in cerebellar lesioned patients *without motor problems* (Schmahmann, Weilburg and Sherman, 2007). With the advent of better imaging techniques, exploration of polysynaptic as opposed to monosynaptic pathways became possible which have revealed cerebro-cerebellar pathways to be much more extensive than previously thought (Krienen and Buckner, 2009). In addition, techniques such as transcranial cerebellar direct current stimulation (tcDCS) have identified cerebellar activations in a range of cognitive tasks such as verb generation whilst aspects of motor control were controlled (Pope and Miall, 2012). An interesting aspect of cognitive impairments in people with cerebellar lesions is that symptoms are often less acute than when a comparable region of the cerebral cortex is damaged (Stoodley and Schmahmann, 2010). There are parallels here with Flourens' earlier



observation that movement is compromised rather than extinguished, and suggests the cerebellum moderates other brain processes rather than initiates them. This line of argumentation leads back to the question of what exactly the cerebellum does to influence other brain regions? An approach to this question is to examine the structure's evolutionary and developmental history.

The cerebellum is comparable across vertebrate phylogeny whilst at the same time being ecologically and behaviourally adapted (Sultan and Glickstein, 2007). As an example, the parafloccular lobes and lobule VIII of the vermis are greatly expanded in bats as a result of echolocation (Paulin, 1993). An interesting question is why have all vertebrates developed cerebella or cerebellar like structures? One reason could be that vertebrae rely on rapid anticipatory movement for survival (i.e. predation/predation avoidance). The problem of anticipation in motor control was introduced in Chapter 2 and it is here where the cerebellum may be of critical importance. Forward models are proposed to explain how the cerebellum functions to overcome prediction problems but does predictive function extend beyond motor control? It was argued in Chapter 2, that the capacity to act with intention in an anticipatory, goal oriented way develops a sense of agency and allows for communication and social engagement long before cognitive processes are first identified. It was further argued that this eventually leads to the development of core mental functions including language. It is logical then, that if core mental processes are developed as an extension of anticipatory motor behaviour, prediction would also be a quality of these processes. Whilst this is easy to contemplate for processes such as language and attention, it is less obvious for others such as emotion. However, if it is considered that emotions are the outcome of *changes in the body* as a result of

perceived event (Damasio, 2000), it can be seen how internal models would be central to this process. In this interpretation, emotions are an amalgamation of autonomic and somatomotor experiences that must be organised sequentially like any other mental activity (Ito, 2008; Levin, 2009).

An evolutionary quandary is that in humans and apes the cerebellum has expanded rapidly relative to the size of the neocortex. This elaboration started in an ape ancestor long before humans and cortical expansion evolved (Barton and Venditti, 2014). Over the course of human evolution the neocortex has tripled in size (Roth and Dickie, 2005), a fact often cited as a primary factor in human intelligence. So why did the cerebellum disproportionately expand given that movement in hominoidea is not characteristically more complex than other animals? One argument suggests the burgeoning use of tools, and thus fine motor control, is responsible but this explanation does not fit linearly with the order of cerebellar expansion in human ancestry. An alternative proposal is that the cerebellum's involvement in anticipatory behaviour, led to increasingly complex predictions about objects and others in the world with development of mental life being a secondary outcome. Evidence for this viewpoint comes from observing the consequences of disruption to the foetal cerebellum such as in cerebellar hypoplasia, Dandy-Walker malformation or Joubert's syndrome (Bolduc and Limperopoulos, 2009). Behavioural/social problems and cognitive and language delays persist in these examples, often (but not always) with motor signs. The presence of delays and deficits in cognitive development does not sit well with a motor view of cerebellar function and further suggests that the cerebellum is performing an operation supportive of both motor and cognitive abilities. Associations have also been made



between cerebellar dysfunction and autism (Fatemi et al., 2012; Becker and Stoodley, 2013). Unusual social interactions, delays in learning to talk, stereotyped language, echolalia, and problems with empathy could all be explained by an inability to understand expectations, or in other words, to predict (Sinha, 2014). These speculations highlight a predictive role for the cerebellum in organizing brain activity including movement. As noted earlier, forward modelling is one proposal for how the cerebellum achieves this. Before discussing this topic, other hypotheses about cerebellar function are introduced such as motor learning, timing and sensory acquisition/processing.

#### *4.4.2 The cerebellum and motor learning*

The cerebellum as a locus for motor learning was first proposed by David Marr in the 1960's (Marr, 1969). From observations of cerebellar structure, the idea was put forward that co-activation of mossy and climbing fibres adapts synapses between parallel fibres and Purkinje cells. In this model, climbing fibres are hypothesised to act as error detectors and Marr proposed 'motor memory' is stored and altered in this way (Strata, 2009). Experimental evidence supporting the hypothesis was put forward by Mario Ito's group. A number of investigations confirmed synaptic weakening occurs in Purkinje cells if a sufficiently large number of parallel fibres are activated. Additionally, small activations of parallel fibres alter synaptic efficacy but *only* in the presence of concomitant climbing fibre activity (Ito, 1982; Ito, 2011, for a review). These studies were the first to experimentally demonstrate a role for the cerebellum in motor learning. Since then a large body of work has further supported these findings. Ojakangas and Ebner (1992) for instance, took single Purkinje cell

recordings from monkeys during a visual-motor learning task. They reported increased climbing fibre activity and changes in simple and complex spike rate during the learning phase of the (reaching) task. Imaging studies also implicate the cerebellum in motor learning. Increased cerebellar activity has been highlighted during learning of conditioned responses (Bloedel et al., 1997; Blazquez et al., 2003) and in learning motor sequences (Jenkins et al., 1994). In the case of learning motor sequences, cerebellar activity is consistently greater during the early phase of a task (Doyon et al., 2002; Ungerleider, Doyon and Karni, 2002; Penhune and Doyon, 2005). It is suggested action parameters are monitored to inform higher cortical structures during this phase. Based on this instruction, areas of pre-motor cortex are modulated to encode the neural basis for action (Ungerleider et al., 2002). It has also been proposed that sensory aspects of cerebellar output continuously influence motor cortex efference (Daskalakis et al., 2004). Here cerebellar discharge is assumed to refine motor signals to the spinal cord and musculoskeletal system through the integration of sensory information. Evidence for this form of learning in humans is provided by electrical stimulation studies where theta-burst stimulation (TBS) is used to inhibit dentate nucleus output (Popa et al., 2012). As a result enhanced and prolonged plasticity was recorded in the M1 region of motor cortex. A similar conclusion was reached by Galea et al. (2011) who showed that stimulation of the cerebellum results in a problem of adaptive control that effects reorganisation of motor cortex. These studies are interpreted as evidence that learning is the cerebellum's primary concern and behavioural studies do not disagree with this proposition. Vestibular ocular reflex adaptations are disrupted by affecting synaptic transmission between parallel fibres and Purkinje cells (De Zeeuw et al., 1998; Katoh

et al., 2005). In addition, increased Purkinje cell and parallel fibre synapses are reported in rats trained to perform complicated movements, as opposed to normal or non-exercised animals (Black et al., 1990; Kleim et al., 1998). The motor learning hypothesis is still debated however, with the primary reason being conflicting evidence regarding the role of Purkinje cell/parallel fibre synapses. Rats and mice for example, which had LTD blocked *in vivo*, were unimpaired in an eye-blink conditioning test (Welsh et al., 2005). Similarly, Burguière et al. (2010), used mutant mice unable to form Purkinje cell/parallel fibre synapses, to demonstrate learning of stimulus–response associations is not hindered in a water maze task.

#### 4.4.3 *The cerebellum and timing*

If motor learning is governed by cerebellar processes, the correct timing of muscle activations underlying motor behaviour is crucial (Hore et al., 2002; Bastian, 2011). Timing is clearly problematic in ataxia, with patients showing timing-deficient symptoms such as late or early arrival on reaching tasks (Manto, 2009). This observation has led to the hypothesis that the cerebellum (in cooperation with other brain regions) acts as a precise timing device (a ‘neural clock’) for the perception and production of internal/external events (Spencer and Ivry, 2013; Ivry and Keele, 1989). A full understanding of the neural basis of temporal processing has proved difficult to resolve. Nevertheless, a large body of literature implicates the cerebellum in a number of aspects of temporal computation and production. Timing of events within the sub-second range are suggested to be under cerebellar control (Ivry and Spencer, 2004; Lewis and Miall, 2003). Experimental evidence supporting this claim comes from studies into interval timing comprehension. Lee et al. (2007), used

transcranial magnetic stimulation (TMS) to show suppression of cerebellar activity affects time perception between auditory tones (participants perceived intervals as being longer). This effect diminishes for longer duration three-second intervals. The results agree with earlier neuropsychological studies that show cerebellar damage leads to impaired perceptual judgement within the 100-600 millisecond range (Nichelli, Always and Grafman, 1996; Lewis and Miall, 2003). A recent meta-analysis of neuroimaging investigations further supports the notion of independent sub- and supra-second time processing networks. The review identified that basal ganglia and cerebellum are primarily concerned with sub-second timing, whereas supra-second timing mainly engages the prefrontal cortex and supplementary motor areas (Wiener, Turkeltaub and Coslet, 2010).

Whilst there is general agreement that the cerebellum is involved in timing processes there is conflicting evidence as to whether the cerebellum is involved in the timing of *auditory* events. Nevertheless, given its role in sensory processes, it is reasonable to assume that auditory timing falls under cerebellar jurisdiction. Evidence for a cerebellar role in auditory timing perception, comes from studies involving people with cerebellar lesions. Ivry and Keele (1989) showed that cerebellar damage leads to deficits in discriminating periods of silence in the intervals between tones. Using the same stimulus, this finding was supported by Mathiak et al. (2004) using fMRI. One issue with these studies is the stimulus is actually silence rather than tones. Better evidence for cerebellar auditory timing, comes from speech processing research which illustrates activation of cerebellar structures when listening to speech. In German, pronunciation of the words ‘boten and boden’<sup>29</sup> can be distinguished by

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<sup>29</sup> In English ‘boten’ and ‘boden’ mean ‘messengers’ and ‘floor’ respectively.

either the pause between syllables or the annunciation of the 't' or 'd' respectively. Mathiak et al. (2002) showed significant cerebellar activation during the former rather than the latter method of discriminating between these two words. These authors suggest that this is evidence that the cerebellum encodes the durational parameters of speech events. However, other studies suggest a more general cerebellar role in auditory processes rather than auditory timing *per se*. Petacchi et al. (2011) for example, used auditory stimuli (tones presented independently) that had neither an explicit or implicit timing component. It was found that the cerebellum was active regardless of whether timing was needed, suggesting cerebellar involvement in general auditory perception, rather than explicitly timing of auditory events.

The studies above investigated cerebellar involvement in the timing of sensory events but timing of motor acts has also been explored (Spencer et al., 2003; Spencer, Ivry and Zelaznik, 2005). In one study, Spencer et al. (2003) demonstrated that production of a continuous movement during a circle drawing task was not compromised in cerebellar patients. However, when starts and stops were introduced (i.e. participants had to time circle drawing), timing variability increased (meaning task performance deteriorated). The authors concluded that the cerebellum is involved in precise timing of discontinuous movement but is not concerned with emergent timing (such as in rhythmic actions) (Spencer et al., 2003). Imaging research supports this notion with independent neural pathways identified for alternate motor event timing. Coull and Nobre (2008) using a different focus showed basal ganglia and cerebellum are active during explicit event timing whereas implicit

timing involves left-lateralised premotor and parietal cortices.<sup>30</sup> However, there is some controversy around the cerebellum operating as a ‘neural clock’ hypothesis. Bo et al. (2008), using the same protocol as Spencer and colleagues, found no difference in timing variability between controls and cerebellar patients for either continuous or discontinuous movements at the sub-second interval level. Further to this, Harrington et al. (2004) failed to find significant deficits in perception or production of timing intervals using tone intervals and finger tapping in cerebellar patients. However, a negative trend was found during a reproduction task in this study but this was attributed to deficits in other brain processes such as working memory, attention or sensory processing.<sup>31</sup> Further evidence contradicting the neural clock hypothesis is that similar timing deficits are produced from injury to non-cerebellar brain structures. A prime example is sub-second timing interval deficits found in Parkinson’s disease (Harrington, Haaland and Hermanowicz, 1998). Similar problems have been described in attention deficit hyperactivity disorder (ADHD) (Rommelse et al., 2008), although this may have cerebellar component.

#### 4.4.4 *The cerebellum in sensory acquisition and processing*

It has long been recognised, that the largest amount of cerebellar input stems from the various sensory structures located throughout the body (Frings et al., 2004). This input was traditionally viewed as being exclusively used in the control of motor

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<sup>30</sup> In this experiment *explicit* refers to participant’s being asked to attend specifically to task duration. *Implicit* refers to timing emergent from attempting to complete a non-timing explicit task

<sup>31</sup> The authors also reported a correlation between individuals producing a deficit in the time reproduction and damage in the middle to superior cerebellar lobules. See Ivry, (2000) for a criticism of this study.

events. This view holds that the cerebellum acts as an integration centre for sensory input and motor output (Bower and Kassel, 1990). More recently, descriptions of cerebellar sensory function have been expanded. Some argue the cerebellum's primary function is to acquire sensory information for general brain activity (Gao et al., 1996; Bower, 1997; Jueptner et al., 1997; Nixon, 2003). This view proposes that the cerebellum is not necessary for a specific behavioural function, but rather supports other brain functions through optimising the collection and quality of sensory input. For example, keeping the gaze of the eyes in the centre of the visual field is important in walking. As described above, this is achieved through cerebellar control of the VOR. In this example the cerebellum operates to ensure the optimal sensory information (vision) is acquired to support the task (walking). A further appeal of the sensory acquisition theory is that it explains a puzzling aspect of cerebellar disease. That is, the peripheral motor system (muscles, nerves etc.) and motor cortex are functionally intact and yet movement is still grossly impaired. This paradox can be explained as insufficient sensory information being acquired for predictions about future states.

The cerebellum is also involved in sensory *processing*. Early evidence supporting this view comes from anatomical studies conducted in the 1970s. The cerebellar tract and cerebellar hemispheres for instance, were found to become active in response to cutaneous stimulation (Shambles, Beermann and Welker, 1978). Later, cerebellar pathways were identified that are not overtly necessary for solving motor control problems. Huang, Liu and Huang (1982) for example, mapped an auditory pathway from the cochlea to the cerebellum. Other physiological studies added to these findings by showing cerebellar activation in the absence of motor activity such as



taste (in animal models) (Hanamori and Ishiko, 1987) and olfaction in humans (Sobel et al., 1998). The latter two findings are important as they are examples of sensory processes where time is not a factor and are also clearly not needed for motor control. Expanding on these findings, and of particular significance to this thesis, is the finding that the cerebellum is not active when moving without sensory discrimination (Gao et al., 1996). Using rapid finger movements to manipulate objects, these experimenters found the dentate nucleus<sup>32</sup> did not respond when digits were moved in isolation.<sup>33</sup> In contrast, when participants used fingers to discriminate between objects (i.e. used tactile sense), the cerebellum became highly active. Further studies support this work, for example, Jueptner et al. (1997) used positron emission tomography (PET) in conjunction with electromyography (EMG), to highlight cerebellar activation during simple flexion and extension at the elbow. After making an initial arm flexion through 90° (an active movement), a motor was then used to manipulate the arm along the same trajectory (the passive movement). EMG recordings confirmed little activity in biceps or triceps during the passive condition. However, for both passive and active movement, a similar level and locus of cerebellar activation was recorded. A direct comparison of passive and active movement revealed only 12% of neuronal activity was attributable to the active condition. Further evidence for sensory processing in the cerebellum can be found in anatomical studies on animals. In an interesting review by Paulin (1993), cerebellar morphology was compared across many mammals and found not to be structurally

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<sup>32</sup> The dentate nucleus is the sole locus of cerebellar hemisphere output (via Purkinje cells). See section 4.3.1 above.

<sup>33</sup> The authors report low levels of cerebellar activation during this condition. However, this activity was attributed to proprioception stemming from contact with the object as in cutaneous stimulation (Shambles, Beermann and Welker, 1978) rather than finger movement).



consistent with the idea of a brain region concerned primarily with motor control. Of particular interest was the cerebellar homology between animals using echolocation to navigate the environment, such as bats and cetaceans. Both the parafloccular and medial lobes are greatly expanded in these species despite dissimilar body physiology and moving in distinctly different ways<sup>34</sup>. As Paulin (1993) notes:

*“When the cerebellum of microbats [and cetaceans] is compared to other mammals, the pattern of relatively enlarged areas is almost exactly the opposite of what would be expected under the assumption that cerebellum is dedicated to control and coordination of movements.”*

(p.45)

That the cerebellum is predominantly concerned with sensory processing in these animals makes the notion of a corresponding function in humans appealing.

However, the idea of the cerebellum as a purely sensory acquisition and monitoring device is controversial. Block and Bastian (2012) for example, used reaching to show cerebellar patients perform as controls during a sensory realignment task (between visual and proprioceptive information). When a motor component was introduced participants’ movement was impaired. This was taken as evidence of a cerebellum primarily involved in motor control rather than sensory processing.

For both the timing and motor learning theories described in this chapter, accurate sensory information is important. Separating motor and sensory components is an issue for all motor research as the act of moving produces an abundant amount of sensory information (Lee, 2005; Synofzik, Lindner and Thier, 2008). With this in mind, it is possible several investigations into cerebellar function could be

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<sup>34</sup> Thrust is almost entirely generated in the ‘lower limbs’ (or thorax) of sea dwelling mammals whereas bats exclusively use the upper limbs for flight.

reinterpreted within the framework of sensory impairment rather than timing or motor learning deficits (Paulin, 1993; Harrington et al., 2004).

#### *4.4.5 Models of cerebellar control*

The involvement of the cerebellum in motor behaviour has made it a central feature in attempts to model movement. An important question for motor control theorists is how predictive information is incorporated into the motor system (see earlier and Chapter 2). As suggested, it is proposed that a primary function of the cerebellum is to make prediction about the outcomes of mental activity. One way this achieved is through the generation of internal models which are generally applied to motor control but can also equally explain mental functioning (Levin, 2009). Two forms of internal model have been described; feedforward and inverse control (see section 2.7.2 for a discussion) and the cerebellum is implicated as the neural structure involved in both (Bastian, 2006; Wolpert, Miall and Kawato, 1998). The interest in the cerebellum as the location of internal models is in part driven by the reality that such a function accounts for many of the timing, learning and motor deficits seen in cerebellar pathology.

Evidence for cerebellar internal models comes from investigations into reaching. In force-field studies, cerebellar patients perform poorly when adapting reaching behaviour under the influence of the field (Maschke et al., 2004). In these investigations, learning aftereffects from adjustments made under perturbed reaching space, are also absent in these patients (as opposed to controls). This finding is interpreted as an inability of the cerebellar groups to generate internal models of the task. Internal models are also implicated in larger scale actions such as walking

(Bastian, 2006; Morton and Bastian, 2006). In an ingenious study, these authors used split-treadmill apparatus to produce different walking speeds for each foot. Whilst not impaired when the asymmetric belt speeds were introduced (described as reactive adaption) cerebellar patients were impaired in predictive aspects of the experiment.<sup>35</sup>

There have also been speculations about the physiological underpinnings of internal models in the cerebellum. It has been proposed that Purkinje cell output represents internal models that are then relayed to higher brain centres (such as the motor cortex) (Ebner, Hewitt and Popa, 2011; Wolpert, Miall and Kawato, 1998). In this model climbing fibre activity is assumed to contain the motor error signals used to modulate output (Imamizu and Kawato, 2012). However, Ebner and Pasalar (2008) documented Purkinje cell spike activity in monkeys performing a circular drawing task in both viscous and elastic force fields. Recordings showed that Purkinje cell activity was largely unaffected (91% of cells) by the introduction of force fields. The authors argue this finding is not consistent with the idea of Purkinje cell spike rates registering an inverse internal model in the cerebellum. Instead, it was proposed that the cerebellum ‘generates predictions of the future state of the system as the kinematic consequences of motor commands’ (Ebner and Pasalar, p.3).

The idea of future states is important in forward modelling. Transmission delays in the sensorimotor apparatus mean the status of the peripheral motor system can never be known (in real-time) (Miall and King, 2008). At the same time recent motor commands will not have reached the musculature. Without an accurate estimate of the state of the periphery, movement is likely to be dysmetric (imagine taking a step

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<sup>35</sup> Reactive adjustments were triggered by feedback mechanisms (such as the acceleration of one of the belts). However, other aspects of the task required feedforward control such as the time both feet were on the treadmill, coordination of phase between legs and step length.

where the start position of the foot is incorrectly interpreted). It is suggested then that motor commands incorporate a *prediction* of the state of the system based on its last known state (Miall et al., 2007). Support for the cerebellum as a state estimator comes from TMS studies that show delays in current state estimates match those found in neural transduction rates in the sensory-motor system (100-300 ms) (Miall et al., 2007; Molinari, Restuccia and Leggio, 2009). In the Miall et al. (2007) study, following TMS stimulation to the ipsilateral cerebellum, directional errors in a reaching task were shown to reflect a motor command 138 ms out-of-date.

The studies presented above suggest cerebellar involvement in internal models manifests in two ways; generation of forward models that include state estimates of the peripheral system and the monitoring of on-going movement.

## 4.5 Brain plasticity

One of the most significant developments for rehabilitation in recent decades is the understanding that the brain undergoes a large amount of reorganisation in response to injury. This is achieved through a number of mechanisms. A primary response to injury is a change in gene expression for various neurotrophins such as nerve growth factor (Lindvall et al., 1994). The increase in neurotrophins initiates a number of repair mechanisms that collectively can be described as brain plasticity.

A primary way the brain responds to damage is to recruit alternate brain regions to assume the functions of the damaged area (Huttenlocher, 2002). Regions adjacent to lesion sites that play a support or associative role become 'unmasked' meaning that they become more active or adopt function of the damaged area (Elovic, Baerga and

Cuccurullo, 2004). Zones distant (or even contralateral) to lesion locations, can also acquire function following injury as evidenced in both animal and human studies. Axelson et al. (2012) for instance, describes contralateral motor cortex reorganisation in lesioned rats. These animals display a distinct pattern of recovery where neural activity first appears in tissue adjacent to the injury (ipsilaterally), followed by activity in both hemispheres. After recovery reaches a peak, motor cortex activity is seen solely in the contralateral hemisphere. Both imaging and TMS studies have confirmed distant cortical reorganisation in humans following stroke (Dimyan and Cohen, 2010; Gerloff et al., 2006). The degree to which reorganisation occurs is dependent on a number of factors. Of critical importance is the amount of residual undamaged tissue. Clearly, greater neuronal volume makes recovery and reorganisation less challenging (Klob, 1999). Existing tissue allows for a level of functionality to be maintained meaning access to facilitatory activity is preserved. However, whilst profound nervous system damage limits the opportunity for functional improvement, elements of recovery are still possible. Examples in animal models show motor recovery after complete ablation of brain areas. Monkeys for example, partially regain upper and lower limb function following hemispherectomy (Burke, Zangenehpour and Ptito, 2010). A similar principle has been established in humans where children are known to recover the rudiments of speech processing and production following left hemispherectomy (Boatman et al., 1999).

A well evidenced form of brain reorganisation is the reattribution of sensory processing in the absence of a specific sensory input also known as cross-modal plasticity. Perhaps the best known examples of this phenomenon are the reassignment of tactile or auditory processing. Visual cortex for example, responds to

auditory stimuli in congenitally blind individuals (Burton, 2003) and to tactile input in sighted people that have lost vision (Merabet et al., 2008). The reorganisation of sensory processing brain areas reflects the unified nature of sensory information once it enters the nervous system. Two aspects of sensory input (in the visual, tactile and auditory domains) are the spatial and temporal components of a behavioural task. It has been shown that these are represented or ‘mapped’ at the neural level (Kilgard et al., 2001). Like any other neural network, these representations are open to modification through experience. Given the interrelated nature of perception and action, it makes sense that changes in the sensory features of a behavioural task evoke plastic changes in the networks associated with that behaviour.

Cortical reorganisation is important in functional recovery and its basis is changes in patterns of neural firing between networks of neurons. The predominant mechanism through which neural behaviour is adapted is through synaptic plasticity (Huttenlocher 2002; Baker and Roth, 2004).

#### *4.5.1 Neural plasticity*

Neuroplasticity is an umbrella term for a number of processes where neurons, or networks of neurons, adapt behaviour and/or physiology under the influence of intrinsic or extrinsic environmental influence (Selzer et al., 2006; Huttenlocher 2002; Møller, 2006). Through repeated exposure to a set of stimuli, excitability or inhibition of a neuron becomes either facilitated or suppressed. Neuronal behaviour is transformed through synaptic, morphological or genetic means but all represent the interface between intrinsic and extrinsic experience. In this regard alterations in neural behaviour are experience-dependent (LeDeoux, 2003). That neural plasticity

is experience-dependent suggests that the converse is also true. If neural pathways are not used, synaptic weakening occurs, also leading to adaptive changes. This is known as the ‘use it or lose it’ principle (Kleim and Jones, 2008; LeDoux, 2003).

Synaptic plasticity can be either short- or long-term. Short-term plasticity is described as alteration in synapse efficacy, lasting within the millisecond to seconds range (Neher, 2007). Because of the rapid decay period, short-term plasticity is found to play a role in computation, working memory and decision making processes (Deng and Klyachko, 2011). Long-term plasticity on the other hand, is a mechanism through which long lasting neuronal adaption occurs (Ledoux, 2003; Huttenlocher 2002; Møller, 2006). Long-term plastic changes by definition do not decay quickly and are semi-permanent (i.e. they are “soft wired”). Both long and short-term plasticity are evoked under a number of conditions. Firstly, a single large pre-synaptic activity burst between two or more neurons, initiates changes at the synapse. Secondly, the same outcome is achieved through smaller but repeated presynaptic activation over time. Both mechanisms are examples of Hebbian principles, which state that firing coincidence between cells is the predominant driver of change at the synapse (Bear et al., 2007; Wolters et al., 2003). The most studied mechanisms of synaptic plasticity are long-term potentiation (LTP) and long-term depression (LTD) (Pedotti and Donoghue, 2003). LTP involves synaptic strengthening in the presence of stimulation whereas as LTD involves synaptic weakening. Both synaptic responses are available within individual cells of the nervous system (Bliss and Lømo, 1973).

Other experience-dependent cellular responses are increases in synapse quantity, greater dendritic arborisation, axon growth and although rare, neurogenesis (Møller,



2006).<sup>36</sup> These mechanisms are the nervous system's main tools in both learning and recovery from injury with a plethora of animal and humans studies amply confirming the plastic nature of the brain (Merzenich, et al., 1984; Møller, 2006; Dobkin, 2005; Baker and Roth, 2004; see Greenwood et al., 2005, for review). However, the same mechanisms that result in positive changes in neural behaviour also apply negatively. This is termed maladaptive plasticity and examples are over-exercising a particular action or adapting compensatory responses to physiological impairment (Takeuchi and Izumi, 2012). Maladaptive plasticity has been implicated in motor problems as diverse as repetitive strain injury, phantom limb pain and dystonia (Neychev et al., 2008; Quartarone et al., 2003; Flor, 2008).

#### *4.5.2 Neural plasticity in neurological disease*

The neural plasticity discussed above focuses on brain responses after acute nervous system injury. Consideration of degenerative disease however, is more complex. Animal research indicates greater function is preserved when lesion formation is slow as opposed to acute (but both resulting in the same damage) (Desmurget, Bonnetblanc and Duffau, 2007). It is argued that slow decline gives the brain time to gradually reorganise and form new neural pathways. However, these studies use localised, artificial lesions where neural damage abates. In nervous system disease this is not the case and continual neural degeneration is typical. In addition neurological pathology tends to produce diffuse, global patterns of neural damage. It is likely then, that at some point, the rate of proximal cell recruitment will be

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<sup>36</sup> The degree to which neurogenesis occurs is still a matter of some uncertainty. Traditionally it was assumed that the brain produced no new cells after maturation. However, more recent findings have confirmed that under certain conditions, the brain undergoes neurogenesis following trauma (see Ming and Song, 2005, for a review).



overtaken by the rate of cellular degeneration. This is supported by the reality that in some cases of neurological disease, as much as 80% of neurons show signs of injury before symptoms appear (Gibb and Lees, 1988). It is feasible that the delay in symptoms reflects function being preserved (or reorganised) until a threshold is reached where adaptive processes are no longer able to compensate. The effects of diffuse nervous tissue damage on functionality can also lead to accelerated symptomology. Diffusion leads to more brain regions being affected and thus greater difficulty in performing rehabilitative acts. This is particularly true where disease affects mobility, as the cost of attempting to engage in rehabilitation (e.g. potentially dangerous falls), further inhibits functional activity.

#### *4.5.3 Neurophysiotherapy*

Despite the clear complexities in treating pathology of the nervous system, a large body of evidence has been accumulated that presents a positive (if mixed) picture of physical intervention. Whilst no ‘cure’ for any neurological disease is known, physical therapy has been shown to improve quality of life and potentially slow pathology in Parkinson’s disease (Keus et al., 2010), cerebral palsy (Ketelaar et al., 2001) Huntington’s disease (Bilney, Morris and Perry, 2003) as well as sporadic reports in cerebellar ataxia (Ilg et al., 2010). Positive responses to treatment suggest successful instigation of neuroplastic principles.

A major challenge for neurorehabilitation is to develop techniques that can exploit the powerful biological mechanisms underlying recovery. Neurophysiotherapy differs from physiotherapy in that its focus is to exploit neural plasticity (rather than healing/strengthening bones, muscles etc.). Despite this distinction, the two

approaches overlap considerably and produce identifiable criteria for maximum recovery. Criteria identified as important are: actual and adaptable performance of the motor problem, repetition and functionality. Physically performing the actual task is primary, as Møeller (2006) states:

*“Physical training is an effective means to promote neural plasticity that can compensate for loss of function and reduce the symptoms associated with injuries to the nervous system.”*

(p.16)

However this statement does not reflect the difficulties of physical training for those with nervous system pathology (Ward and McIntosh, 2003). Movement is typically poorly executed and often requires compensatory actions. A complication from training in a compromised way is that unwanted factors can be engaged and become permanent features of movement behaviour. As described earlier, all movement has an underlying neuronal basis and that includes compensatory movement where maladaptive neural pathways can form and hinder recovery (Takeuchi and Izumi, 2012). Not being able to perform an action has been recognised in the rehabilitation field where the advent of mechanical and prosthetic aids, as well as sensory and environmental manipulations, is common. These manipulations attempt to ensure whole actions, with the complete range of motion, are engaged. Neurorehabilitation techniques also confront ‘learned non-use’ (where a patient stops using a limb etc.). One such technique is constraint-induced therapy (CIMT) where, in hemiplegia for example, the non-affected arm is restrained forcing the impaired arm to be used (see Charles and Gordon, 2005, for review).

Essential to relearning any movement is repetition over time (Classen et al., 1998; Winstein, Wing and Whittall, 2003). Repetition is central to encouraging long-term plasticity and forms the basis of all neurophysiotherapy programmes (Nudo et al., 2000). However, simple repetition is not enough to evoke permanent changes in motor behaviour (French et al., 2007; Winstein, Wing and Whittall, 2003). Instead movement should be repetitive *and adaptable*. Although this appears counter intuitive, it signifies that the basic skill (and form) underlying action should be developed and applied in different scenarios.<sup>37</sup> For example, to practice reaching objects should be of different sizes and placed at alternate distances etc. As Winstein and Stewart (2006) suggest:

*“It is this ability to adapt that provides an individual with the capability to perform a task over time ([and induce] relatively permanent change).”*  
(p.92)

Having to adapt encourages participants to produce appropriate motor solutions to novel movement problems and an extension of this is making exercises increasingly difficult to counter the effects of learning plateaus (Winstein and Wolf, 2009). As Nudo et al. (2000) argue, it is learning that drives plasticity and therefore, challenge should continually be introduced.

Functionality is another important component of successful movement rehabilitation (also known as task-specificity [Winstein and Wolf, 2009]) (Shepherd, 2001). Functional rehabilitation bases ‘exercises’ on tasks that are meaningful for the client. One way of achieving this is to incorporate real-world applications into training

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<sup>37</sup> See Chapter 3 for a discussion of the invariant kinematics produced in different reaching behaviour.

programmes (French et al., 2007). The benefits of functional, as opposed to undirected exercise, are known for walking, reaching and balance rehabilitation (Langhammer and Stanghelle, 2000; Rensink et al., 2009). There are a number of reasons why this may be so. Motivation is one factor which is arguably increased by including goals that reference real world activity. Psychology may play a role as it is arguably more satisfactory to lift a cup of tea without spilling, than to complete ten repetitions on a weight machine. In addition, attention may be more focused when exercises are relevant to the individual. Finally, since the human brain has evolved in interaction with the environment, and for interacting within that environment, it could be argued that functional exercises preserve the natural coupling between perception and action. This places functional activity within the framework of ecological perception and Gibson's ideas of affordance in the environment (Gibson, 1979/86). Performing a task within its natural environs evokes responses in a variety of brain areas associated with that task. In the example of lifting a cup of tea without spilling, drinking is afforded to the observer and with it, the time-correlated multimodal experiences of the act (e.g., seeing the cup, smelling the tea, movement towards the cup, feeling the cup in one's hand, tasting the tea). That a single stimulus initiates many different responses is recognition of the reality that one-to-one structure-functions are rare in brain circuitry. Instead structure-functions are characterised by many-to-one relationships which has been termed 'degeneracy' (Noppeney, Friston, and Price, 2004). Degeneracy has been recognised since early observations that remote brain areas undergo synaptic weakening with damaged brain regions (a phenomenon known as diaschisis) (Finger, Koehler, and Jagella, 2004). To keep a task functional then is a way to activate task related networks of

neurons and to increase the potential for recovery in individuals who have an associated brain area affected.

#### 4.5.4 *Neurophysiotherapy and ataxia*

As mentioned, a key factor in neurorehabilitation is repetition of adaptable form. For people with ataxia, it is clear that cerebellar damage makes well-formed, repeatable actions difficult, thus reducing the prospect of evoking plastic mechanisms. For those with severe ataxia, falls, injury and objects being knocked or dropped may lead to mistrust of the body. Under these circumstances it is likely that movements will be performed tentatively, without full range of motion and compensatory strategies will develop. Severe ataxic symptoms may also reach a stage where performance of ‘real world’ exercise is restricted. These factors suggest that failure to respond to treatment is related solely to the functional properties of the cerebellum. Timing and/or sensory deficits are likely to obscure movement goals making repetitive and well-formed motion difficult (Bower, 1997; Ivry, Keele and Diener, 1988). Movement start and termination in particular would be compromised. A cerebellar role in motor learning would also confound rehabilitation (Strata, 2009). Here the very mechanism necessary for recovery of well-formed movement is impaired. However, there are limited reports of successful rehabilitation after cerebellar stroke (Kelly et al., 2001) and in cerebellar degeneration (Martin et al., 2009; Ilg et al., 2007; Čakrt et al., 2012). Nevertheless, few ataxia rehabilitation studies have attempted to take into account the nature of the deficits associated with cerebellar dysfunction (this is discussed further in Chapter 5).

In review, this chapter has introduced the basic anatomy and function of the cerebellum. It also has identified the key strategies that should be used for successful neurorehabilitation. Exercises should be conducted with adaptable form, account for the fact that the central mechanism for timing and sensory monitoring may be faulty, and provide prospective information (a goal) that might be otherwise obscured. Ideally this information will be delivered through an unimpaired (or less impaired) modality. The best candidate would be a modality not typically involved in the sensory guidance of bodily actions, and thus potentially less affected by cerebellar ataxia. That modality is the auditory system. The focus of the next chapter then is to test on-going, dynamic sounds in a clinical population with cerebellar ataxia.

# Chapter 5 – Experiment 2: Swaying with Sonic Guides in an Ataxic Population

## 5.1 Introduction

Experiment 1 demonstrated that the kinematics of a reaching action can be influenced by manipulating the properties within a guiding sound. More specifically, by making sounds continuous and prospective, the position of the peak velocity, the velocity of approach and coordination of the hand with the end of sound at the target can be altered. The next step in this thesis is to test if providing additional sensory information improves motor control in a clinical population. As the cerebellum may be involved in the predictive aspects of sensory processing and motor behaviour, movement problems as a result of cerebellar disease may in particular benefit from auditory guides of this nature. The present study then, investigates the influence of continuous auditory guides on movement control in cerebellar ataxia. To do so, sonic guides were developed for the action gaps of neurophysiotherapy balance exercises. The exercises consisted of displacement (weight-shifting/sway) of the body in the medial-lateral direction with the aim of improving motor control as assessed by movement smoothness. Smoothness was measured by recording the rate of change in acceleration or ‘jerk’ (Hogan and Sternad, 2009). The experimental task was to

perform the neurophysiotherapy exercise with or without sonic-guides. Sonic-guides were based on the changing tau between the start and end of each exercise. Following the results of Experiment 1, all sonic guides were programmed with k values of 0.5. In a second part to the experiment, participants mentally rehearsed sonic guides and coordinated swaying to them as if the auditory guides were playing. As the cerebellum may impair motor imagery, auditory imagery learnt in association with the swaying was tested instead. Jerk was again used as an estimate of how fluently participants were swaying. This chapter also discusses the inappropriateness of using the  $\tau_G$ -equation (Lee, 2005, see section 2.8.3) to analyse the data produced in this study.

## 5.2 Recovery of balance skill

The ultimate goal of this thesis is to improve movement control in ataxia. In cerebellar disease, the movement issue that impacts quality of life the most is difficulty in walking.<sup>38</sup> At the root of walking complications in ataxia are difficulties of balance (Diener and Dichgans, 1992; Morton and Bastian, 2007). For this reason the exercises chosen for this study targeted core balance skill.

### 5.2.1 Exercises to improve balance

Balance rehabilitation techniques focus on controlling displacement of the centre of mass (COM) in relation to a ‘felt’ stability boundary (Haddad et al., 2006). In neurological disease, limits of stability are often overestimated (Kamata et al., 2007).

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<sup>38</sup> Participants were interviewed to discuss the impact of ataxia on their lives before testing.



To create instability is one way the COM can be altered to initiate adaptive motor control responses. The method is the bedrock of many balance retraining programmes such as those developed to reduce falls in the elderly (Chang et al., 2004; Bieryla and Madigan, 2011). Balance boards (Gieger et al., 2001; Diracoglu, 2005), uneven surfaces (Rose, 2011) or tilting platforms (Maurer, Mergner and Peterka, 2006) are used to generate instability and force adjustments in and control of the COM. The suggestion is that by engaging relevant muscles, experiencing the forces produced by motion and challenging stability limits, ‘body awareness’ is increased and motor control improved (Chang et al., 2004; Diracoglu, 2005). Exercises that challenge stability also force participants to adapt to altering kinematics. This is a feature of normal movement behaviour that can be practiced (see section 4.5.3). For example when walking, distance, speed and accuracy of foot placement, differs from step to step meaning inertial forces (and movement kinematics) are different at alternate points in the stride (Rose and Gamble, 2005). Taking a step forward generates momentum in the posterior direction which must be controlled before the next step. Here ‘sway’ is created primarily in the anterior-posterior axis. Once in motion, COM is transferred over the weight bearing leg creating sway in the lateral axis (Rose and Gamble, 2005). Practicing control of sway in medial-lateral and anterior-posterior directions therefore, is a useful exercise for balance and walking recovery. Ideally practice would be realised through walking but for many, due to incapacity following degenerative disease, this is not possible. However, weight-shifting in a static position mimics several of the forces experienced during ambulation whilst stability is far greater and falling less likely. Static stance then can be used to explore full range of motion in relation to a sensed

stability boundary. In addition, the forces generated can be exaggerated (i.e. by swaying faster and further) which can potentially lead to an increased training effect.

### 5.2.2 *Swaying to encourage plasticity*

Swaying can be used to follow the principles of neurophysiological rehabilitation and encourage neural plasticity (see section 4.5.1). Weight-shifting is simple to repeat but produces enough variability to not be stereotypical. From one sway to the next fluctuations in distance and speed of motion mean the mover has to adapt to maintain balance. As in experiment 1 (Chapter 3), adaption in a healthy adult would mean movement form remaining similar regardless of the scale or dynamics of the action.<sup>39</sup>

Swaying can also be easily modified to increase task difficulty. If support is used for example, it can be gradually reduced until swaying is unassisted. Alternatively, feet can be brought closer together to limit the base of support and increase instability. Shifting body mass is also functional as sway is a feature of all movement activity especially during upright tasks (such as running or walking). Being upright engages all the relevant muscle groups and sensory systems involved in balance maintenance. This engagement is as opposed to physiotherapy techniques where movement is broken down into components such as practicing weight-shifting either sitting down or when on the knees.

That swaying is repetitive, adaptable and functional means that as an exercise it overlaps with other effective rehabilitation techniques (for example Proprioceptive

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<sup>39</sup> In the reaching experiment, it was predicted that invariant kinematics would be produced for the reach. Similarly, invariant kinematics are likely to be produced by swaying actions. For example, a bell-shaped velocity profile would be produced if motion was recorded from the sternum angle.

Neuromuscular Facilitation (PNF) or Bobath therapy<sup>40</sup>). Shifting body mass is also part of coordination training often in conjunction with other physiotherapy such as strength training etc. (Lange et al., 2010).

### 5.2.3 *Swaying with cerebellar ataxia*

To sway efficiently requires adequate sensory input. Unfortunately, in cerebellar disease sensory deficits are well documented (see section 4.3.3) (Bower, 1997; Jueptner et al., 1997). Visual, vestibular and proprioceptive deficits affect the capacity to sway effectively in a controlled manner and in severe cases, the ability is completely disrupted. Compromised somatosensory feedback is particularly problematic as the predominant sensory information for controlling weight-shifting is articular information from the body. Receptors at the ankle and knee joints are especially important in regulating balance (Lephart, Pincivero and Rozzi, 1998). Sensory disruption then could be a main cause of inability to access rehabilitative exercises and for the well-documented difficulties in motor rehabilitation in people with cerebellar disorders (e.g. Martin et al., 2009). That compromised sensory experience may play a role in cerebellar disease raises the question; can augmenting or substituting impoverished sensory information improve motor control? This question is the main focus of this experiment.

### 5.2.4 *Enhanced sensory information in ataxia*

Using additional sensory information in neurorehabilitation has been established over

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<sup>40</sup> PNF emphasises complete range of motion and ‘real world’ purposeful activity (Bradley et al., 2007). Parts of the ‘new’ Bobath concept encourage functionality. However, in both literature and practice, there is considerable confusion as to what constitutes Bobath therapy (see Tyson et al., 2009 for review).

a number of years (for example, Thaut et al., 1998; Feys et al., 2006). Nevertheless, studies that augment or substitute sensory information in cerebellar disease are limited. Biofeedback in the form of visual feedback from the transformed output of a posturography platform (which records perturbations of the body), has been used to show people with ataxia improve on a range of dynamic exercises (Jobst, 1989). However, this study included individuals with extra-cerebellar brain disorders/insults (e.g to the brainstem or vestibular apparatus) and is not known to what extent results apply specifically to cerebellar disease. Other studies show, either directly or indirectly, that augmenting sensory information in ataxia may be beneficial. Crowdy et al. (2000) for example, demonstrated that looking at foot placements and mentally rehearsing stride before stepping causes individuals with cerebellar ataxia to walk with less variability. In this study, looking and mentally rehearsing can be thought of as additional visual information. Novel techniques, such as wearing Lycra garments, have been proposed and are currently the topic of investigation (Cassidy, Kilbride and Holland, 2009). Wearing tight fitting Lycra increases stimulation of skin receptors potentially increases somatosensation and physically reduces tremor by constraining muscle activity. The technique has been applied successfully in other neurological conditions such as cerebral palsy where improvements in proximal stability have been recorded (Nicholson et al., 2001). A recent study used an electrotactile device<sup>41</sup> placed on the tongue to give balance feedback to people with cerebellar ataxia. The tactile device delivers electric pulses to the tongue's surface in relation to the position of the head and it was found that the alternative sensory input

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<sup>41</sup> This is the BrainPort device designed by Professor Paul Bach-y-Rita's laboratory. It has been used in various settings to improve sensory feedback (Bach-y-Rita, 2004).

improves static balance (Čakrt et al., 2012). Investigations such as these, demonstrate the feasibility of augmenting sensory information in cerebellar disease. As yet however, the auditory system has never been used as a method to do so. Further to this, guides based on a motor control variable have not been tested in ataxia or any other clinical population and this study is the first to do so.

### 5.3 Auditory stimuli and ataxia

Chapters 2 introduced the relationship between sound and movement and the usefulness of sound in conveying on-going, dynamic information. However, using auditory stimuli in ataxia may be problematic as some forms of the disease present with hearing loss<sup>42</sup> (Hoche et al., 2008) indicating cerebellar involvement in auditory processes. In fact a number of studies convincingly show that the cerebellum is active in both passive listening and pitch discrimination (Wolfe, 1972; Petacchi et al., 2011; Parsons et al., 2009). Parsons et al. (2009) demonstrated that cerebellar damage leads to problems discriminating between higher or lower pitches presented independently. However, in most cases of cerebellar disease (and particularly in the early stages) people with ataxia do not appear hearing impaired in a significant way (i.e. most people with cerebellar damage can engage in conversation, listen to music etc.). This suggests that sonic guidance in cerebellar disease is possible but that the nature of the auditory deficit present and the qualities of the stimuli being used must be taken into consideration.

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<sup>42</sup> Hearing loss is a recognised symptom in Friedreich's ataxia (Rance et al., 2010) however this could be due to brainstem degeneration. Recently hearing loss has also been reported in cases of SCA (e.g. Hoche et al., 2008).

### 5.3.1 *Dynamic pitch in ataxia*

Despite a role for the cerebellum in auditory processing, the specifics of that role are yet to be defined. Of relevance to this study is the question of whether the identification and understanding of continuous, modulating pitch tones (i.e. auditory tones that get higher or lower) is affected by cerebellar disease. Moreover, it is not known if the ability to extract predictive information from auditory stimuli (i.e. auditory looming or time-to-contact information) is disrupted following cerebellar damage. However, research suggests that separate brain mechanisms are involved in processing tonal and dynamic pitch. Johnsrude, Penhune, and Zatorre (2000), concluded that detection of different pitch tones recruits bilateral primary auditory cortex with some subcortical involvement (including the cerebellum). In contrast, identification of pitch direction<sup>43</sup> is attributed to lateral Heschl's gyrus, a finding supported by imaging studies (Warrier et al., 2009; Schneider et al., 2005). To date, no reports of damage to Heschl's gyrus in cerebellar ataxia have been recorded, suggesting that perception of modulating pitch guides may be unimpaired even if deficits in discriminating between pitch tones are present.

## 5.4 Auditory imagery

### 5.4.1 *Why auditory imagery?*

A secondary aim in this study is to test the effects of moving to mentally rehearsed sonic guides. This line of enquiry is pursued as, whilst the sonic guides could be a

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<sup>43</sup> Pitch direction refers to whether a pitch rises or falls. For the listener, how pitch direction changes can simulate auditory motion.

way to approach novel motor problems in everyday situations, it is impractical to develop and play sounds for each motor problem encountered. It would be more appropriate therefore to learn the ‘form’ within the sounds and then mentally apply this as and when required. It is also likely that for some individuals and in particular those with neurological impairment, synchronising movement to external auditory guides will be problematic (Grahn and Brett, 2009). Using self-generated ‘auditory’ guides circumvents this difficulty and offers predictions about ‘what is coming next’ and internal knowledge of movement duration before initiation. A further benefit from using auditory imagery is that the ‘tone’ of the real sonic guide would not impact the listener. A complaint during pilot work in this study was that sustained periods of using the sonic guides was ‘off-putting’.<sup>44</sup>

#### *5.4.2 Auditory imagery research*

Auditory imagery is defined as neural activity in the auditory cortex in the absence of sound (Zatorre and Halpern, 2005). It has been evidenced in a number of fMRI studies and shown to engage the same neural correlates as real auditory processing (Yoo et al., 2001; Krusemer et al., 2005; Hubbard, 2010). Waking up with a ‘tune in the head’ is an experience familiar to most people. What research shows about this phenomenon is that humans possess high temporal accuracy in replicating auditory events (Halpern, 1988). It is also common to move to these imaginings for example, when singing to one’s self, people often tap the feet or dance. It is clear therefore, that imagined sound can guide movement behaviour in much the same way as external auditory cues. Research has established that when learning to play an

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<sup>44</sup> Over the course of this study, experimenters came to agree with this sentiment. The issue of sound quality is addressed in Chapter 7.

instrument the motor act and auditory feedback become interrelated so that presentation of the sound in isolation activates the corresponding motor control region. The benefits of this auditory-motor union are not yet fully understood, but one suggestion is that the sound prepares the motor system for the initiation of action (Blakemore and Frith, 2005). In this regard, auditory stimuli can be thought of as priming/preparing the motor system for movement.

Auditory imagery is also known to elicit motor responses in relation to learnt auditory-motor transformations (Haueisen and Knosche, 2001; Lahav et al., 2007). Violinists and piano players for example, display premotor cortex activity when imagining familiar musical sequences (that they know how to play) (Kristeva et al., 2003; Meister et al., 2004).<sup>45</sup> These findings make it plausible, indeed likely, that rehabilitative movement can also be learnt in conjunction with auditory stimuli and imagined at a later time to prime/aid movement.

Motor imagery is already an active area of research for improving movement behaviour, particularly in stroke (de Vries and Mulder, 2007) or hemiparesis rehabilitation (Stevens and Stoykov, 2003). Motor imagery activates the same movement related brain structures that are stimulated during movement preparation and performance (Jeannerod, 1994). One of the benefits of using motor imagery for nervous system disease is that motor behaviour is rehearsed in a 'well formed' manner without the limitations of physical and/or sensory impediment. The application of motor imagery requires introspection where kinaesthetic feelings are experienced as opposed to simply imagining an effector moving in the mind's eye.

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<sup>45</sup> The piano players imagined playing a Bartok piece and the violinists imagined a musical sequence.



Grush (2004) highlights how motor imagery must emulate proprioceptive sensation as bodily feeling and sensation are integral to the motor image or plan (i.e. the output of the motor areas) that is activated in premotor areas by imagery. This is termed ‘faux’ proprioception and is an important factor in how motor imagery operates (Grush, 2004). A finding relevant to this idea is that motor images can be honed by external auditory cues. Heremans et al., (2012) report that ‘imagery vividness’<sup>46</sup> is increased when congruent sounds are presented whilst imagining. An question therefore, is whether auditory imagery (that reflects a learnt auditory motor-transformation) can similarly benefit motor imagery? What this would offer, more than motor imagery alone, is twofold. Firstly, mental rehearsal of the motor act would be placed within a multisensory context. As the brain assimilates coincident sensory stimuli as a unified percept, using imagined auditory sounds to guide imagined movement, may initiate activity in interrelated networks (Stein and Meredith, 1993). Secondly, in some cases, the ability to perform motor imagery might be impaired following neurological damage. If motor imagery emulates the body’s proprioception, damage to the motor system will likely also compromise this representation (Grush, 2004). There is evidence to support this, for example, motor imagery has been shown to be poorly timed following cerebellar damage (Grealy and Lee, 2011) and produce abnormal activation patterns in Parkinson’s disease (Cunnington et al., 2001). It is possible therefore, that auditory imagery can compensate if motor imagery is impaired, particularly if it is associated with a motor act.

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<sup>46</sup> Imagery vividness was assessed using a visual analogue scale.

To summarise, this second experiment has dual purpose. It is an investigation into the efficacy of sonic guidance for improving movement control in people with cerebellar ataxia. As in Experiment 1, it is expected that the tau information within the auditory guides will provide prospective guidance and lead to positive changes in swaying behaviour. The second aim of the study is to investigate if auditory imagery (of the sonic guides) also improves swaying. It is anticipated that the changing pitch, which represents the movement's dynamics, will be quickly learnt/memorised and successfully self-generated to improve movement. Similarly it is projected that following self-generated guides without the burden of coordinating to an external sound source will further facilitate movement control. In all cases it is predicted that weight-shifting will be smoother as measured by a decrease in normalised jerk.

## 5.5 Methods

### 5.5.1 *Participants*

Twenty adults, 11 males and 9 females, (Mean age  $50.9 \pm \text{SD } 15.39$ ; Range 25-80 years), diagnosed with various forms of ataxia were recruited from across the UK. Recruitment began in Scotland through local branches of Ataxia UK, before being expanded to other regions of the United Kingdom. The order of the selection process meant that participants in the experimental group were predominantly from Scotland with the control group being recruited from around the UK. The inclusion criterion for being involved was a diagnosis of cerebellar ataxia. Many participants had idiopathic ataxia with three having additional diagnoses (see Table 5.1). Participants had varying movement ability and a preliminary assessment was made using four

**Table 5.1** Participant information for the experimental (subjects 1-10) and control (subjects 11-20) groups.

Subject	Age (yrs)	Sex	Ataxia type	Mobility	Onset <sup>a</sup> (yrs)	Ataxia Rating (SARA)*				
						Gait (0-8)	Stance (0-6)	Sitting (0-4)	Speech (0-6)	Score (21/28) <sup>b</sup>
1 <sup>§</sup>	38	M	Ins	Wc	20	8	4	2	3	14/17
2 <sup>§</sup>	49	F	Cb,Dys	Wk	17	4	3	2	2	9/11
3 <sup>§</sup>	48	F	Cb, Mg	Wc, Wa	29	5	4	2	3	11/15
4	38	M	Cb	Unaided	24	1	0	0	2	1/3
5	72	M	Cb	Ws	4	3	2	0	1	5/6
6 <sup>§</sup>	33 <sup>d</sup>	F	Idi	Wa	20	4	1	3	0	8/8
7 <sup>§</sup>	58	F	Cb	Wc	28	6	4	2	1	12/13
8	40	M	Cb	Wk	12	3	2	1	4	6/4
9 <sup>§</sup>	53	F	Cb	Wc; Wk	27	6	4	1	4	11/15
10 <sup>§</sup>	80	M	Cb	Wc; Wa	50	6	4	2	2	12/14
11	59	M	Cb	Ws	38	4	2	1	1	7/8
12 <sup>§</sup>	25	F	Idi	Wc	11	7	5	3	2	15/17
13	65	M	Cb	Ws	8	2	2	1	2	5/7
14	50	M	Cb	Ws	5	3	2	1	0	6/6
15 <sup>§</sup>	56	F	Cb,B12	Ws	17	2	2	1	0	5/5
16 <sup>§</sup>	48	M	Idi	Wc,Wa	3	6	4	2	1	12/13
17	64	M	Sca 6	Ws	5	1	1	0	3	2/5
18	39	F	Sca 2	Wa	10	2	2	1	1	5/6
19 <sup>§</sup>	67	F	Sca 6	Wa	9	3	3	1	1	7/9
20	49	M	Cb	Unaided	3	1	1	0	4	2/6

Note. Ataxia type: Ins = Ataxia caused by cerebellar insult, Cb = cerebellar ataxia, Idi = idiopathic cerebellar ataxia, Sca = spinocerebellar, Dys = Dystonia, B12 = Vitamin B12 deficiency, Mg = Myasthenia gravis Mobility: Wc = wheelchair, Wk = walking frame, Ws = walking stick, Wa = walk assisted (e.g. holding a person's arm).

a Onset refers to years since symptoms began rather than number of years since diagnosis.

b The first score is the maximum obtainable score for posture related items. The second score includes speech.

\* Categories adapted from the Scale for the Assessment and Rating of Ataxia (SARA).

d Reported deafness in the right ear.

§ Assisted during the swaying task.

measures adapted from the Scale for the Assessment and Rating of Ataxia (SARA)

(Schmitz-Hübsch, 2006) (Appendix C) (Table 5.1).<sup>47</sup> No participants reported

hearing loss outside of normal ageing except one who had deafness in the right ear

<sup>47</sup> Four (from eight) assessment criteria were adapted from the SARA (Appendix C). Three focused on motor skill and the other, vocal ability. Scores are based on the experimenter's judgement and are provided as general guide to participant's ataxia rather than a clinical assessment.

(see Table 5.1). All participants gave written and informed consent and testing complied with the code of ethics at The University of Edinburgh.

### 5.5.2 Equipment

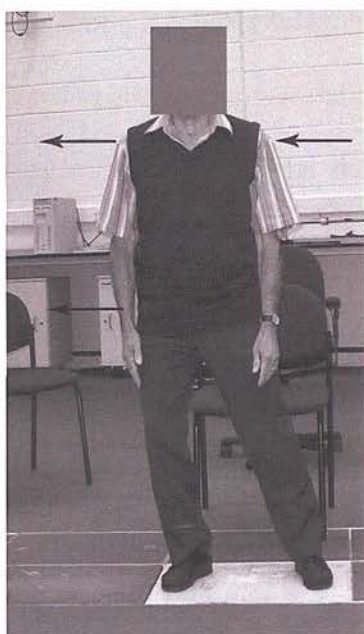
Swaying was recorded using a Kistler forceplate. The plate measured 800 x 600 mm and registered the three components of the resultant ground reaction force vector (vertical, anterior-posterior, and medial-lateral). Data was collected and exported through Qualisys™ motion tracking software. Sonic guides were played through a Dell™ PC using standard stereo speakers. A pole (microphone stand) was used as an object to focus vision on.

### 5.5.3 Sonic guides

Guides were created the same way as in Experiment 1 (see section 3.4.2), except mean duration was calculated from the average of ten sways in a healthy adult. Sonic guides of seven different durations were created around the mean (1.2 seconds) by adding or subtracting values of 0.1 seconds. Thus sonic guides were programmed with durations of 0.9 s, 1.0 s, 1.1 s, 1.2 s, 1.3 s, 1.4 s and 1.5 s. In accordance with the findings of Experiment 1, each guide carried a  $k$  value of 0.5. Guides were randomised using [www.random.org](http://www.random.org) and ordered into five minute long MP3 files containing an indefinite number of sounds. Silence periods of 0.7, 0.8 and 0.9 seconds were used to separate guides with the order randomised as above.

#### 5.4.4 The lateral sway and trial set up

Lateral sway was used as the experimental task in this study. The motion practiced shifting the body's mass in the medial-lateral axis. Participant's started in natural stance, upright with gaze fixed on a pole placed three meters to the front.



**Figure 5.1** A participant performing the lateral sway. Arrows indicate direction of motion for a single sway.

Subjects shifted bodyweight laterally (as shown in Figure 5.1) until a 'stability boundary'<sup>48</sup> was experienced. The exercise was based on neurophysiotherapy for patients recovering from stroke (Geurts et al., 2005) or to help maintain balance in the elderly (Bieryla and Madigan, 2011). A complete sway consisted of a controlled stop at the stability boundary in coordination with the termination of the sonic guide. A return from this position to the stability boundary in the other direction following the next sonic guide completed a weight-shift in the opposite direction. Feet were placed approximately

shoulder width apart and maximum displacement from left to right (and vice versa) constituted a single sway. Participants were instructed to not bend at the waist and instead to engage the whole body in the swaying action. Before trials began, subjects were given verbal instructions, a demonstration and the opportunity to practice. Participants were also asked to not treat guides as rhythmic and 'bounce' from one guide to the next. Instead directions were given to bring each sway to a controlled

<sup>48</sup> Peak distension before instability occurs.

stop and to follow the ‘instruction’ within each guide. Participants were encouraged to rest or stop at any time during testing when necessary.

#### 5.5.5 *Standing on the force plate*

As foot placement is problematic for individuals with cerebellar disease (Manto, 2002) participants were allowed to place the feet where most comfortable (and thus stable). However, same stance was maintained between trials, as was the need for both feet to be completely on the force plate at all times. For tall individuals, natural foot placement was hindered during scissors stance due to the dimensions of the force plate.<sup>49</sup> Eleven participants out of twenty required assistance while swaying (see Table 5.1). Assistance involved an experimenter standing either side of the participant holding out a hand to grab if necessary. Several participants held on for the duration of the recording period but this did not disguise tipping or overbalancing. It did however stop falls and participants who elected to be assisted were supported in the same way for the rest of testing. Regardless of whether assistance was requested, all subjects had experimenters standing to the side to help if necessary. For both exercises, participants were asked not to lift the feet from the force plate and to relax the arms at the side (where possible).

#### 5.5.6 *Experimental design*

The experiment consisted of one baseline period and two testing periods. In the baseline period, participants performed the sway exercises without sonic guidance. In the testing periods, exercises were performed with the sonic guides and then using

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<sup>49</sup> For one participant, taking a full stride meant overshooting the force plate. Foot placement was compromised in this individual but was approximately the same throughout testing.



auditory imagery. As memory for auditory events persists after sounds are no longer present (Sams et al., 1993) a counterbalanced design could not be used (as auditory memory would interfere with no sound conditions). Instead a staggered design was employed, so that direct comparisons could be made between control and experimental groups. In the experimental group the testing sequence was ABC (where A = No Sound, B = With Sound and C = Imagined Sound). In the control group, the sounds and imagined guides were not introduced until three baseline conditions had been completed therefore testing was AAABC. All recorded trials consisted of lateral swaying (described in section 5.2.3), recorded over periods of forty five seconds. Two trials were completed and averaged for each condition (no sound, sonic guidance, imagined sound). Overall the experimental group took part in six trials; two without sound (condition 1, Pre), two with sounds playing (condition 2, With Sound) and two using auditory imagery (condition 3, Imagined Sound). Between each trial participants rested for three to five minutes. For the control group, swaying was performed in exactly the same way but no sounds were played for the first six trials (i.e. no experimental group condition two or condition 3). As the first three conditions (AAA) were to be compared to the first conditions (ABC) in the experimental group, the control group conditions were named 'condition 1, Pre', 'condition 2, No Sound' and 'condition 3, No Imagined Sound'. Sonic guide and auditory imagery conditions (condition 4, With Sound and condition 5, Imagined Sound) were then introduced to complete the same protocol as the experimental group. Overall controls performed ten trials (five conditions). Controls also rested for three to five minutes between trials. The entire protocol took approximately one hour to complete for each participant.

## 5.6 Data analysis

### 5.6.1 *Normalised jerk*

A defining feature of well-formed movements is that they are smooth (Rohrer, 2002). Smooth movement does not contain (large) deviations in trajectory and a single peak bell-shaped velocity profile is produced. Following cerebellar damage, movement is ataxic with multiple stops and starts, changes in acceleration/deceleration, ‘bumpy’ velocity profiles with multiple peaks, and several subcomponents.<sup>50</sup> A measure of movement smoothness is jerk, the instantaneous rate of change in acceleration and the third order time derivative of position (Hogan and Sternad, 2009). High levels of jerk correlate with problems in trying to regulate motor control (Wininger et al., 2009), and reflect increased changes in acceleration/deceleration and number of subcomponents in movement (Hogan and Sternad, 2009). Conversely, decreased jerk is indicative of less fragmented movement with fewer velocity peaks (Hogan, 1984; Hogan and Sternad, 2009). Low levels of jerk may also indicate improved timing in the muscle contractions underlying movement (Krebs et al., 1999). This assumption is based on the idea that subcomponents represent the breakdown of triphasic muscle activity (Cooke and Brown, 1994). Jerk has been used as a clinical assessment tool (e.g. Teulings et al., 1997) and a measure of motor dysfunction in cerebellar patients (Goldvasser, McGibbon, and Krebs, 2001). However, not all studies using jerk have been able to distinguish between pathology and healthy controls. Wininger, Kim, and Craelijs, (2009) for example, compared people recovering from stroke to controls and did not detect significant differences. Nevertheless, for the present study, there

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<sup>50</sup> A subcomponent in this context is defined by a point in the movement where zero is reached in the velocity profile after movement initiation.



are advantages in using jerk to analyse movement data. COP data from people with ataxia is likely to consist of several subcomponents.<sup>51</sup> By using jerk, these subcomponents can be expressed as a single score to give a complete measure of the whole action. As a result, subtle changes following intervention are more likely to be identified as one more or less movement subcomponent will alter overall jerk. In this regard jerk measures are more sensitive than measures which focus on the qualities of individual subcomponents.

Different measures of jerk have been used in clinical settings such as integrated absolute jerk (Goldvasser et al., 2001) or mean squared jerk (Wininger, Kim, and Craelius, 2009). However jerk can also be calculated using the first derivative of force (yank).<sup>52</sup> An advantage of calculating jerk in this way is that there will be less noise in the data as for this study, force data would only need to be differentiated once as opposed to three times for position. Jerk is dependent on the size and duration of the movement so data must be normalised with respect to time and amplitude (Hogan and Sternad, 2009). Dividing the sum of the jerk by mean speed achieves this as it has aspects of both time and amplitude (velocity = amplitude/duration) (Hogan and Sternad, 2009). Using mean speed to normalise jerk is in line with Krebs et al. (1999).

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<sup>51</sup> COP represents the input from multiple joints rather than a single effector. Cerebellar ataxia is known to cause dysnergia which results in the decomposition of movement trajectories.

<sup>52</sup> As yank and jerk are equivalent the term jerk will continue to be used throughout this thesis. Force = mass x acceleration. As mass is constant, the first derivative of force is proportional to the derivative of acceleration i.e. jerk.

### 5.6.2 Jerk analysis

Centre of pressure (COP) and force (F) data were exported as text files from Qualisys™ software. Data was smoothed using a Gaussian  $\sigma 11$  (giving a cut-off frequency of 8 Hz) in KaleidaGraph. The first fifteen seconds of each trial were removed to take into account participants who needed a longer period of time to stabilise before swaying began. COP data of the medial-lateral axis (Y) was plotted and the first ten sways in each trial extracted. Start and end points were identified by maximum displacement to either the left or right where velocity had reached zero. As there was drift (noise) once weight-shifts had been brought to a stop, data with Y velocity less than 3% of the peak velocity were removed from the start and end. X and Y components of force data were differentiated once with respect to time to give jerk. So that jerk in both axes would be considered in the analysis, tangential jerk (TJ) was computed using the formula;

$$TJ = \sqrt{(x_j^2 + y_j^2)} \quad (\text{Equation 5.1})$$

where  $x_j$ , and  $y_j$  = amount of jerk recorded in each axis.

Times for the start and endpoints in the positional data were then applied to the TJ so that the sum of the jerk could be calculated for each individual sway before being divided by mean speed. The jerk<sup>-m/s</sup> score of sways recorded over the two trials (10 x 2) were then aggregated to give an overall jerk score per condition (20 sways).

## 5.7 Results

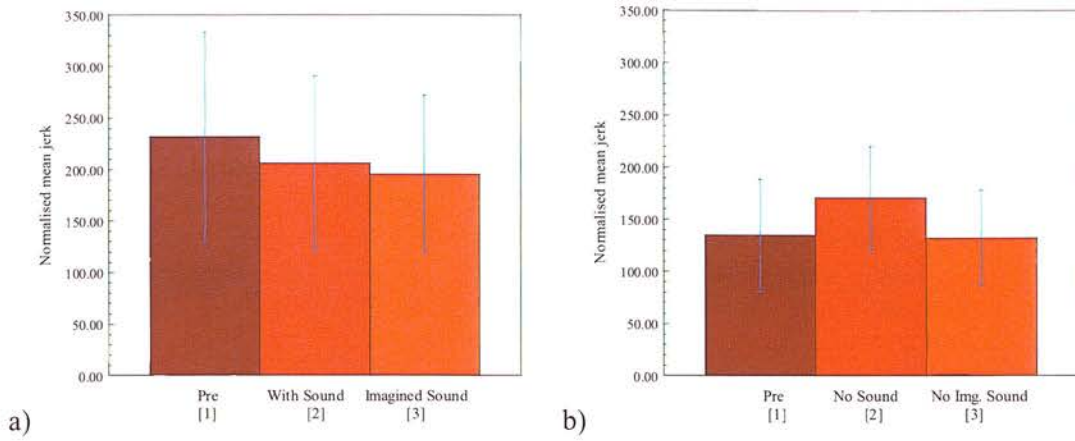
### 5.7.1 Swaying analysis - part one: within group comparisons

Mean normalised jerk for conditions 1-3 is presented in Table 5.2 and Figure 5.2(a and b) for experimental and control groups. Overall controls produced less jerk than the experimental group in each condition. This reflects that collectively, the experimental group rated higher than controls on the experimenter's Scale for the Assessment and Rating of Ataxia (SARA) mobility score (89 as opposed to 66, see Table 5.1). To test for significance an independent t-test was conducted but no significant effect of mobility score was found ( $t(18) = 1.278$ ,  $p = 0.05$ ). However, further investigation using Mann-Whitney U-tests revealed that the experimental group produced significantly higher levels of jerk than controls in the first condition (Pre) ( $U = 13.0$ ,  $p = 0.009$ ).<sup>53</sup>

**Table 5.2** Mean and standard deviation of normalised jerk ( $m/s^3$ ) for experimental and control groups.

	Pre (no sound)	With Sound	Imagined Sound
Experimental Mean	231.89	206.22	195.62
Experimental SD	101.67	84.660	76.306
	Pre (no sound)	No Sound	No Imagined Sound
Control Mean	134.68	170.35	132.14
Control SD	53.54	49.99	45.931

<sup>53</sup> Testing for skew and kurtosis showed data was non-normally distributed so non-parametric tests were used.



**Figure 5.2 a and b** Total mean normalised jerk ( $\text{m/s}^3$ ) with standard deviation bars for the first three conditions. a) Experimental group. b) Control group.

Moreover, the experimental groups was found to be statistically higher on number of years since the onset of symptoms ( $U = 17.5$ ,  $p = 0.014$ ). It was not unexpected therefore that movement problems were greater in the experimental group and that higher jerk scores were recorded. This makes sense given that a greater number of the experimental group used wheelchairs than controls.

To test the effects of the sonic- and imagined guides on lateral weight-shifting between the groups, a mixed  $2 \times 3$  (group  $\times$  sound condition) repeated measures ANOVA was conducted. Before doing so, a data exploration was carried out and scores were found to be non-normally distributed. A correction was made by taking the log of each score as described by Field (2005). No significant main effect of sound condition was found ( $F(2, 34) = 3.26$ ,  $p = .051$ ). This indicates that jerk scores did not significantly change between conditions in either group during the lateral swaying task. However, the  $p$ -value recorded was very close to significance suggesting that with greater statistical power (i.e. a larger group size), significance would have been reached. Nevertheless, a significant interaction effect was found between experimental and control groups ( $F(2, 34) = 4.17$ ,  $p = .024$ ). This indicates

that participants in the experimental group improved from condition-to-condition whereas control group participants did not. To test for statistical differences between each condition in each group individually, one-way repeated measures ANOVAs were conducted. The experimental group, produced no significant effects between conditions ( $F(2, 16) = 2.02, p = 0.17$ ). For the control group Mauchly's test of sphericity assumption was found to be violated ( $\chi^2(2) = 10.47, p < 0.05$ ) and a Greenhouse-Geisser estimate ( $\epsilon = 0.59$ ) was accepted instead of the normal F-ratio. A significant effect between conditions was found ( $F(1.16, 10.41) = 5.88, p = 0.04$ ). However, it was between conditions two and three and is not discussed here as it does not demonstrate a practice effect but rather a return to baseline. As presented earlier significant differences were found between groups before testing began. These differences are important as age, disease onset and disease type, correlate strongly with mobility.<sup>54</sup> That the groups differed significantly suggests treating clinical population like this as homogenous makes little sense. In addition to between groups differences, disparate scores were produced *within* groups. For example, jerk scores ranged from 130 to 490 in the experimental group and 52 to 295 in controls. Such large variances potentially disguise changes in jerk score on an individual basis, and raise questions as to whether the sample can be assumed to be randomly drawn from the same target population. As a result of these inconsistencies, it was decided to treat subjects as individual cases.

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<sup>54</sup> Correlations were run between all variables and SARA ratings. As expected, significance at the  $p < 0.05$  level (one-tailed) was found between disease onset and gait ( $R^2 = 0.444$ ) as well as gait and overall jerk score ( $R^2 = 0.397$ ).

### 5.7.2 Swaying analysis - part two: auditory guides

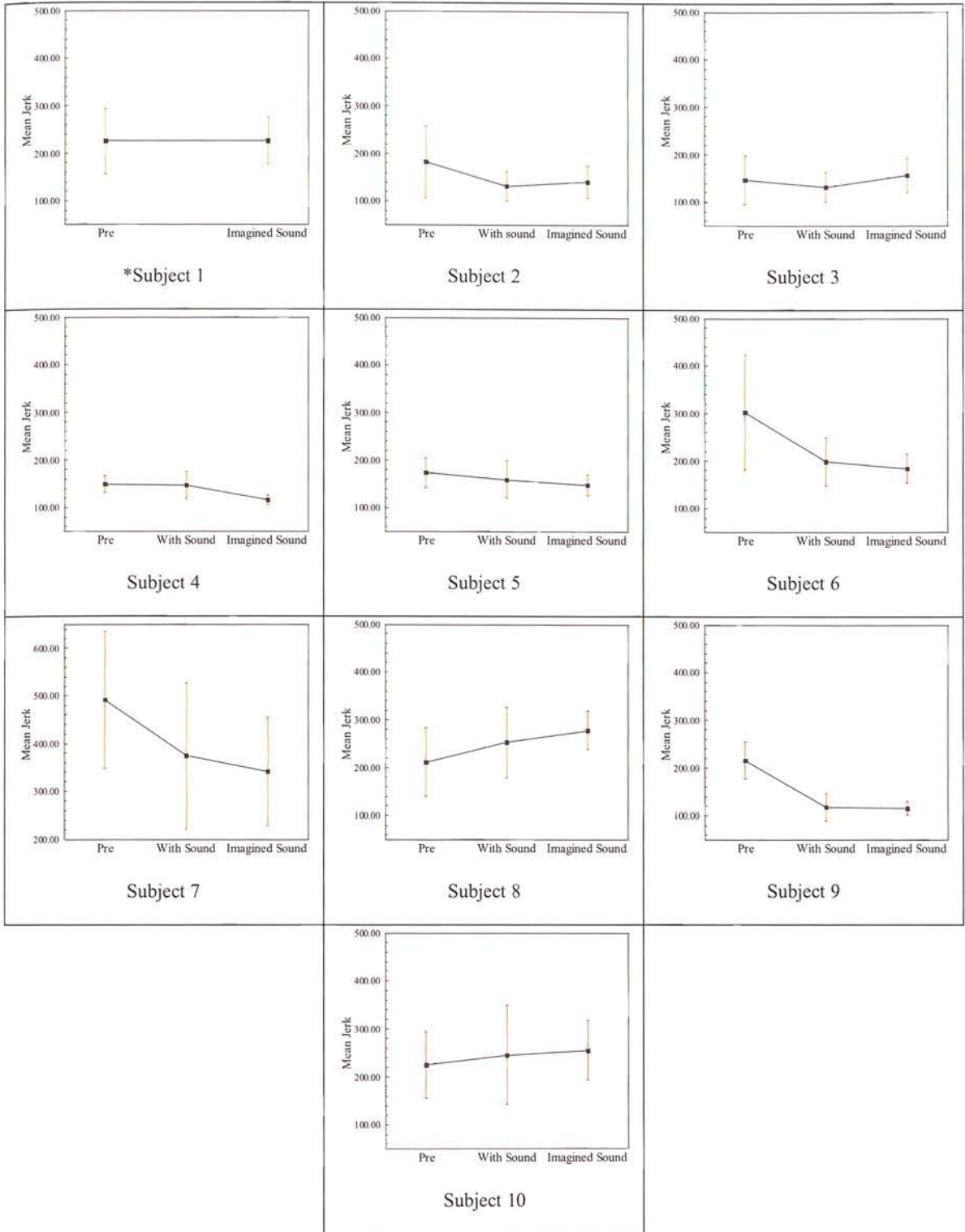
Individual normalised jerk scores were calculated for each participant in the experimental group (displayed in Table 5.3 and Figure 5.3). The first comparison in this group was made between conditions one (Pre) and two (With Sound).

**Table 5.3** Mean normalised jerk ( $\text{m/s}^3$ ) and standard deviation of conditions (20 sways), Pre [1], With Sound [2] and Imagined Sound [3] for participants (P) in the experimental group.

Condition	P 1	P 2	P 3	P 4	P 5	P 6	P 7	P 8	P 9	P 10
Pre	225.34	182.06	146.21	148.95	173.01	302.44	490.83	210.49	215.30	224.25
(SD) [1]	(68.65)	(73.83)	(51.30)	(17.81)	(31.12)	(120.6)	(143.1)	(71.25)	(38.68)	(69.11)
With Sound	*N/A	131.77	131.14	146.72	159.32	197.98	374.11	252.26	117.36	245.36
(SD) [2]		(31.66)	(31.21)	(27.61)	(39.22)	(50.55)	(152.2)	(73.81)	(28.46)	(104.1)
IS	225.73	140.99	156.94	115.71	147.33	184.19	342.13	277.46	115.08	254.93
(SD) [3]	(49.29)	(33.06)	(36.20)	(9.84)	(22.27)	(29.79)	(112.3)	(39.82)	(14.33)	(61.86)

\*Subject 1's data comes from a pilot study where the 'With Sound' condition was not recorded.

Figure 5.3 shows that seven participants produced less jerk during the With Sound condition than at baseline and two produced more. Independent sample t-tests were used to test for significance. Four out of nine participants produced significantly less jerk moving to sounds than at baseline (see Table 5.4). The remaining five recorded no significant change, meaning that overall, 44% of participants in the experimental group produced lower jerk scores whilst moving with sonic guides.



**Figure 5.3** Mean normalised jerk ( $\text{m/s}^3$ ) with standard error bars across three conditions, Pre, With Sound and Imagined Sound, for each individual in the experimental group.

\* Subject 1's data comes from a pilot study where the 'With Sound' condition was not recorded.



**Table 5.4** Independent sample t-test results for Pre vs. With Sound (experimental group) Pre vs. No Sound (control group).and Pre vs. With Sound (control group). If negative p is shown it denotes a negative t-value and thus the direction of the effect.

Experimental	Sub 1	Sub 2	Sub 3	Sub 4	Sub 5	Sub 6	Sub 7	Sub 8	Sub 9	Sub 10
Pre vs. With Sound	--*	p <.008	N/S	N/S	N/S	p <.003	p <.024	N/S	p <.0001	N/S
Control	Sub 11	Sub 12	Sub 13	Sub 14	Sub 15	Sub 16	Sub 17	Sub 18	Sub 19	Sub 20
Pre vs. No Sound	N/S	N/S	Neg p<.0001	N/S	N/S	Neg p<.0001	Neg p<.0001	N/S	N/S	N/S
Pre vs. With Sound	N/S	p<.006	Neg p<.0001	N/S	N/S	Neg p<.000	Neg p<.0001	p <.007	p <.003	N/S

Table guide; N/S = non-significant. Neg = negative t-value was recorded (i.e. more jerk produced).

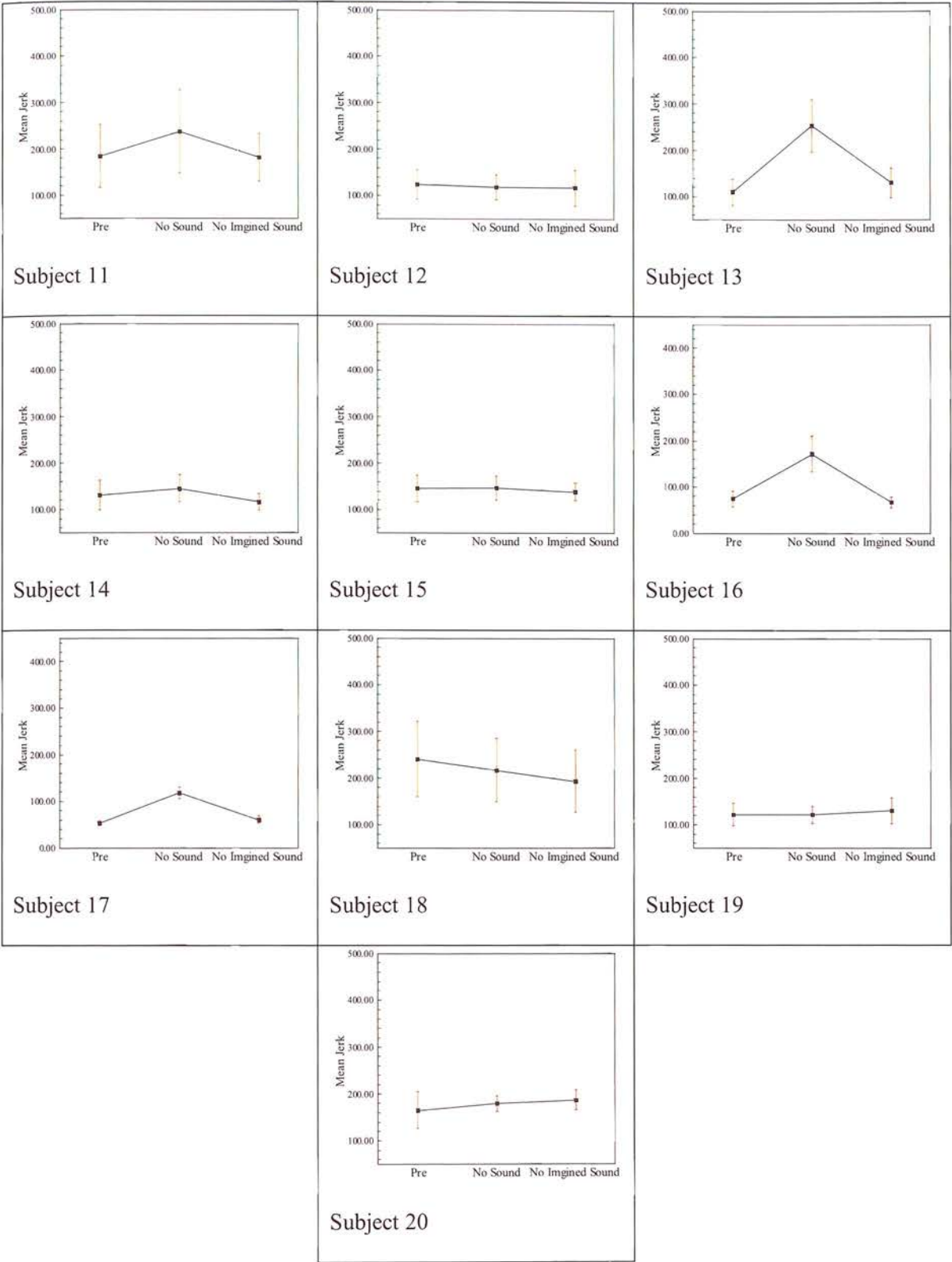
\*Subject 1's data comes from a pilot study where the 'With Sound' condition was not recorded.

Controls were then investigated using corresponding conditions, Pre vs. No Sound. Results for each participant are presented in Table 5.5 and displayed in Figure 5.4. Figure 5.4 shows that seven participants in the control group generated higher jerk in the No Sound condition than in the Pre condition. Independent sample t-tests (also presented in Table 5.4) revealed that no participant in the control group significantly

**Table 5.5** Mean normalised jerk ( $\text{m/s}^3$ ) and standard deviation of 20 sways in each condition, Pre [1] With Sound, [2] No Imagined Sound, [3] With Sound [4], and Imagined Sound [5] for individuals in the control group.

Condition	Subject 11	Subject 12	Subject 13	Subject 14	Subject 15	Subject 16	Subject 17	Subject 18	Subject 19	Subject 20
Pre	183.49	123.40	110.61	130.47	145.03	74.30	52.82	240.33	121.57	164.80
(SD) [1]	(67.97)	(31.83)	(28.33)	(31.90)	(29.08)	(16.80)	(4.89)	(79.86)	(23.82)	(38.95)
No Sound	236.53	117.97	252.34	144.39	146.00	170.97	118.00	217.05	121.54	178.66
(SD) [2]	(89.31)	(27.09)	(56.37)	(28.93)	(25.36)	(38.52)	(12.34)	(67.99)	(18.52)	(16.71)
NIS	181.58	116.95	130.26	116.11	138.88	67.42	60.53	193.12	129.99	186.60
(SD)[3]	(51.42)	(38.84)	(32.46)	(18.05)	(18.84)	(11.31)	(7.35)	(66.43)	(27.92)	(20.57)
With Sound	156.85	91.57	295.41	128.72	136.17	150.30	113.74	175.85	98.20	181.14
(SD) [4]	(36.10)	(28.30)	(60.91)	(17.56)	(25.11)	(38.42)	(15.55)	(45.85)	(23.34)	(24.57)
IS	183.24	118.08	119.94	113.07	122.5	44.26	52.76	160.90	98.23	149.40
(SD) [5]	(51.97)	(24.32)	(35.18)	(16.67)	(23.03)	(7.71)	(9.45)	(49.03)	(15.13)	(23.69)



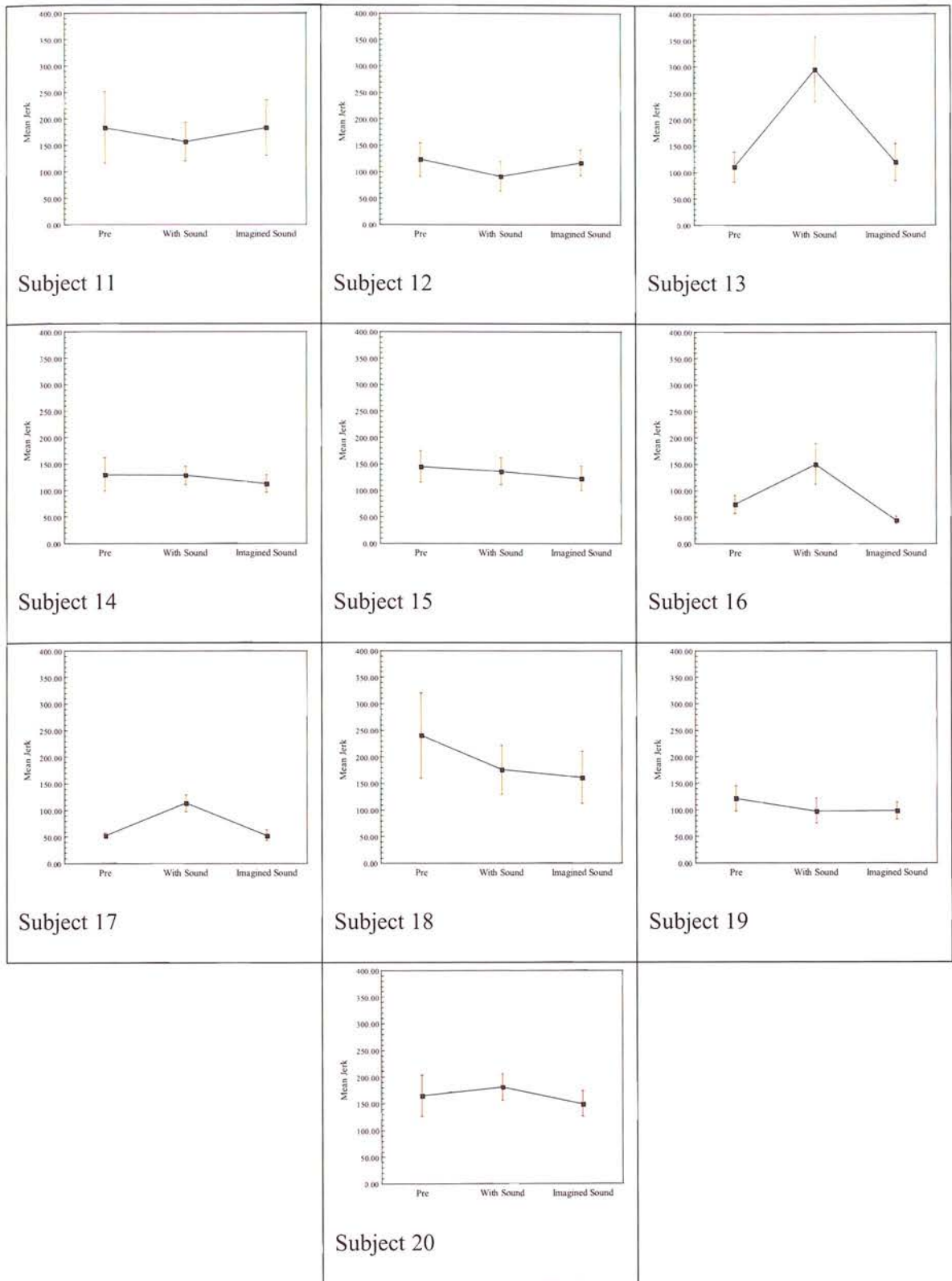


**Figure 5.4** Mean normalised jerk ( $\text{m/s}^3$ ) with standard error bars across all three conditions, Pre, No Sound and No Imagined Sound, for each individual participant in the control group.

improved movement smoothness in condition two. On the contrary, three participants were significantly less smooth with the others producing no significant change. To compare the percentage of improved scores between experimental and control groups (44% vs. 0%), a one tailed, Fisher Exact Probability test was conducted and the difference between groups was found to be significant at the  $p < 0.03$  level.

Following on from this analysis, the effects of introducing the sonic guides to the control group were explored. Pre vs. With Sound were compared and results are presented in Table 5.5 and displayed in Figure 5.5. To test for significance, independent sample t-tests were conducted and results are presented in Table 5.4.

The results of the sonic guide condition are ambiguous. Three participants produced significant reductions in jerk whereas three others scored significantly higher. Hence, 33% of controls produced lower jerk scores following the introduction of the sonic guides. This percentage partially supports the first analysis in that for some, following sonic guides increased movement smoothness. However, it must be noted the same percentage of controls produced significantly less movement smoothness.



**Figure 5.5** Mean normalised jerk ( $\text{m/s}^3$ ) with standard error bars across conditions, Pre, With Sound and Imagined sound for each participant in the control group.

### 5.7.3 Swaying analysis - part three: auditory imagery

The next analysis was to investigate the effects of auditory imagery on movement smoothness. Pre and Imagined Sound conditions in the experimental group were compared to the Pre and No Imagined Sound conditions, for controls. Scores are presented in Tables 5.3 and 5.5, and plotted in Figures 5.3 and 5.4 respectively. As in the previous investigation, the number of significant results for each group was used to assess the effects of imagined auditory guides on swaying. Independent sample t-tests were carried out for each individual and are reported in Table 5.6.

**Table 5.6** Independent sample t-test results for Pre vs. Imagined Sound (experimental group), Pre vs. No Imagined Sound (control group) and Pre vs. Imagined Sound (control group).

Experimental	P 1	P 2	P 3	P 4	P 5	P 6	P 7	P 8	P 9	P 10
Pre vs. IS	N/S	p <.024	N/S	p <.0001	p <.002	p <.000	p <.002	Neg p <.001	p <.0001	N/S
<b>Control</b>	<b>P 11</b>	<b>P 12</b>	<b>P 13</b>	<b>P 14</b>	<b>P 15</b>	<b>P 16</b>	<b>P 17</b>	<b>P 18</b>	<b>P 19</b>	<b>P 20</b>
Pre vs NIS	N/S	N/S	Neg p <.016	N/S	N/S	N/S	Neg p <.005	N/S	N/S	Neg p <.040
Pre vs. IS	N/S	N/S	N/S	p <.05	p <.005	p <.003	N/S	p <.001	p <.003	N/S

Table guide; N/S = non-significant. Where p values are recorded = significant effect found. Where p values are preceded by Neg it means a negative t-value was recorded (i.e. more jerk produced).

Table 5.6 shows that six out of ten participants in the experimental group showed significant decreases in jerk when swaying to imagined auditory guides. One person scored significantly higher with the remaining three producing no change. Overall 60% of participants in the experimental group improved movement smoothness when swaying using auditory imagery. For the control group no participant produced a significant improvement between Pre vs. No Imagined Sound (see Table 5.6). Further to this, three participants produced scores with significant increases in jerk. To test for significance between the two groups percentages (60% vs. 0%) a one

tailed, Fisher Exact Probability test was run and found to be significant at the  $p < 0.005$  level.

How controls performed when using imagined auditory guides was then tested. Figure 5.5, shows that six participants recorded less jerk in the Imagined Sound condition compared to Pre, with the other four being approximately the same. Independent sample t-tests (Table 5.6) revealed that five out ten participants showed significantly lower jerk when using auditory imagery with five participants showing no change. The improved weight-shifting in this condition adds support to the previous result which showed that swaying to imagined guides increases movement smoothness in the majority of participants. These results suggest that in general, participants found moving to imagined guides easier than auditory guides. In the experimental group, 60% improved in the imaginary condition compared to 44% when using the sounds. This finding was mirrored in the control group with percentages of 50% and 33% respectively. However, Fischer Exact Probability tests showed that there was no significant difference ( $p > 0.05$ ) within each group when using the auditory compared to imaginary guides.

## 5.8 Discussion

### 5.8.1 Introduction

The aim of Experiment 2 was to test if predictive and continuous auditory guides could improve movement smoothness in people with cerebellar ataxia when performing functional neurorehabilitation exercises. A second part of the study tested the same idea using auditory imagery instead of actual sounds. The first investigation

revealed that nearly half of participants showed decreased levels of jerk when swaying with sonic guides. Lower jerk scores indicate that individuals were swaying with fewer changes in acceleration and less subcomponents (Krebs et al., 1999). The result provides evidence that sensory augmentation is an effective way to approach movement rehabilitation in some cases of cerebellar disease. In addition the finding suggests the auditory system is an appropriate sensory domain for delivering additional movement information. This is consistent with auditory augmentation investigations where improved motor control in people with neurological disease has been found (e.g. biofeedback studies [Dozza, Horak, and Chiari, 2007] or rhythmic cueing [Thaut et al., 1996]). Results from the second part of this study, found that following mental rehearsal of movement-based sonic guides, also increases movement smoothness when performing the exercises. This finding is in agreement with numerous studies that show mental rehearsal improves performance of motor acts (e.g. de Vries and Mulder, 2007). However, this study adds to the field by showing that mental imagery of a sound learnt in association with a motor act also assists motor performance. In doing so an additional technique for motor-rehabilitation is identified in cerebellar ataxia and potentially for other nervous system disorders.

### *5.8.2 Augmented sensory information*

The primary finding from this study is that, in some cases of cerebellar ataxia, additional sensory information improves movement smoothness. Results agree with the small quantity of studies that confirm augmented sensory information benefits people with cerebellar disease (e.g. Crowdy et al., 2000; Čakrt et al., 2012) and

supports theorists who have argued that sensory acquisition/processing is a primary function of the cerebellum (Bower, 1997; Parsons et al., 1997; Gao et al., 1996; Jueptner et al., 1997). Bower (1997) proposes that the cerebellum operates to optimise the motor system to acquire sensory information. This implies that if enough sensory information is made available, the cerebellum's acquisition role becomes diminished. From a perception-action context (i.e. Gibson, 1986; Lee, 2005), it can be understood how acquiring sensory information from ataxic movement would produce 'ataxic' sensory feedback. It makes sense therefore, that offering a clear source of movement information *without having to move* will mitigate or diminish the need to optimally direct motor behaviour for sensory acquisition. If guides abrogate the need for a cerebellar role in sensory acquisition, the auditory stimulus must be delivering sufficient movement information to extra-cerebellar regions involved in motor control. One suggestion (as in Chapter 3) is that direct movement information is delivered to the premotor cortex (PMC), an area known for sensorimotor transformation. Zatorre, Chen and Penhune, (2007) demonstrated that dorsal premotor cortex (dPMC) is involved in extracting 'higher-order features of the auditory stimulus' for temporal organisation of motor activity. The same authors show that ventral premotor cortex (vPMC), is responsive to auditory information associated with movement (Zatorre, Chen and Penhune, 2007). Data from this study suggests that movement information is extracted from the stimulus in the vPMC after being segregated in the ventral auditory pathway and then used to enhance the premotor signal. PMC (and specifically the vPMC) is part of numerous motor control related pathways to subcortical structures such as the cortico-basal ganglia-thalamic loop (Nakano, Kayahara and Nagaoka, 2005). The



presence of motor control loops that do not include the cerebellum highlights alternate ways through which additional sensory information can be delivered for sensorimotor control. The PMC is also populated by numerous multisensory mirror neurons (Ferrari et al., 2003; Rizzolatti et al., 1996) some of which respond to auditory aspects an action (e.g. paper ripping) (Kohler et al., 2002). It is possible then, that an auditory signal conveying the specific spatio-temporal characteristics of an action stimulates the ‘action-recognition’ systems and increase activity in the motor networks. This proposal agrees with Lahav et al. (2007) who showed that non-musicians, who have recently learnt a novel musical sequence on the piano, display mirror-neuron system activity (that includes PMC) for ‘auditory-action’, when listening back to the musical piece. The auditory-action recognition system is an explanation as to how music ‘affords’ listeners a way to move such as, dancing, foot tapping etc. (Clarke, 2005) or how to coordinate with others during musical performance (Schögler, 1998). In this study the sounds afford the listener the time and space within which to act (sway).

Guides may also have been influential through affecting brain regions associated with modulating pitch. Unlike pitch tones which activate the cerebellum, modulating pitch (or frequency sweeps), may be caused neural responses in extra-cerebellar brain areas such as Heschl’s gyrus (Johnsrude et al., 2000; Warrier et al., 2009). As Heschl’s gyrus is also interconnected with pre-motor cortex, this implies another network through which the auditory guides may deliver appropriate information for audiomotor transformation (Chen, Penhune and Zatorre, 2008b).

If the sonic-guides are supplementing poor cerebellar output it would suggest that the robust auditory stream is overcoming poor cerebellar visual and proprioceptive



sense. This agrees with Čakrt et al. (2012), who showed that increased proprioceptive information given through the tongue, lessens movement problems. A similar effect could be occurring in this study, particularly as a new (auditory) information stream is being introduced rather than simply adding to an existing (impoverished) one.

The discussion so far has centred on the properties of the sensory auditory-movement information and how it might be integrated into the nervous system with or without cerebellar involvement. However, whilst sensory integration explains decreased jerk scores for some participants overall (including for those who improved), movement was still greatly degraded. This reality suggests that the guides either, do not offer ‘enough’ sensory stimulation, or that cerebellum based sensory deficits are not the only source of problems present in this cohort.

### *5.8.3 Intrinsic guidance and prediction*

If auditory guidance reduces the need for sensory acquisition and leads to increased sensory awareness, it is worth considering how this translates into smoother movement. A key aspect of increased sensory arousal is that goal orientation can be defined more clearly. The importance of prediction in motor control was stressed in Chapter 2, tested in Chapter 3 and in Chapter 4 it was proposed that the cerebellum plays a key role in this behaviour for multiple mental activities. It is argued in this study that where participants improved, the addition of prospective sensory information allowed for better predictions regarding the task. It is proposed that better prediction contributed to the formation of a more accurate internal guide for the action (e.g. a motor image or feed forward model). The immediate outcome would be that initial movement trajectories would be more accurate, generating less

error and require fewer adjustments (as evidenced by less subcomponents being recorded).

Whilst it is clear that guides represent a reach trajectory (the gap between effector and goal), it is not clear how they support coordination of limb and body dynamics, particularly if signals returning from the body are compromised by cerebellar damage. The production of a motor command is dependent on an accurate ‘state estimate’ of the peripheral motor system (Miall et al., 2007). However, Chapter 2 argued that goal orientation is the organizing principle around which motor elements are coordinated (Bernstein, 1967). In this experiment, as guides provide clear goals it is possible that premotor organization is improved. This is in agreement with reaching experiments that show a visual goal can overcome absent proprioceptive sense by providing ‘enough’ information to register spatial awareness and calibrate limb dynamics (albeit imperfectly) (Ghez et al., 2000; Bernier, Chua and Franks, 2005). Data from this study suggest that auditory goals elicit motor organization in the same manner.

A stronger motor control signal would also mean a clear efference copy generated for comparison between predicted and actual movement paths. In cerebellar research, it is still debated whether the ability to use feedback for online adjustments is compromised. Force field experiments indicate that cerebellar patients are not impaired when adapting to trajectory perturbation during reaching (i.e. online control is close to normal) (Smith and Shadmehr, 2005). However, the ‘bumpy’ velocity profiles and increased subcomponents typical of ataxic movement suggest otherwise (i.e. ‘bumps’ represent dysmetric responses to feedback error) (Tseng et al., 2007). Data from this study suggest that cerebellar disease does cause problems in online

control as smoothness was improved by supplying a sensory feedback signal throughout the action. What is not clear is whether the guides lessen the need for an efference copy? The predictive and temporal characteristics of the sounds suggest that online comparison between self-generated movements and guides would be adequate for control regardless of the efferent copy of motor commands. Further evidence that prediction is a key aspect of this study comes from looking at movement variability at movement termination. This variability is attributed to abnormal EMG patterns where onset of antagonist activity is delayed (Hallet et al., 1991; Hore, Wild and Diener, 1991). Delays result in the sudden and rapid changes in acceleration and deceleration as a target is approached. Improved jerk scores imply that antagonist activity is being initiated more appropriately (ahead of time) and that actions are being performed closer to a single coordinated sway with fewer trajectory errors (and less dysmetric responses).

A different argument is that comparison between internal models and sonic guides is facilitated by the temporal aspects of sound. Growing evidence suggests that internal models are represented temporally in neural firing rates (see for example Lisberger, 2009). As mentioned visual information is spatial and requires a transformation before comparison with an internal model can be made (Optican, 2005). Auditory information is temporal abrogating this additional step meaning the speed and precision of comparisons between predicted and actual trajectories could be facilitated. This proposition is supported by a study that demonstrated the slow transmission rate of visual information hinders movement performance in some cases of cerebellar disease (Beppu, Suda and Tanaka, 1984).

Data for participants who improved in this study supports both the possibility of influencing the formation of the motor signal and/or providing online feedback in agreement with studies that show auditory stimuli adapt/support internal models (Ghez et al., 2000; Oscari et al., 2012).

#### 5.8.4 *Cerebellar timing*

Findings from this study could be interpreted as support for a cerebellar internal clock (Ivry et al., 1988; Spencer et al., 2007; Ivry and Keele, 1989). If the timing device was not functioning, it is logical that an external ‘timekeeper’ could provide the required temporal information to guide movement. The temporal clarity offered by an auditory timekeeper increases this possibility meaning that the sonic-guides could be acting as a secondary (external) timing mechanism to support the damaged cerebellum. However, the internal clock hypothesis is not well supported by this experiment. Timing information was deliberately obscured by randomising sound durations and presenting guides stochastically. Participants therefore could not use the previous guide’s duration to make an estimate of the current guide. Given this design, it is difficult to see how the guides could supply movement timing to the cerebellum in advance. A different problem with the internal clock hypothesis is that the cerebellar timing literature reports the cerebellum is only involved in the perception and timing of sub-second events (Ivry and Spencer, 2004; Lewis and Miall, 2003; Nichelli et al., 1996). In this experiment, the vast majority of auditory guides (and the sways) were of durations of one second or above (the range was from 0.9s to 1.4s). It is unlikely therefore, that the deficits in swaying recorded are related to faulty cerebellar timing. As earlier, decreased jerk suggests improved timing of the

contractions between the muscles involved in controlling the sway (in line with Hogan and Sternad, 2009; Bastian, 2011) (see below). However, this more reflects participants using prospective and online- information made available *once the sound has begun*, rather than an internal timing device.

#### 5.8.5 Imagined sound discussion

The original purpose of testing mental rehearsal of the sounds was to see if the form of the guides could be learnt and applied to motor solutions out of the laboratory. This was confirmed as the auditory imagery condition produced a strong effect, increasing movement smoothness in the majority of participants. Experimental group results show that the spatio-temporal characteristics of the guides can be quickly learnt and self-generated to guide movement. Findings from this work support studies that show motor imagery enhances motor control following brain injury (de Vries and Mulder, 2007; Stevens and Stoykov, 2003). Reports in the literature describe motor-imagery problems in cerebellar patients (e.g. Grealy and Lee, 2011; González et al., 2005) although this was not directly tested in this group. However, this experiment did not use motor imagery but rather, *imagined auditory guides* which were *actively moved to*. The majority of participants were not compromised in this activity suggesting that imagined auditory guidance is a good way to improve movement. Overlap between brain areas activated by auditory and motor imagery suggests that auditory imagery of a motor act could be useful where motor-imagery deficits are present. Some of the reasoning behind using auditory imagery was the assumption that audiomotor associations would formulate through practice with the real guides, just as occurs in musicians learning instruments (Kristeva et al., 2003;

Meister et al., 2004). It is question however, whether enough time/practice had passed for this to transpire as in general these associations develop over much longer periods of time (Haueisen and Knosche, 2001; Lahav et al., 2007). Nevertheless, rapid auditory-motor connections have been evidenced in musicians playing small, fast, sequences of motion, with the fingers (Bangert and Altenmüller, 2003). It is not known if integration of larger, slower actions, in multiple body joints with unmusical sounds, form as precipitously. It could be argued however, that the movements employed in this study, despite using the whole body relatively slowly, are simple and stereotyped and may encourage fast auditory-motor associations so that imagery of the guides initiates activity in the motor systems. It is argued that the auditory imagery is influences the motor system in the same way as motor imagery. This is through the emulation of faux proprioception being delivered to the pre-motor areas (Grush, 2004). In other words, the embodied feeling of swaying with the real guides in a coordinated fashion would be experienced through imagining the guides. An interesting idea is that scores in the imagery testing may have been higher because the (faux) information returning from the body was of higher quality than that generated by the movements. This hypothesis fits well with the earlier discussion of sensory acquisition deficits being a cause of movement problems in ataxia (Bower, 1997) particularly as the most abundant sensory input to the cerebellum comes from the somatosensory system. However, it must be considered that rather than being imagery being self-generated, sonic guides may have been being stored locally and remembered by participants (time between auditory and imagery testing was not long enough to completely extinguish auditory memory). This is important as generating mental imagery stimulates different process than memory retrieval. If participants

were relying on auditory memory the parameters of the sound would guide swaying rather than an audiosomatomotor gestalt being activated. In this instance, it is unlikely that additional proprioceptive information would be delivered to the motor systems. A different issue was that the spatio-temporal aspects of the imagined sounds could not be controlled for in this experiment. There is the possibility therefore that participants were producing auditory imaginings unrelated in duration to the swaying actions. However, results do not support this notion.

An advantage for participants in the imagined sound condition was that they could rehearse the temporal dynamics of the sound ahead of time. In the sound condition guides had to be presented before prospective information could be extracted. It is also a factor that listening and synchronising with something self-generated and internal, is likely easier than with something imposed and external. In one task participants are attending whilst having something imposed, whereas in the other, they are cooperating with themselves. As additional tasks are known to cause problems in ataxia (Ilg et al., 2013), it is possible that participants improved in the imagined sound condition as a function of less interference whilst swaying.

#### *5.8.6 Short-term motor learning*

The cerebellum is implicated in the short-term learning of motor acts (Penhune and Doyon, 2002). As the motor problem in this study involved repeat actions, it might be expected that motor adaption would occur. Adaption would mean efferent motor signals from higher brain structures (i.e. motor cortex) to the spinal tracts, are modulated by cerebellar structures. Activation of the pathways involved lead to ‘learning’ through inhibition of M1 motor cortex efference (Daskalakis et al., 2004).

If this is occurring, the question is how the sounds could influence this network? Integration of movement information through non-cerebellar pathways or increased cerebellar output, are two possibilities (see earlier discussion on sensory augmentation). However, most of the research on the cerebellum and short-term motor memory suggests that once a task is learnt, activity subsides (e.g. Toni et al., 1998; Ungerleider, Doyon and Karni, 2002). There is a question therefore as to whether the swaying exercises can be considered a ‘new’ learning experience and if the cerebellum would normally be active in this scenario. Perhaps for some participants weight-shifting was novel but for others this is unlikely. Nevertheless, short-term rapid learning, is a primary step in the long-term retention of motor acts (Nudo, 2013). Long-term changes in movement control therefore would indicate whether the auditory guides are activating networks that moderate motor cortex output or not. This topic is explored further in Chapter 6.

#### *5.8.7 Other considerations from this study*

A number of studies show that the cerebellum is involved in auditory processes (e.g. Parsons et al., 2009; Sens and de Almeida, 2007). The precise role unclear but this is an important question if the auditory system is to be used for delivering additional sensory information in cerebellar disease. Auditory processing is localised within the cerebellum. Click sounds for example, initiate neural responses in lobules VI, VII, VIII (Colin, Ris and Godaux, 2001). For participants who improved in the present study, it is apparent that auditory deficits are not an issue. It is possible therefore that the location of cerebellar damage determined which participants improved, and which did not.



As understanding of cerebellar function has expanded over the last decade, so have the number of cognitive processes attributed to this sub-cortical structure (Stoodley, 2012). One such process is the direction and maintenance of attention (Gottwald et al., 2002; Schweizer et al., 2008). This cerebellar function also includes attention to motor acts (Akshoomoff, Courchesne, and Townsend, 1997). It is plausible therefore that the auditory guides may influence attention and there are two ways this is likely to happen. First, attention may be focused towards the sounds where instructions within the guide dictate action (i.e. a top-down process). Alternatively sounds may focus attention back towards the body so that movement is monitored and referenced to the guides (a bottom-up process). The predictive nature of the guides is important to both proposals as anticipation of an event is crucial to directing attention toward it. As posited in Chapter 4, prediction is a primary function of the cerebellum (Allen et al., 1997). As nervous system injury often includes a lack of awareness of the body, a related proposition is that the act of moving in time with something external, reaffirms feelings of self or connection with the body (i.e. through practice, a sense of agency is experienced). This hypothesis draws on the development literature where it has been argued that moving in synchrony with music or vocal rhythms, develops a sense of self and being with others (Schögler and Trevarthen, 2007). In the case of neurological disease this would mean expectations once again being met and predictive behaviour becoming meaningful once more.

## 5.9 Implications, limitations and further directions

That some participants responded to the intervention is encouraging, particularly as novel techniques were being tested in this work. However, a number of participants did not respond positively in either sonic guide or imagined sound conditions. This reality likely reflects the lack of homogeneity of the cohort. Other than groups being statistically different in some baseline measures, participants within each group had varied symptoms and movement abilities.<sup>55</sup> Heterogeneity was also a product of incomplete diagnoses with many participants classified with idiopathic cerebellar ataxia which provided poor understanding of underlying neurological damage. It is possible therefore that positive results (and vice versa) could be related to patterns of neural damage rather than the qualities of the sounds. Lack of clear diagnoses also hindered pre-identification of functional problems that could have provided greater clarity in the results. For example, spinocerebellar ataxia types 2, 3 and 7, present with auditory complications attributable to extra-cerebellar brainstem degeneration (Hoche et al., 2008). In this cohort, only one participant had a diagnosis where a prediction of hearing ability could be made before testing (participant 18; SCA 2). In light of these problems, this study would have benefited greatly from a group presenting with the same form of cerebellar ataxia. In an ideal world, age and disease onset would also be controlled. However, finding participants that matched these criteria was beyond the scope of this research and even recruiting twenty people with cerebellar disease able and willing to take part required a nationwide search. Nevertheless, further testing could have lessened the effects of poor diagnoses. For

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<sup>55</sup> To demonstrate this case files have been produced to explore two participants in more depth. These are presented in Appendix D.

example, tests of hearing ability (such as perception of pitch tone and pitch glide) would have been appropriate and helpful to interpreting results. Tests of vision and proprioceptive sense likewise would have been beneficial.

Heterogeneous groups also weakened the opportunity to draw strong conclusions regarding cerebellar function. Results support the general idea that task specific, predictive sensory information helps in controlling ataxic movement but the nub of how and what the guides influence remains obscure. A better controlled cohort would limit this problem. Patients with SCA 6 would be a particularly useful group to work with, as neural damage in this form of the disease is restricted almost exclusively to the cerebellum, perceptual deficits are apparent and no peripheral neuropathy is found (Stevanin et al., 1997). A small group with SCA 6, or indeed a single case study, may lead to a deeper understanding of the effects of the auditory stimuli in relation to cerebellar function.

With regards to the mental rehearsal of sounds, the experiment could be improved by clarifying if participants were using auditory memory (of the recently played sounds) or self-generating auditory imagery. An experiment with sufficient time between testing for auditory memory to diminish would be appropriate for answering this question. This problem is approached in Chapter 6.

Controlling for fatigue, a known feature of ataxia (Brusse et al., 2011), was a problem in this experiment. It is clear for example, that wheelchair users are more likely to tire than those who walk unaided. In particular fatigue may have been a factor in the control group results as participants completed six trials rather than three. However, that may have been offset by the fact that controls were ‘fitter’ than the experimental group as determined by the SARA scores (this was unintended as

participants were randomly assigned). It is also a reality that all participants completed the testing and a third of controls produced a positive effect irrespective of the extra trials they had undertaken.

A final issue with this study is the level of analysis employed. Whilst behavioural data can answer many important questions in scientific research, many of the most intriguing points raised by this work remain unanswered by this method. Perhaps most intriguing are questions of what happens at the neural level. Does sensorimotor integration occur in relation to rehabilitative sounds for action? Can we show activation of motor cortex when listening to rehabilitative sounds? Did the sounds stimulate areas of the motor system or do they affect cerebellar structures? To answer questions like these, neural measures are necessary and therefore it is suggested that fMRI is used to study single participant before and after a period of training. Such an exploration would be of immense value to studies of rehabilitative sounds and neurorehabilitation science as a whole.

## 5.10 Summary of experiment two results

It is proposed that additional sensory input makes up for a shortfall in the sensory function of the cerebellum. This function is sensory acquisition rather than processing (Bower, 1997). Data suggests that if enough meaningful information is offered the acquisition function of the cerebellum is mitigated. Two proposals were advanced for how additional sensory information may be integrated once in the nervous system. The first was that, as the sounds are movement based, spatio-temporal characteristics of the sway directly initiate responses in the higher

processing areas of the brain (such as premotor cortex). The second proposal is that the guides support an existing but impoverished sensory function within the cerebellum increasing its output. Both proposals assume that movement information within the guides goes through sensorimotor transformations, and contribute to the formation of a motor image or internal model that is used for anticipatory intrinsic guidance. It is also suggested that the guides may act as an external comparator to monitor movement progression.

The findings from the auditory imagery testing add support to the idea that the cerebellum is involved in sensory acquisition. It is argued that audiomotor associations are rapidly developed so that imaging sounds contributes to the mechanisms of intrinsic guidance in much the same way as real sounds. The possibility that more meaningful information is given through the emulation of proprioception is considered. It is reasoned that, as a large proportion of cerebellar input is from the somatosensory system, imagined guides support impoverished sensory function within the cerebellum.

### 5.11 Issues using the $\tau_G$ -equation

A number of papers have used the  $\tau_G$ -equation as a way to measure and assess motor performance (for example, see Austad and van der Meer, 2007). The equation is part of a broader hypothesis that uses recursive regression to test how well a movement matches a proposed neural correlate (the  $\tau$ -guide). The neural correlate is described as a ‘flow of neural energy’ in the nervous system that follows a ‘ $\tau_G$ -pattern’ and specifies the underlying information needed to guide action (Lee, 2005) (see section

2.8 for a more in-depth discussion of this topic). As sonic guides were computed using the  $\tau_G$ -equation, a potential method to investigate the data in this study was to test how well swaying matched the  $\tau$ -guide. In Chapter 3, an analysis was run using the trajectory path of the hands. Almost perfect  $\tau_G$ -guidance was found for all sound conditions (see Appendix B). However, as described in this section, this is not unsurprising and in the opinion of this author means little outside of the realm of curve fitting. Of concern was the fact that k-values did not reflect reaching behaviour in a meaningful way. This is one of several issues encountered when applying the  $\tau_G$ -analysis to centre of pressure data from this study. Essential to any analysis is confidence that the measure used satisfies a number of criteria. The measure must represent what is being tested (i.e. does the data explain what is being measured?). Additionally, in rehabilitation studies, the measure must be able to discriminate between dissimilar types of action and be sensitive to subtle changes in behaviour. Most importantly, reliable and consistent results need to be produced. After using the  $\tau_G$ -equation in Chapter 3 and with two people in this Chapter, it can be concluded that these criteria are not met. The purpose of this research is to test the influence of sonic-guides on movement behaviour in cerebellar ataxia. Therefore an alternative analysis tool was selected to measure movement changes (jerk). A discussion of the issues encountered in the preliminary analysis is presented below but before doing so  $\tau_G$ -theory is briefly revisited.

### 5.11.1 $\tau_G$ -analysis

The tau guide (i.e. the hypothesised movement guide generated in the brain) is calculated using the formula;

$$\tau_G = 0.5(t - T_G^2/t) \quad (\text{Equation 5.3})$$

where  $T_G$  is the duration of the action gap and  $t$  is time (from zero to  $T_G$ ).

Tau theory predicts that movements are controlled by coupling the time-to-closure of an action gap (e.g., a distance to be covered by a limb movement) to the tau guide ( $\tau_G$ ). The time-to-closure of the motion gap (tau of the movement) is calculated following the equation:

$$\tau_m = x/\dot{x} \quad (\text{Equation 5.4})$$

Where  $x$  specifies the action-gap to the end of the movement (at a particular data point) and  $\dot{x}$  equals the time derivative of  $x$  (velocity). Regardless of the dimension of  $x$  (e.g., distance, force, pitch), the dimension of tau is thus time. The theory predicts that movement is controlled by coupling the tau of the movement to the internal tau guide.

$$\tau_m = k\tau_G \quad (\text{Equation 5.5})$$

where  $\tau_m$  = movement tau,  $k$  = a constant and  $\tau_G$  = the tau guide.

To test whether a movement is tau-guided, a recursive linear regression analysis is conducted. This analysis starts at the target point (e.g., touching a target) and using an iterative process determines the proportion of the movement towards this target that is tau-guided. Three variables are important in this analysis,  $R^2$ , the percentage of the movement that appears  $\tau_G$ -coupled and  $k$ .  $R^2$  is pre-set by the experimenters at

0.95, meaning that 95% or more of the variance in the data needs to be explained by the linear regression model in order for that section of the movement to be deemed ‘tau-guided’. Data points are removed from the start of the movement towards the end until this value is reached. Percentage coupling is found by dividing the remaining number of data points by total number of data points in the movement. The slope of the regression gives an estimate of  $k$ , providing the  $R^2$  is close to 1. In this case, the regression slope indicates where in the movement peak velocity occurs and how long periods of acceleration and deceleration will be. The closer the value to one, the later the peak velocity in the movement and the harder contact is at the goal. A value above one indicates the effector is still accelerating at contact, resulting in collision. These scores are the values on which judgements of how well a movement is  $\tau_G$ -guided are based.

#### *5.11.2 Exploring movement data for two participants using the $\tau_G$ -equation*

Using the protocol described above, data for two participants with cerebellar ataxia and a healthy control were explored analysed. Participant one had serious difficulty walking unaided whereas subject two walked without problems. For the experimental set up and data collection see section 5.5 above. Movement along the medial-lateral (Y) axis was analysed, as this was the axis along which the majority of movement in the weight-shifting exercise took place. The axis along which the majority of the movement took place was selected. For the weight-shifting exercises this was the medial-lateral (Y) axis. Data was smoothed using a Gaussian filter  $\sigma$  11 (sampling frequency was 500 Hz). To account for noise, data points less than 5% of the peak velocity were removed from the start and end of the movement. Movements with



amplitude of less than 0.02 mm were considered noise and excluded from the analysis. Data were analysed using TauGui, a custom program in MATLAB (The MathWorks, Inc.).<sup>56</sup> Mean percentage coupling and mean k value were computed for before and after the test variables were introduced as well as at two months follow-up and are presented in Table 5.11.<sup>57</sup>

**Table 5.7** Mean percentage and k values for conditions Pre-intervention, Imagined Sound and Two Months follow up for two ataxia participants and a healthy control.

	Pre %	Pre k	IS %	IS k	2 Mth %	2 Mth k
Subject 1	78.94	0.48	47.6	0.66	71.74	0.55
Subject 2	70.66	0.46	87.11	0.34	97.47	0.31
Control	78.68	0.35	*n/a	*n/a	*n/a	*n/a

\*The control did not take part in the two month follow up so only baseline data are reported for this participant.

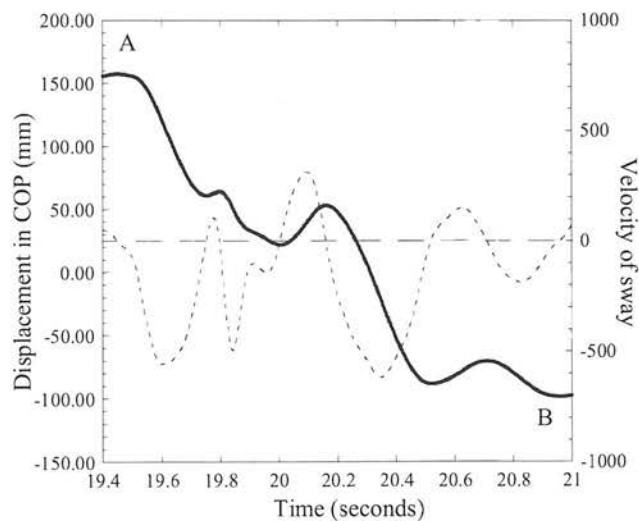
Percentage coupling is the main outcome measure for this analysis with high percentage coupling indicative of tau-guided movement. For subject one, immediately after intervention, percentage coupling decreased (i.e. movements were less tau-guided) and after two months this participant was still not performing at baseline. In contrast, subject two steadily improved until at two months follow-up percentage coupling was high (97.47%) (see Table 5.11). Visually, participants appeared to have less problems weight-shifting, which was corroborated verbally by the participants. This suggests that the percentage coupling scores reflect two different processes in these participants. For one an increase reflects improvement, for the other a decrease. A likely explanation for this difference is that participant one's baseline movements consist of more subcomponents, from which a 'mean

<sup>56</sup> The TauGui was programmed by David Skulina, 2005.

coupling' is derived. As swaying improves, subcomponents 'blend', meaning longer continuous motion but 'bumpier' movement trajectories and velocity profiles. However, the opposite pattern occurs in the results for subject two. At baseline sways were already completed in a single motion with one velocity peak. As this participant improves *increased* coupling scores are recorded. This preliminary exploration highlighted a significant issue. The direction of coupling scores (higher or lower) has different meaning depending on the original movement ability of the participant.

### 5.11.3 Subcomponents

People with advanced ataxia do not move in smooth, coordinated ways and as a result produce jerky centre of pressure profiles, even when repeating stereotyped actions. Figure 5.6 shows COP data of a sway 'action-gap' in the medial-lateral axis from peak left to peak right. The action-gap is broken into smaller subcomponents as



**Figure 5.6** The typical movement profile of a person with ataxia performing a single sway (left to right) (solid line). The 'action-gap' (A to B) is broken into a number of subcomponents (as bound by zero to zero in the velocity profile [the dotted line]).

denoted by velocity returning to zero multiple times rather than once. ‘Steps’ are also formed where velocity moves towards zero without reaching it.

A central tenet of  $\tau_G$ -theory as stated by Lee (2009) is;

*“An action-gap is the separation between the current state an animal is in and the goal state to be achieved by action.”*

(p. 841)

It is difficult to argue that the endpoint of each of these subcomponents is ‘the goal state to be achieved by action’. However, as discrete movements are defined by zero to zero velocity, each of the sub-action-gaps is treated as an individual movement in the  $\tau_G$ -analysis. In the example of Figure 5.6 above, five subcomponents are analysed (two are too small to be included). The  $\tau_G$ -score for this particular sway suggests that each subcomponent is tightly  $\tau_G$ -guided with the average coupling score 98%.<sup>58</sup> This result suggests this person with ataxia is not impaired at generating or executing  $\tau_G$ -guides for small movements. However, that the brain prescribes guides for these subcomponents is debatable as the endpoints of subcomponents do not represent movement goals. Subcomponents have been described as representing failure of coordinative muscle activity (Krebs et al., 1999) or adjustments to perturbations in original trajectory. It makes little sense to suggest subcomponents are  $\tau_G$ -guided (i.e. planned for by the nervous system *ahead of time*).

In discussing subcomponents, it is worthwhile considering what they represent in centre-of-pressure data. COP trajectories are the outcome of multiple body parts being stabilised to control the COM (Haibach et al., 2007). In this regard COP is not

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<sup>58</sup> Percentage coupling for each component was; 97.2%, 98.11%, 97.73%, and 97.5%.

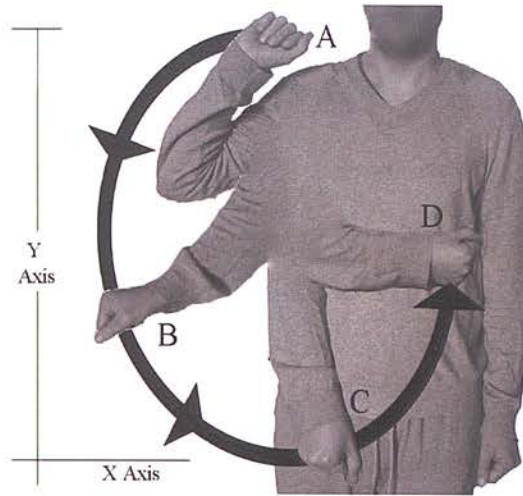
directly perceived but rather, is the outcome of controlling motion sensed in other body parts (for example at the ankle, knee or hip joints). Perturbations of the upper torso, head or arms also register in COP trajectories. This includes body movement outside of the main direction of motion. For example, it is not uncommon to lurch backwards (i.e. in the anterior-posterior direction) from the waist when swaying medial-laterally). In this example the lurch may affect velocity/trajectory in the medial-lateral direction.

#### 5.11.4 Issues of single axis and centre of pressure data

Single axis data has been used in many  $\tau_G$ -studies (e.g. Austad and van der Meer, 2007). However, using single axis data introduces misleading start and endpoints. At any point within a single axis, where the trajectory moves perpendicularly to that axis, velocity will be zero. In addition, for a continuous motion where the trajectory passes from one axis to another (i.e. along a curved path) the velocity will *always* produce a gradually decelerating/accelerating velocity profile<sup>59</sup> regardless of how the effector is moving. To demonstrate this, a simple experiment was set-up. A hand was marked for Qualisys motion capture before being swung in an arcing circle. Instruction was given to still be increasing velocity at peak distension (point C in Figure 5.2).

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<sup>59</sup> This is based on velocity being calculated from single axis positional data by differentiating once with respect to time.

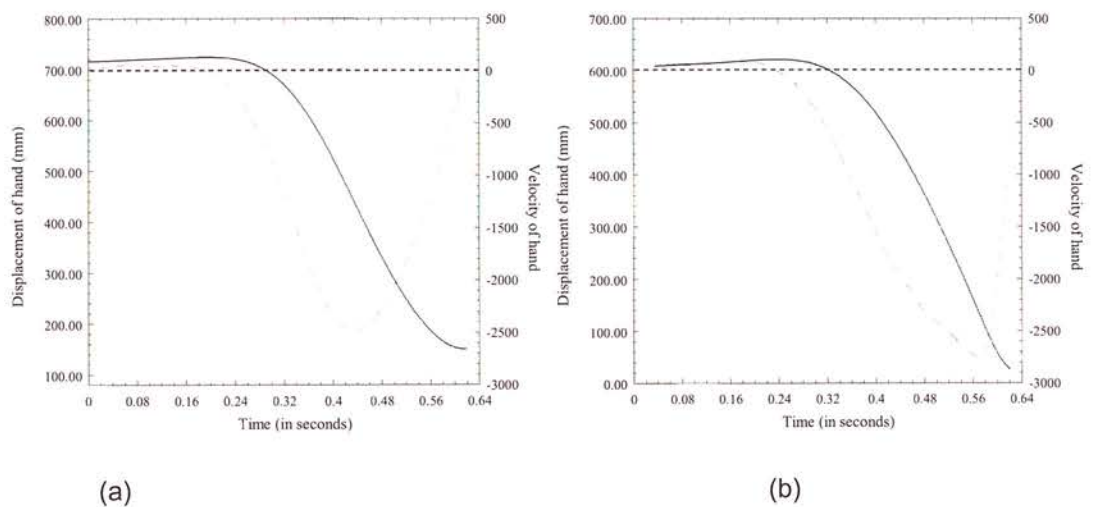


**Figure 5.7** Hand swinging from start point A to rest at point D. Hand speed was still increasing at point C.

Figure 5.7, shows the greater part of the hand's trajectory is in the Y-axis. However at point C, At C, the vertical velocity of the hand is zero, while the horizontal velocity is at its peak. Figure 5.8 (a) plots the position and velocity of the hand using Y-axis data only. Movement in the Y-direction starts at approximately 0.24 seconds (point A) and full extension is reached after 0.64 seconds (point C, where the hand begins to ascend towards the head). At this point, in the Y-axis the hand's velocity reaches zero. A complete movement has been recorded displaying a bell-shape velocity curve with clearly defined start and end points (bounded by zero to zero velocity). A  $\tau_G$ -analysis performed on this movement shows high  $\tau_G$ -guidance with a coupling score of 98%. However, this result only represents a portion of the hand's motion. It is known that speed is increasing at C (as the participant was instructed to do so) meaning that if the movement is being  $\tau_G$ -controlled, the participant would have to be monitoring decreasing velocity in the Y-axis whilst simultaneously increasing hand speed in 3-dimensional coordinates. This seems improbable as a control strategy. In addition, remembering that the tau-guide is described as the flow

of neural energy following a  $\tau_G$ -pattern, it is difficult to understand how control in one axis would operate in this context. The axis is defined in a world-centred frame of reference (as opposed to body-centred). The positions of the X- and Y-axes are defined by the experimenter, meaning that results do not directly reference the direction of the forces generated by the muscles or the torques on the joints involved. In this sense results are artificial. In the arm swinging example, four neural flows of energy would be required, three to proscribe ahead of time the movement information for the passage of the hand through each axis and a an overriding  $\tau_G$ -guide to control the complete motion (presumably by proscribing information to the same muscles as the sub- $\tau_G$ -guides). Figure 5.8b is the same movement. However, data from the X, Y and Z axes have been combined by creating a single movement vector (Rodger and Craig, 2011) using;

$$R = \sqrt{X^2 + Y^2 + Z^2} \tag{Equation 5.5}$$



**Figure 5.8(a and b)** Movement of the hand using Y-data only (a). (b) The same movement using the single sway vector of combined positional data (R).



Figure 5.8b gives a more accurate picture of the hand's trajectory. As can be seen at 0.64 seconds (point C), velocity has not reached zero. The result shows that using single-axis data introduces false start and endpoints but also that velocity in a single axis bears little relation to the actual motion. The same types of problem are found

**Table 5.8** Comparison between start time, end time, percentage  $\tau_G$ -guidance, and number of steps\* for single-axis (Y) and 3-dimensional vector (R) data of the same sway trial of an ataxia participant.

Start(s)	End(s)	Percent	Steps	Start(s)	End(s)	Percent	Steps
Y	Y	Y	Y	R	R	R	R
0.96	1.492	74.16	3	0.96	1.492	47.19	3
2.074	2.216	97.22	1	2.074	2.636	50.71	2
11.142	11.824	21.35	3	11.15	11.448	98	1
18.482	19.948	23.98	6	18.502	20.058	6.8	7
20.734	21.54	98.02	2	20.73	21.634	44.37	3
22.056	22.428	61.5	2	22.066	22.446	26.18	2
25.212	25.63	90.48	1	25.166	25.738	46.34	3
Average		66.67		Average		45.66	

\* Steps indicate adjacent segments in the velocity profile where a period of acceleration is followed by a period of deceleration within one sway motion. Between steps, velocity does not reach zero, whereas between sway movements velocity returns to zero.

when  $\tau_G$ -analysis is applied to a person with ataxia. Data presented in Table 5.9 shows the results of a  $\tau_G$ -analysis on Y and R data from the same section of swaying data from a person with ataxia (subject one from 6.2.2).

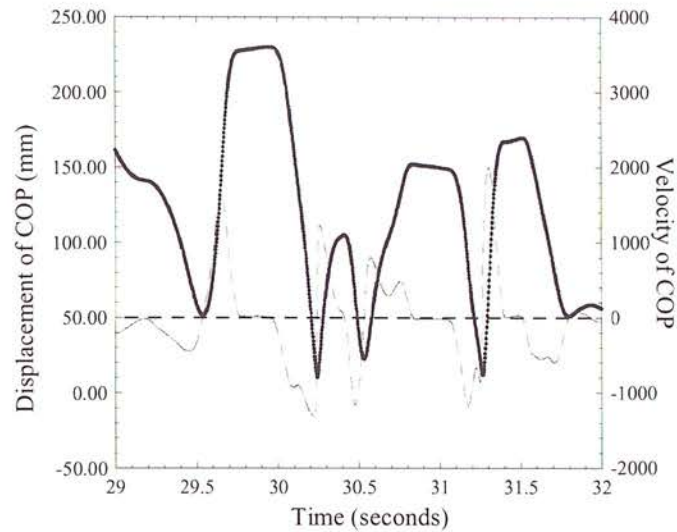
Table 5.8 shows starts and particularly end points vary between sets. In this sense these data do not represent action-gaps sensed by the actor but rather, are the product of the experimental design and data analysis. It should also be recognised that in some Y vs. R data comparisons, small differences in start and end points (and thus sway duration) have dramatic effects on coupling scores. For example, at 22.056 to

22.428 seconds the Y-data coupling score is 61.5%. For the corresponding time in the R-data (22.066 to 22.446 seconds) the coupling score is 26.18%. In this example small differences have changed the movement from being reasonably well guided to not at all. The obvious answer to this problem is to not use single axis data. However, further issues regarding  $\tau_G$ -analysis exist which further question its accuracy as a measure of motor dysfunction.

#### 5.11.5 The sensitivity of the $\tau_G$ -analysis

The sensitivity of the  $\tau_G$ -analysis refers to how well this analysis discriminates between qualitatively different types of movement, in particular between well-controlled movements and uncontrolled movements. In Figure 5.9, a section of data is displayed where an ataxia participant loses control and overbalances a number of times whilst swaying. The flat lines starting at 29.6, 30.8 and 31.9 seconds, each represent a moment where experimenters have intervened and ‘caught’ the participant to stop falling. Zero velocity is recorded for the duration of the intervention. The movement preceding the flat lines are clearly not well controlled





**Figure 5.9** A section of data showing a participant with ataxia swaying in the medial lateral axis. At several points the actor overbalances before being steadied by the experimenters.

however, a  $\tau_G$ -analysis was conducted and percentage coupling scores of 97.5, 65 and 98% recorded. In other words, two out of three movements were highly  $\tau_G$ -guided according to this analysis. A further uncertainty is that  $k$  values for the falls were 0.3, 0.4 and 0.15 respectively. This does not make sense given that  $k$  denotes how hard something arrives (see Chapter 2) (Lee, 2005). In this example  $k$  values are too low to identify falls even when cushioning from the experimenter's intervention is accounted for. A concern with this example is that neither the mean percentage coupling nor the  $k$ -values distinguish these falls from well controlled actions. Whilst the example is rare, the inability of the  $\tau_G$ -analysis to identify such clear aberrations in movement behaviour is a serious problem for a measure attempting to evaluate motor dysfunction.

### 5.11.6 Inconsistencies in the $\tau_G$ -analysis data

Ataxia is a degenerative disease where at a certain stage movement is continuously impaired. This means movement problems are identifiable through observation each time an action is performed. An accurate assessment should reflect this in its analysis (i.e. scores for each action will cluster around the mean). However, this was not found in the  $\tau_G$ -analysis with sway scores inconsistent from one to the next. Table 5.9 reports scores for a single ataxia participant (subject one from section 5.2.2) swaying over one trial. Mean coupling percentage for the trial is 64% yet few individual sway scores are close to this. Movements with low scores of approximately 30% or less were found, as well as movements with high scores of percentages of 90% and above associated with tight  $\tau$ -coupling. These data suggest that the ability to generate tau guides switches on and off from one movement to the next, within one trial. Although theoretically possible, this explanation is

**Table 5.9**  $\tau_G$ -scores for an ataxia participant lateral swaying over a single trial. Sway number and percentage coupling score are shown.

Sway No.	%	Sway No.	%	Sway No.	%	Sway No.	%
1	72.8	6	83.17	11	23.59	16	30.52
2	98.81	7	98.99	12	17.7	17	85.73
3	97.76	8	28.42	13	91.81	18	22.35
4	97.49	9	9.37	14	97.84		
5	71.05	10	99.01	15	26.94		Mean %
							<b>64.08</b>

unsatisfactory. Since all sways were completed successfully, the results raised questions as to whether  $\tau_G$ -guidance is necessary for motor control.

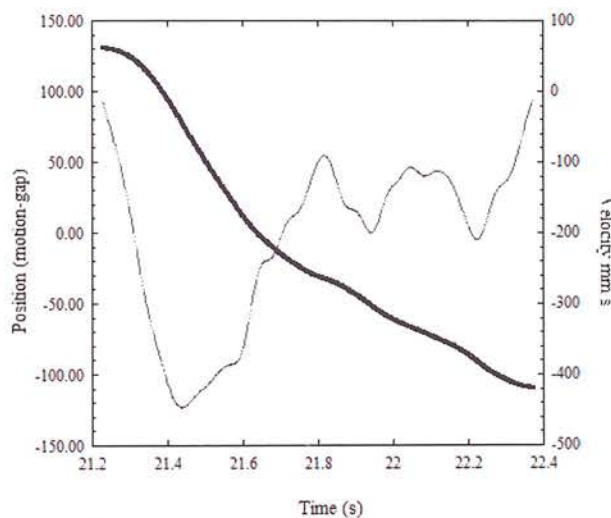
### 5.11.7 Further issues with consistency

Motion data is often noisy particularly at the start and end of actions because velocity is low at these points. This is an issue when calculating tau as Lee, Craig and Grealy, (1999) note;

*“...the estimates of  $(\dot{x})$  are noisy; and since that value appears in the denominator of the formula for  $(\tau)$ , this noise would be amplified in the calculation of  $(\tau)$ ”*

(p. 2032)

This means data from the slower parts of an action (i.e. the start and ends) must be removed. However, it is imperative that removing data does not affect results and has equal influence on all data. This was found not to be the case when applying a  $\tau_G$ -analysis to COP data. In Figure 5.10 (below) a single sway extracted from the larger



**Figure 5.10** A single sway from which 3% and 4 % of the peak velocity was removed.

analysis is plotted. The sway is highlighted as an example of the anomalies that appeared in the data when exploring the removal of noise. Two analyses were



performed. In the first analysis data were removed from the start and end points if movement velocity was less than 3% of the peak velocity. In the second analysis data of movements with a velocity less than 4% of the peak velocity were removed. The first analysis revealed a percentage coupling score of 98.8% and the second analysis 33%. To confound results further,  $k$  values of 0.1 and 0.9 were recorded, respectively. In terms of the  $\tau_G$ -hypothesis, the first analysis describes a well-controlled motion arriving gently at its goal and the second analysis a poorly controlled motion nearly colliding with the endpoint.

#### 5.11.8 Conclusions

The issues discussed above are not intended to contribute to the debate on how action is guided or on the  $\tau_G$ -hypothesis as a whole. However, it is difficult to ignore the outcomes of this exploration. As the crux of the  $\tau_G$ -hypothesis is that movement follows a mathematical formula produced in the brain, the fact that these data do not fit that model (without manipulation or ignoring the meaning), challenges the  $\tau_G$ -hypothesis. However, the concept of intrinsic guidance is still central to motor control and its properties worthy of attention. A number of useful lines of enquiry have been pursued, such as temporal coincidence between patterns of neural energy and sensory stimuli (Grothe and Klump, 2000) or data showing activation of cerebellar Purkinje cells code for precise timing of motor output (Thier et al., 2000). This section shows that in its present form, the  $\tau_G$ -hypothesis is not a useful way to explore intrinsic guidance or, in the opinion of this author, movement as a whole. More pressingly, the aims of this thesis were to monitor changes in movement ability in individuals with and without cerebellar ataxia. Using the  $\tau_G$ -equation proved to be

unreliable, inconsistent and unrepresentative of the movement performed in this work so an alternative was found. Whether the issues related to the  $\tau_G$ -equation can be solved is debateable. However, providing evidence for or developing the  $\tau_G$ -hypothesis is not the focus of this research.

## Chapter 6 - Applying Sonic Guides over Two months

### 6.1 Introduction

Experiment 2 demonstrated that coordinating actions with continuous and predictive, auditory guides, instantaneously decreases levels of jerk in some cases of cerebellar disease. In addition, it was shown that moving to mentally rehearsed sonic guides also produced less jerk in several participants. The next part of this research was to investigate the effects of performing lateral swaying exercises more smoothly over a longer period of time. This study attempts to answer two main questions. After two months of exercising with sonic guidance, do participants sway in a more controlled manner *in the absence of the sounds*? Secondly, does this same practice translate to improved walking ability? To investigate these questions, seven members of the experimental group (from Chapter 5) followed a sonic guide exercise programme (SGEP), which included swaying in the medial lateral and anterior posterior axes, in coordination with auditory and imagined guides. After two months participants returned to the laboratory and were tested on lateral swaying and walking. Changes in mean jerk for weight-shifting, and foot placement angle and stride length for walking, were used to assess performance using a pre-test post-test design. For the swaying it was predicted that training with the guides would lead to decreases in jerk or, if improvements had been previously found (in Chapter 5), these would remain

stable. As the training programme targeted core balance, and as core balance is important in stabilizing upright tasks, it was estimated that foot placement would be less variable and that stride length would increase in the ambulation task.

### *6.1.1 Applying neurorehabilitation in cerebellar disease*

This study attempts to encourage changes in brain plasticity using the principles of neurorehabilitation; functionality, adaptability and repetition (see section 4.5.3 for discussion) (Carr and Shepherd, 2003). A major challenge for this research is that cerebellar damage precludes participation in neurorehabilitation programmes based on these principles. Rehabilitation of mobility for example, would optimally include active participation in an ambulation task. However falls, or fear of falls, are common in cerebellar pathology meaning that this is often not possible, particularly in the later stages of the disease (van de Warrenburg et al., 2005). The ability to adapt movement form is also impaired in cerebellar disease as ataxia is known to increase when different constraints are put on a task. People with cerebellar atrophy for example, display degraded movement when moving at different velocities (Topka, Konczak and Dichgans, 1998) and have difficulty controlling multi-joint interaction torques (Bastian, Zackowski, and Thatch, 2000). Experiment 2 (Chapter 5) addressed these issues by compelling participants to experience some of the forces encountered when walking and to engage the systems involved in maintaining upright balance. Participants were also forced to adapt movement kinematics to altered guide durations (if they were being followed correctly). The next stage of the thesis is to build on Experiment 2 by applying the third principle of neurorehabilitation - repetition.



### 6.1.2 *The effects of practise on plasticity*

It is well understood that practice leads to learning and improved performance across all activities (Langhorne, Coupar and Pollock, 2009) and the basis of learning is neural plasticity (see section 4.5.1). One to three months post-acute injury, the brain is at its ‘most plastic’ (i.e. there is a period of relatively rapid, automatic reorganisation within this time window). It is advocated that this is the optimal time for engagement in neurorehabilitation and that significant amounts of functional recovery are likely to occur in this period (Krakauer et al., 2012). Neurological recovery however, is by no means restricted to this time frame and functional gains can be found/initiated for years post injury (Cohen and Hallet, 2003).

Repetition of a specific act is vital in initiating long-lasting changes in plasticity and thus, motor behaviour (Duerden and Laverdure-Dupont, 2008). There is a question however, as to what constitutes enough practice for plastic changes to occur? As mentioned in Chapter 4, short-term changes occur in neurons instantaneously in response to incoming stimuli (Nudo, et al., 1996). Nevertheless, these connections weaken just as rapidly in the absence of continued input, suggesting further intensity and duration are necessary for longer-term change. The question of ‘how much neurophysiotherapy’ was addressed by Shiel et al. (2001) in a study comparing two groups of patients recovering from brain injury. One group was given ‘intensive’ rehabilitation (i.e. extra hours), whereas controls were given a regular programme. The intensive course group recovered faster and showed greater functional gains on a number of tests including motor skills (Shiel et al., 2001). However, intensity and duration of rehabilitation programmes for neurological diseases are much more difficult to determine. The relatively slow pace of neural degeneration means that

there is no period post-injury when the brain is ‘most plastic’. In addition, damage is often diffuse, greatly complicating the capacity for unmasking effects and brain reorganisation. However, positive changes in movement behaviour have been observed following short periods of training. Physical programmes of 4-10 weeks for example, improved motor behaviour in neurological disorders such as cerebellar or Parkinson’s disease (see Ilg et al., 2010; Hirsch et al., 2006). Nevertheless, these facilitatory effects may diminish post-training which reflects the on-going neural degeneration underlying neuropathology (Hirsch et al., 2006). This factor suggests neurorehabilitation in nervous system disease should be approached differently. Other than being an on-going part of a person’s daily routine, training programmes must be continually restructured to challenge ‘ceiling effects’ encountered through practice.

### 6.1.3 *Motor learning*

An important aspect of neurorehabilitation is motor learning or, as is often the case, re-learning. As previously discussed the cerebellum may be involved in this process (see section 4.4.2) (Penhune and Doyon, 2005). Cerebellar roles in monitoring error feedback (crucial in motor adaption) (Kawato and Gomi, 1992; Tseng et al., 2007), storage of motor memories (Marr, 1969; Ito, 2012) and refining motor cortex efference (Daskalakis et al., 2004) have all been put posited. However, observations that cerebellar activity declines after movement becomes ‘automatic’ or learned, have led to proposals that the cerebellum is only involved in the early stages of motor learning (Toni et al., 1998; Doyon et al., 2002) or may represent only the consolidation of motor memories (Penhune and Doyon, 2005). A movement is

temporarily represented at the neural level (through short-term plasticity) for a number of hours post practice (Nudo et al., 1996; Krakauer, Ghilardi and Ghez, 1999). If another movement is learnt within this ‘consolidation window’, the original representation is disrupted and learning hampered. However, if the action is repeated the representation becomes more stable. Animal models (Kellet et al., 2010) and human imaging studies (Doyon and Ungerleider, 2002), have identified that consolidation of a motor act involves neural activity that occurs in a sequence through different brain regions. Doyon and Ungerleider, (2002) report that high neural activity is found in the prefrontal cortices (perhaps due to the cognitive aspects of a task) followed by increased firing in separate structures such as the striatum or cerebellum. Once consolidated, there is some debate about where motor memories are stored. Modifications to the M1 in motor cortex are frequently cited as a way in which memories are stored (Galea et al., 2011) however; the cerebellum is also reported to retain motor memories (Herzfeld et al., 2014; Ito, 2012). Whilst positive findings from Experiment 2 were interpreted as potential short-term learning of the swaying (e.g. motor adaption), it could not be established if consolidation or long-term storage had occurred.

#### *6.1.4 Core balance training and dynamic balance*

In section 5.2.1, the importance of destabilising exercises for ambulation training was introduced. This is because walking displaces COM and maintains it outside of the stability boundary. COM is transferred from leg-to leg for each step (Kuo, Donelan and Ruina, 2005) and as each foot lifts from the ground the base of support becomes periodic monopedal stances (Vaughan, Davis and O’Connor 1999; Bauby



and Kuo, 2000). Propulsion is generated and then equally counteracted whilst gravity and the body's inertia are simultaneously monitored (Kuo, Donelan and Ruina, 2005). Ambulation viewed in this way is a series of controlled falls (O'Conner and Kuo, 2009). Two components of walking are an equilibrium centre (for balance) and a locomotor centre (to generate the rhythmic patterns of the limbs) (Ienaga et al., 2006). To maintain equilibrium requires core stability which refers to the coordinated contraction of the diaphragm, abdominal and pelvic floor muscles (Willson et al., 2005). These contractions limit lumbar spine movement and help to return the body to equilibrium after perturbation. All movement affects core stability to some degree and control of this central balance mechanism depends on prospective coordination, rather than strength or endurance of the trunk muscles (Borghuis, Hof and Lemmink, 2008). Anticipatory adjustment of the musculature involved in core stability maintenance therefore, must be part of any 'motor image' or motor program elicited for motor control. An inability to generate anticipatory control is one explanation for the increased postural sway and difficulty in controlling limb dynamics seen in neurological patients (Borghuis, Hof and Lemmink, 2008). Measures of core stability, such as postural sway, have been shown to predict falls when walking in neurologically impaired persons (Agrawal et al., 2011). These findings have been replicated in cerebellar patients (e.g. Bakker et al., 2006; Diener et al., 1984) opening up the potential for improving the motor problems associated with the disease by increasing core stability. More recently studies have emerged exploring this possibility (e.g. Tabbassum et al., 2013). As the exercises used in this work target control of core stability this testing aims to add to this consideration.

## 6.2 Methods

### 6.2.1 Participants

Seven members of the experimental group from Chapter 5 took part in the weight-shifting task. Five were males and two were females (mean age=50.6  $\pm$ SD 18.6; range 33-80 years). Two participants could not take part in the gait testing leaving five participants in the walking test (one female and four males: mean age=52.6  $\pm$ SD 21.7 range 33-80 years). All subjects were recruited through Ataxia UK, East or West Scotland branches. One participant reported deafness in the right ear (see Table 6.1).

**Table 6.1** Information for participants who took part in the two-month follow-up study.

Subject	Age (yrs)	Sex	Ataxia type	Mobility	Onset <sup>a</sup> (yrs)	Ataxia Rating (SARA)*				
						Gait (0-8)	Stance (0-6)	Sitting (0-4)	Speech (0-6)	Score (21/28) <sup>b</sup>
1 <sup>§</sup>	38	M	Ins	Wc	20	8	4	2	3	14/17
4	38	M	Cb	Unaided	24	1	0	0	2	1/3
5	72	M	Cb	Ws	4	3	2	0	1	5/6
6 <sup>§</sup>	33 <sup>d</sup>	F	Idi	Wa	20	4	1	3	0	8/8
8	40	M	Cb	Wk	12	3	2	1	4	6/4
9 <sup>§</sup>	53	F	Cb	Wc; Wk	27	6	4	1	4	11/15
10 <sup>§</sup>	80	M	Cb	Wc; Wa	50	6	4	2	2	12/14

Note: Ataxia type: Ins = Ataxia caused by cerebellar insult, Cb = cerebellar ataxia, Idi = idiopathic cerebellar ataxia. Mobility: Wc = wheelchair, Wk = walking frame, Ws = walking stick, Wa = walk assisted (e.g. holding a person's arm).

<sup>a</sup> Onset refers to years since symptoms began rather than number of years since diagnosis.

<sup>b</sup> The first score is the maximum obtainable score for posture related items. The second score includes speech.

\* Categories adapted from the Scale for the Assessment and Rating of Ataxia (SARA).

<sup>d</sup> Reported deafness in the right ear.

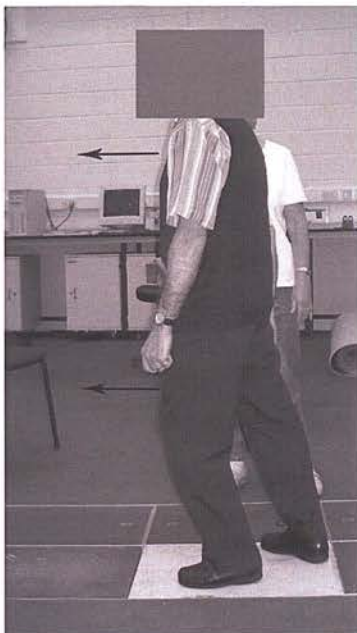
<sup>§</sup> Were assisted during the weight-shifting task

### 6.2.2 Equipment

Participants were given either a CD or MP3 file containing the sonic guides described in section 5.4.3. For this study the MP3/CD was made to be five minutes long and a different order of sound presentation was created for each day of the

week. This was to lessen the potential for learning the guide sequence. MP3/CDs were played at home on personal music devices. Swaying was recorded using a Kistler force plate. Data were collected and exported through Qualisys™ motion tracking software following the same procedure as in Experiment 2. A pole (microphone stand) was used as an object to focus vision. For the walking test, Qualisys Track Manager captured positional data (at 500 Hz) of each foot in three dimensions. A single 20mm reflective marker was attached to each foot placed at the base of the third metatarsal. The walking space was demarcated by two pieces of masking tape on the floor five meters apart. A chair was placed behind each mark. Positional foot data were outputted through Qualisys motion tracking software to a standard Dell computer.

### 6.2.3 The sonic-guide exercise programme



**Figure 6.1** An ataxia participant performing the scissoring stance sway direction of motion for a single sway.

Two types of sway based on neurophysiotherapy were used in the exercise programme: the lateral sway introduced in Chapter 5 (see section 5.4.4) and the ‘scissors’ sway. The scissors sway practices moving the body’s mass in the anterior-posterior axis (A-P). Start position constituted a step forward with one foot whilst keeping the trunk upright and gaze fixed on a pole placed three meters to the front. Participants then leaned into the leading leg, keeping the trunk upright and the back leg straight. The knee of the leading leg would bend as the torso pushed advanced and subjects



shifted bodyweight forward until a ‘stability boundary’ was felt (see Figure 6.1). A complete sway consisted of a controlled stop at the stability boundary in coordination with the termination of the sonic guide. A return from this position to start stance, while following the next sonic guide, completed a weight-shift in the opposite direction. The leading leg was alternated and participants were given instruction in how to use the exercises in conjunction with the sounds (i.e. to not bend at the waist and engage the whole body) following the same protocol as Chapter 5. Participants were asked to split practice time between the two swaying exercises. For the scissors sway, they were requested to follow the guides on the CD/MP3 for a minimum of 2.5 minutes with the left leg leading and then repeat with the right leg forwards. Participants were then instructed to perform the lateral swaying for 2.5 minutes following the guides. The same protocol was then repeated, except this time participants were asked to sway to mental imagery of the sounds without the guides playing. The total exercise programme lasted for a minimum of 15 minutes.<sup>60</sup> Safety was encouraged at all times and participants were instructed to use household objects such as walls, chairs, sofas or banisters for support where necessary. A timesheet was supplied so that participants could keep track of exercise completion. In addition to the programme, participants were encouraged to apply (mentally) sonic-guides to everyday activities such as regular exercise or an action like vacuuming the house. The rationale was to further increase/practise learning the pattern/form of the changing pitch glides.

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<sup>60</sup> As described, MP3 files were five minutes long. However for some participants, swaying for this length of time for each exercise and repeating with mental imagery, proved too difficult. A minimum sway time was given instead of 2.5 minutes for each exercise.



#### 6.2.4 *Experimental design*

The testing consisted of a pretest-posttest design. For the swaying part of the study, Pre and Imagined Sound (IS) conditions from Experiment 2 acted as baseline measures for comparison with the Two Month (2M) data. Both baselines were selected so that long-term gains could be properly assessed. After completing the two-month SGEP, participants returned to the laboratory to perform the lateral sway exercises as described in section 5.5.1. However sounds were not played at this stage and prompting to use auditory imagery was not given. This was because the efficacy of using both had already been established in Experiment 2 and this part of testing was more concerned with the outcomes of training and how well (or indeed if) participants had ‘absorbed’ the form of the sonic guides.

For the walking test, participants sat in one of the chairs and waited for an auditory ‘beep’ to sound. The beep signified the onset of motion capture. Upon hearing the cue, participants stood up and walked towards the marker/chair at the opposite side of the room. Once the mark had been passed, participants turned and headed back towards the first marker/chair. This was repeated as many times as was comfortable within a sixty-second recording. Participants were offered assistance, which consisted of an experimenter walking alongside the participant offering an arm to hold if necessary. Participants that used walking aids were asked to use assistance rather than the aid. This was done so that foot placement represented a natural walk rather than a compensatory strategy developed in response to walking aids. Assistance meant the experimenter’s arm was extended for participants to hold onto rather than the experimenter supporting the participant. As in Experiment 2, assistance affected outcome scores but did not disguise tipping or overbalancing. If

requested during the first recording session, assistance was used throughout the rest of testing. Participants were encouraged to stop if they felt tired or uncomfortable. Walking trials lasted for one minute and were repeated twice. Walking was recorded at baseline and after the two-month intervention where participants returned and were retested. Where possible participants returned at the same time of day and the order of trial presentation was kept the same.

## 6.3 Data analysis and results

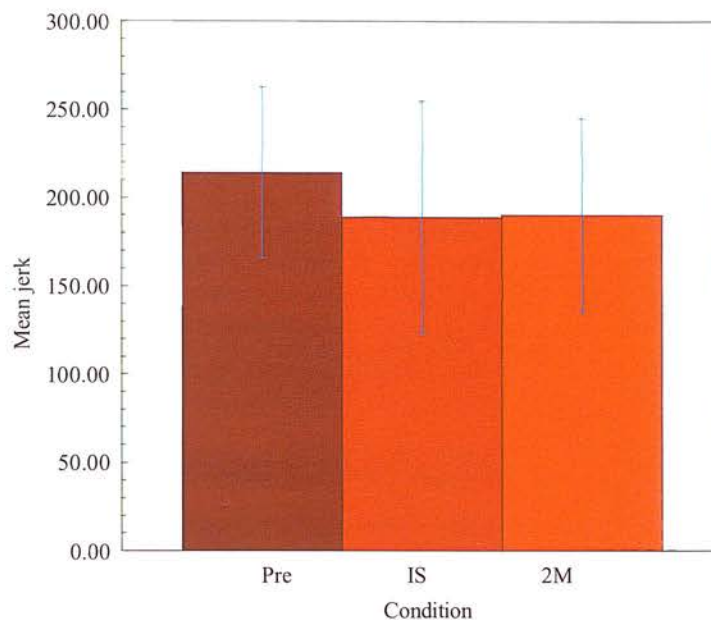
### 6.3.1 *Data analysis for swaying*

Jerk scores were calculated using the same protocol as Experiment 2 (see section 5.6.2). Force was differentiated once with respect to time to give jerk. The jerk for each sway was then normalised with regards to time and amplitude by dividing jerk scores by mean velocity. The first ten sways from each trial were taken to give twenty sways per condition. These were then averaged to give mean and standard deviation of jerk in each condition for each individual.

### 6.3.2 *Results one: within group comparison*

The first analysis investigated if there were changes in sway behaviour in the group after two months. Jerk scores are plotted in Figure 6.2. This figure indicates that participants produced less jerk in 2M than in the Pre condition and that scores are similar to the IS baseline condition (with scores of 190.3, 214.3, 188.6 respectively). To test for significance a repeated measures ANOVA was conducted. No significant effect of condition on jerk score was found ( $F(2, 12) = .947, p < 0.4$ ). The result

suggests that as a group, participants were not swaying more smoothly after two months of practice with the SGEP.



**Figure 6.2** Mean normalised jerk ( $\text{m/s}^3$ ) with standard deviation of the mean for the group in conditions, Pre, Imagined Sound and Two months.

However, jerk scores were not significantly *worse* at two months than in either the IS or baseline conditions. Given that participants were not listening to sounds and had not been instructed to imagine guides, this result indicates that some aspect of the SGEP training had been retained. Despite the group analysis findings, the possibility of significant improvements in movement smoothness on an individual basis could not be ruled out. To explore this further, and as the cohort suffered from the same homogeneity problems as Experiment 2, participant's scores were explored individually.

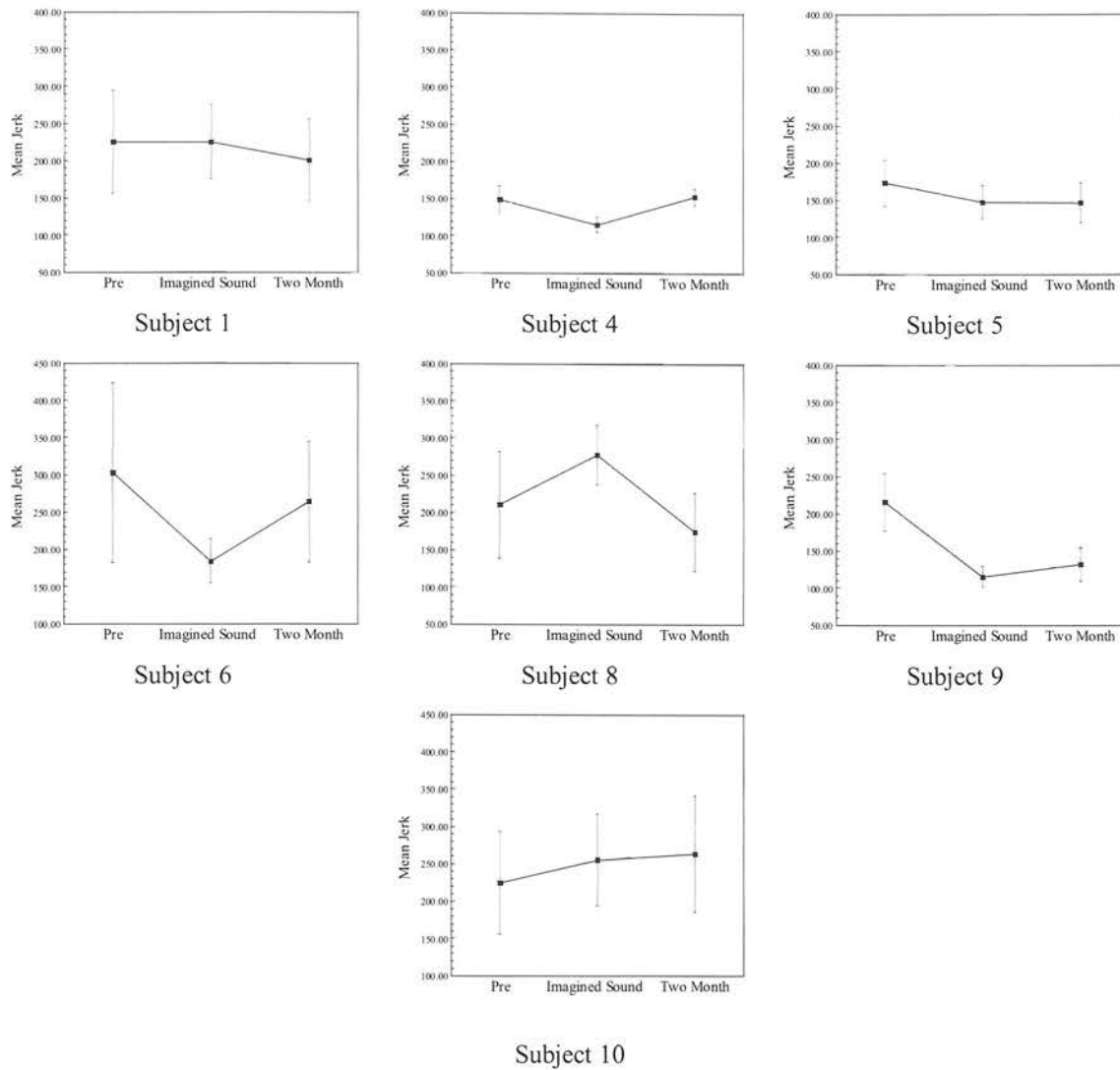
### 6.3.3 Results two: individual analysis Pre vs. Two months (2M)

To investigate which participants may have maintained or improved jerk scores from Experiment 2, individual mean jerk was compared between Pre and 2M. Scores are displayed in Table 6.2 and plotted in Figure 6.3. At 2M, five participants showed less jerk than at Pre (see and Figure 6.3). Independent sample t-tests were carried out to test for significance and an effect of increased movement smoothness was found in two participants (P5 and P9). No other participant recorded significant changes (see Table 6.3).

**Table 6.2** Mean normalised jerk ( $\text{m/s}^3$ ) and standard deviation (20 sways) for participants (P) in conditions, Pre, Imagined Sound (IS) and Two months (2M).

Condition	P 1 <sup>§</sup>	P 4	P 5	P 6 <sup>§</sup>	P 8	P 9 <sup>§</sup>	P 10 <sup>§</sup>
Pre (SD)	225.34	148.95	173.01	302.44	210.49	215.30	224.25
[1]	(68.65)	(17.81)	(31.12)	(120.6)	(71.25)	(38.68)	(69.11)
IS (SD)	225.73	115.71	147.33	184.19	277.46	115.08	254.93
[3]	(49.29)	(9.84)	(22.27)	(29.79)	(39.82)	(14.33)	(61.86)
2M (SD)	200.93	152.76	145.79	263.68	174.16	131.65	263.37
[4]	(54.47)	(10.78)	(26.34)	(80.53)	(52.76)	(22.47)	(78.27)

§ Were assisted during the weight-shifting task



**Figure 6.3** Mean normalised jerk (m/s<sup>3</sup>) with standard error bars for conditions, Pre, Imagined Sound and Two months, for each participant in the two-month follow-up.

**Table 6.3** Independent t-test results for Pre vs. Two months (2M) and Imagined Sounds (IS) vs. Two months (2M) for participants (P) who took part in the SGEP.

Condition	P 1 <sup>§</sup>	P 4 <sup>a*</sup>	P 5 <sup>*</sup>	P 6 <sup>§a*</sup>	P 8 <sup>†</sup>	P 9 <sup>§a*</sup>	P 10 <sup>§</sup>
Pre vs. 2M	N/S	N/S	p <.003	N/S	N/S	p <.0001	N/S
IS vs. 2M	p <.05	Neg p<.0001	N/S	Neg p<.0001	p <.000	Neg p<.02	N/S

Note: N/S = non-significant. Neg = significantly negative t-score (i.e. higher levels of jerk recorded).

<sup>a</sup>Participants who recorded significantly *lower* jerk scores between the Pre and With Sound conditions in Experiment 2

<sup>\*</sup>Participants who recorded significantly *lower* jerk scores between the Pre and Imagined Sound conditions in Experiment 2.

<sup>†</sup>Participants who recorded significantly *higher* jerk scores between the Pre and Imagined Sound conditions in Experiment 2.

<sup>§</sup> Were assisted during the weight-shifting task

Both of the participants who showed significantly lower levels of jerk after the SGEP produced lower jerk scores when using imaginary auditory guides in Experiment 2. Overall 29% of participants performed significantly smoother weight-shifting behaviour after two months with 71% showing no change.

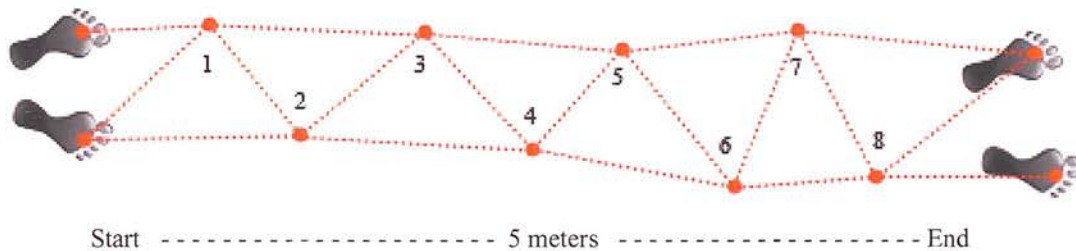
#### *6.3.4 Results three: individual analysis Imagined Sound (IS) versus Two months (2M)*

The next comparison was made between Imagined Sound (IS) and Two months (2M) (see Table 6.2 and Figure 6.3). Figure 6.3 shows that three participants produced less jerk, three produced more jerk and the final participant recorded no change. Paired sample t-tests revealed a significant effect for jerk score in five participants. Two participants (P1 and P8) recorded significantly less jerk, whereas three participants (P4, P6 and P9) produced significantly higher levels of jerk after two months than in the IS condition. Scores for two subjects (P5 and P10) did not change significantly (see Table 6.4). Both participants who displayed decreased jerk in this study previously recorded lower jerk scores between Pre and IS conditions in Experiment 2. In contrast, all three participants that recorded significantly higher jerk in this analysis had shown smoother swaying between the Pre and IS conditions in Experiment 2 (see Table 6.3).

Overall, when comparing the IS baseline and 2M follow up, 29% of participants produced significantly lower jerk scores, 29% did not change with close to half of the group (42%) producing significantly higher levels of jerk at two months than in the IS baseline condition.

### 6.3.5 Foot placement angle analysis

The trajectory of the foot markers was analysed in Qualisys Track Manager. A trace of the marker's path was displayed to aid foot placement identification. The 'floor' in Qualisys was rotated so that the 'view' was directly above the placement of the feet. The Qualisys display of the feet's movement for the complete trial was then played and captured as an AVI movie file using desktop screen capture software. These movies were then transferred to MaxTRAQ software where angles between foot placements were calculated. The angle created between the start and rest of one foot and the placement of the opposing foot was computed (see Figure 6.4). If the angle was opposite the start and end placement of the left foot it was named 'right' and



**Figure 6.4** Schematic of the experimental set up for walking the task. The red dots represent foot placement. Numbers represent the angle ( $^{\circ}$ ) of one foot in relation to the other after one step has been taken. Angles 2, 4, 6 and 8 are 'right' angles and angles 1, 3, 5 and 7 are 'left' angles in this example.

vice versa. The angle increased or decreased as a function of the spatial relationship between the feet. As participants took two steps to get into stride, the first angle was excluded from the analysis. Likewise, as participants slowed as the marker was approached the last angle in each trial was also excluded.



### 6.3.6 Results: walking angle

Mean and standard deviation left and right angles were calculated for the whole trial.

Scores were derived for Baseline and following the two-month SGEP for each individual. Results are displayed in Table 6.4 and Figure 6.5.

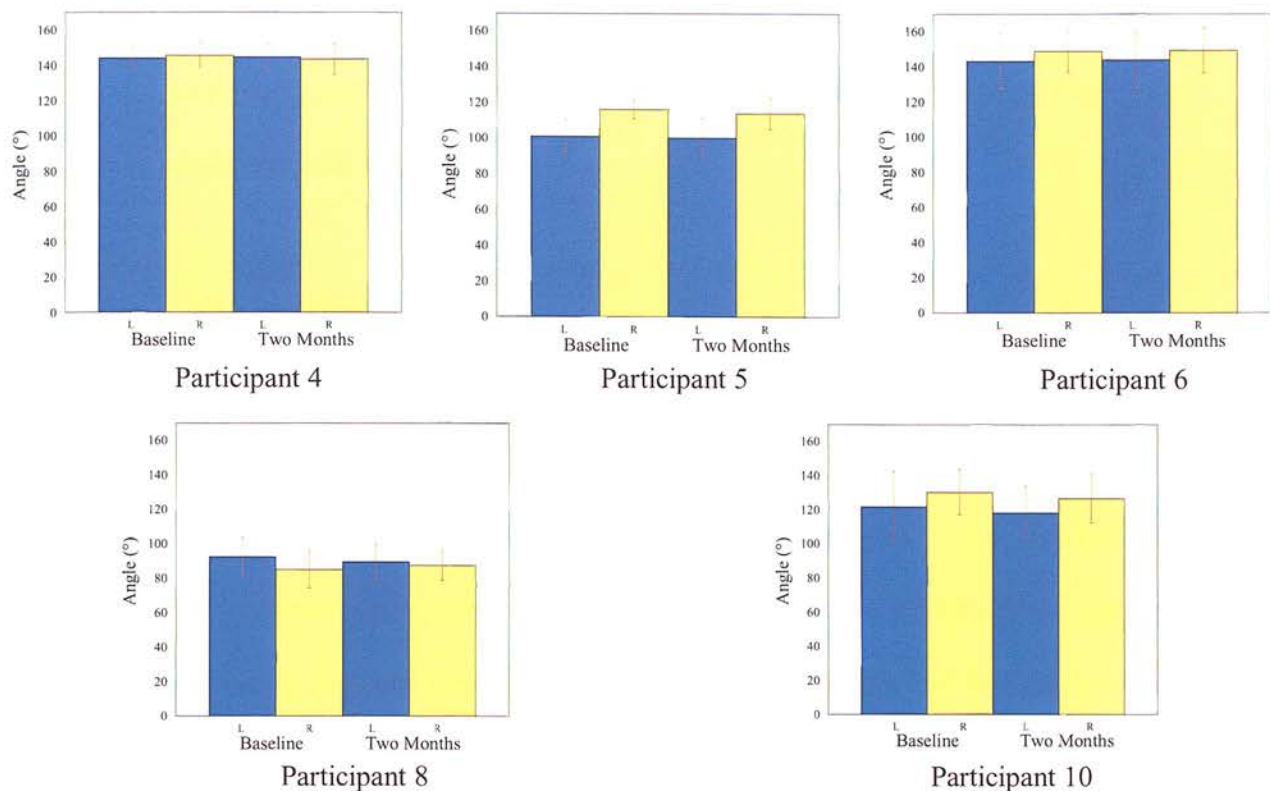
**Table 6.4** Mean and standard deviation of the angle (°) between left and right feet for each participant (P).

	P 4		P 5		P 6*		P 8		P 10*	
Foot	L	R	L	R	L	R	L	R	L	R
<b>Baseline</b>	144.0	144.7	101.3	100.3	143.2	144.0	92.4	89.6	121.9	118.4
<b>(SD)</b>	6.4	7.4	9.0	11.0	15.8	16.5	11.1	9.9	20.7	15.5
<b>2M</b>	145.5	143.4	116.2	114.1	148.8	149.4	85.0	87.4	130.4	126.7
<b>(SD)</b>	7.0	8.5	5.1	8.70	12.0	12.8	10.7	8.8	13.0	14.2

\* Participants that used support (the arm of the experimenter) whilst performing this task.

Table 6.4 and Figure 6.5 suggest that there are changes in the angle between foot placements in several individuals after two months. To test for changes in the group an independent samples t-tests was used to compare the combined left and right angles at Baseline and at 2M. No significant effect of SGEP was found for either foot angle ( $t(4) = 1.60, p = 0.19$  and  $t(4) = -1.24, p = 0.28$  respectively).

Data was further analysed using independent t-tests conducted for each individual and results are displayed in Table 6.5. Significant effects for foot angle were found in three individuals (P5, P8 and P10). Data show a significant increase of both right and left foot angle in P5 and P10 with P8 showing a decrease in the left foot angle. No other significant changes were recorded. However, changes in foot angle are not a sign of better or worse walking but rather different strategies. Variability on the other hand is feature of walking dysfunction so F-ratio was used to compare standard



**Figure 6.5** Mean angle (°) of foot placement with standard deviation bars. The graph displays the left foot as blue and the right foot is yellow.

deviation between Baseline and 2M. Two out of five participants showed significantly less variability in the left foot angle at 2M (participants five and ten).

**Table 6.5** t-test results (1 and 2) and F-ratio of variance test results (3 and 4) for angle (°) of foot placement at Baseline (Pre) and Two months (Post) for each participant (P). Negative values indicate negative t-values and hence the direction of the effect.

Conditions	P 4	P 5	P 6*	P 8	P 10*
1 R Pre vs. Post	X	-p=.0001	X	X	-p=.043
2 L Pre vs. Post	X	-p=.0001	X	p=.013	X
3 R Pre vs. Post	X	X	X	X	X
4 L Pre vs. Post	X	-p=.008	X	X	-p=.027

Note. X = non-significant result.

\* Participants that used support (the arm of the experimenter) whilst performing this task.

Both of these participants previously showed changes in walking angle in left and right feet. To explore the strategies that people were engaging, walking angle was then correlated with step length.

### 6.3.7 Step length data analysis

Step length is the linear path between subsequent foot placements of the same foot. To calculate step length, positional data from the Y-axis (walking direction) of each foot was smoothed using a Gaussian filter 11 (cut-off frequency of 8 Hz) and then differentiated once with respect to time to give velocity. Zero velocity crossings were used to identify start and end points of swing phases for each foot in KaleidaGraph. The length of each step was then calculated for each foot individually in millimetres and averaged over the two trials for Baseline and 2M. First and last steps for each foot were excluded to account for the untypical steps at the initiation and termination of the walk.

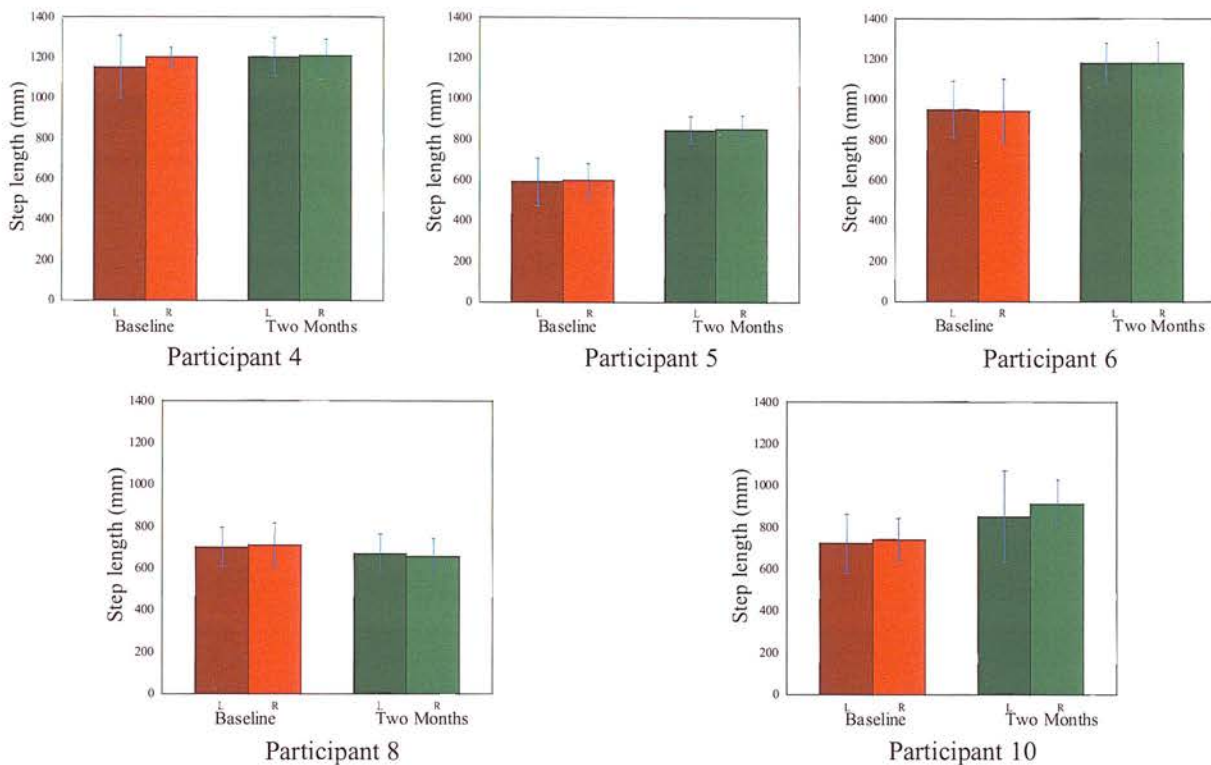
### 6.3.8 Results: step length

Mean and standard deviation of step length are displayed in Table 6.6 and Figure 6.6. An exploration of Figure 6.6 shows a marked discrepancy in three participants for step length at 2M compared to Baseline. To test how step length changed in the group, independent samples t-tests were used. No significant effect of step length in either the right or left foot was found ( $t(4) = -1.98, p = 0.12$  and  $t(4) = -2.231, p = 0.08$  respectively).

**Table 6.6** Mean and standard deviation of step length (mm) for each foot at Baseline and 2M for each participant (P).

	P 4		P 5		P 6*		P 8		P 10*	
	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left
<b>Baseline</b>	120.0	115.4	59.8	59.0	94.9	94.1	70.2	71.2	73.9	72.0
<b>(SD)</b>	(4.7)	(15.4)	(8.1)	(11.7)	(15.7)	(13.9)	(10.1)	(9.2)	(10.1)	(14.0)
<b>2M</b>	120.8	120.2	85.2	84.5	118.0	118.2	65.6	67.0	91.1	85.1
<b>(SD)</b>	(8.3)	(9.4)	(6.2)	(6.4)	(10.3)	(9.7)	(8.3)	(8.9)	(11.5)	(21.7)

\* Participants that used support (the arm of the experimenter) whilst performing this task.

**Figure 6.6** Mean step length (mm) with standard deviation bars. The left and right feet at Baseline are shown in shades of red. The left and right feet are shown at Two months in green.

To investigate the group further, t-tests were conducted on the step length data of each individual (see Table 6.7). A significant effect of step length was found (in both feet) in three participants (P5, P6 and P10). Results show that individuals were taking

longer steps with each foot after two months. The other two participants showed no significant change. F-ratio was then used to compare standard deviation. One participant (P5) showed less variability in step length (in both feet) after the two-month intervention with no other significant effects found.

**Table 6.7** t-test results (1 and 2) and F-ratio of variance test results (3 and 4) for step length Pre and Post SGEF for each participant (P).

Condition	P 4	P 5	P 6*	P 8	P 10*
1 R Pre vs. Post	X	p=.0001	p=.0001	X	p=.01
2 L Pre vs. Post	X	p=.0001	p=.0001	X	p=.0001
3 R Pre vs. Post	X	p=.05	X	X	X
4 L Pre vs. Post	X	p=.05	X	X	X

Note. X = non-significant.

\* Participants that used support (the arm of the experimenter) whilst performing this task.

### 6.3.9 Summary of results

To summarise, two participants (P5 and P10) consistently produced different walking behaviour following the two month intervention. Both recorded changes in left and right feet between Baseline and 2M. P5 recorded changes in mean and variability on the majority of variables tested whereas P10 showed differences in mean scores only. Of the other three participants, two registered changes of angle in one foot, with no improvement in variability for any measure. The results of the walking test are related to other experiments carried out in this thesis. Results of Experiment 2 and 3 are important in interpreting the results in this chapter. Data for all three experiments are presented in Figure 6.7.



**Figure 6.7** Results for all testing for the seven participants (P) who took part in the two-month intervention programme. Green indicates positive findings whereas red indicates negative. Purple signifies a significant change that is neither positive nor negative (i.e. changes in angle). Lighter shade represents a larger angle, the darker shade, a smaller one. Blue indicates no significant change.

Condition	P 1	P 4	P 5	P 6	P 8	P 9	P 10
Results Experiment 2 – Chapter 5							
Pre vs. WS							
Pre vs. IS							
Results Experiment 3 – Chapter 6							
Pre vs. 2M							
IS vs. 2M							
Angle R							
Angle L							
Angle RV							
Angle LV							
Step R							
Step L							
Step RV							
Step LV							

Note. Pre= baseline, WS= with sound, IS= imagined sound, 2M= Two-month; Angle: R= right foot, L= Left foot, RV= Right variability, LV= Right variability; Step: R= right foot, L= Left foot, RV= variability, L= variability.

The first noticeable aspect of this table is that only two participants who took part in the swaying test at 2M had shown less jerk in Experiment 2 when swaying with the guides (P6 and P9). One of these maintained a significant difference at 2M (P9). Four participants had shown improved jerk scores in Experiment 2 using the auditory imagery (P4, P5, P6 and P9). However not a single participant maintained these scores at 2M. In fact P4, P6 and P9, produced more jerk after two months than during the IS condition at the first recording. Neither participant who improved in 2M in this chapter responded to the guides or imagery in the original testing (P1 and P8).

For the walking task, of the three who recorded changes in angle of the feet (P5, P8 and P10), two had not responded to guides or imagery in the first testing (P8 and P10). A slightly more positive finding was that two participants who had responded during Experiment 2 imagery, produced improved stride length here (P5 and P6). However neither participant maintained imagery gains at 2M. One participant who did not show changes in walking angle (P6) produced longer steps suggesting a wider stance was being used.

The question of whether changes in core stability improve ambulation could not be answered by these data as only one participant took part in the walking (P5) who had improved at 2M. A confounding result was that P10 did not show improvements in any of the swaying experiments yet recorded changes/improved scores on four out of eight walking variables. This indicates that other factors were influencing results.

## 6.4 Discussion

### 6.4.1 *General findings*

The swaying exercise and walking follow-up produced mixed findings in this experiment. Results failed to convincingly show an effect of the SGEP in improving movement smoothness in cerebellar disease. This result suggests that the cerebellum is directly involved in the formation or storage of motor memories. However, an alternative hypothesis is; what if motor memories are not actually relied on? This would imply that each action is the result of the current situation requiring the acquisition of accurate sensory data for motor command formation. Whilst lack of findings in this study supports this idea (i.e. removal of guides leads to impoverished



sensory acquisition) there is abundant evidence that motor memories are stored and used by the nervous system.

That auditory imagery of the guides could be learnt and become a feature of motor control was also not well supported. However, it must be noted that motor imagery problems are recognised in cerebellar patients (Grealy and Lee, 2012). It is possible therefore that compromised imagery could be a reason for the poor results found in this part of the thesis. Nevertheless, participants did not demonstrate imagery deficits in the original testing (although guides had been presented within five minutes) and two out of four maintained greater smoothness at 2M. This hypothesis is therefore discounted.

There was some evidence of improvement in walking as increased step length is accepted as a sign of improved ambulation in neurological disease (e.g. Thaut et al., 1996). However, given the results of earlier tests it is incongruous to attribute these changes to the auditory guides. It is more likely that physical factors such as increased lower body strength or psychological factors such as confidence, motivation or less inhibition were responsible for improvement (the results from P10 are evidence for this). In general it is concluded that movement-based sonic-guides may be useful for accessing rehabilitation exercises but they must be available (or recently played) to do so. Data from this work also confirms the difficulty of motor rehabilitation in people with cerebellar ataxia.

#### *6.4.2 Motor learning in the cerebellum*

The lack of motor improvement after two months of practice supports studies that show the cerebellum is involved in motor learning (Doyon and Ungerleider, 2002).

Three ways the cerebellum may contribute to this process were introduced earlier; modulation of motor cortex activity, consolidation of learnt movement behaviour or storage of motor memory

#### 6.4.2.1 *Modulation of motor cortex*

In Chapter 5 the possibility was raised that anticipatory movement information within the sounds was either directly activating PMC or increasing cerebellar output resulting a better defined motor signal. Motor adaption modifies motor commands by responding to error feedback (Tseng et al., 2007). Improvements in the previous study suggested that the predictive nature of the guides reduces error and thus the need for the cerebellum in generating motor corrections (cerebellar activity is reduced when a movement becomes learnt). This hypothesis is supported in this work by the fact that removal of the guides led to a return of symptoms. It is argued therefore, that the cerebellum is critically involved in short-term learning through motor adaption (Galea et al., 2011). A possible cause for reduced cerebellar activity in motor adaption is related to the *size* of the motor error (Criscimagna-Hemminger, Bastian and Shadmehr, 2010; Tseng et al., 2007). These authors showed that error size drives motor learning by introducing small errors gradually and large errors abruptly in people with severe cerebellar degeneration. Smaller errors led to stronger and longer lasting motor memories. In Experiment 2, swaying improved but was still greatly compromised and consisted of large errors. It is likely this continued when using the SGEP at home meaning that limited motor adaption would occur. The minimal improvements found in this data support this notion.

#### 6.4.2.2 Consolidation of motor memory

Data from this study strongly suggests that consolidation of motor memories is disrupted in cerebellar disease. A further conclusion is that the effects recorded in Experiment 2 are likely sustained as a result of non-cerebellar networks rather than increased cerebellar output. This assessment is based on the reality that modulation of motor cortex (predominately M1) occurs through closed cerebellothalamocortical loops. It is difficult to see therefore, how continual activation (with smoother movement) of this pathway over a two month training period could fail to modify motor cortex (and subsequently motor behaviour) (Popa et al., 2012; Daskalakis et al., 2004). What these data also suggest is that the transfer of neural signals generated by motor adaption to a consolidated representation is wholly dependent on the cerebellum. This proposition is in agreement with numerous studies that implicate the cerebellum in the consolidation process (e.g. Doyon and Ungerleider, 2002; Galea et al., 2011; Krakauer and Shadmehr, 2006). It also implies that while alternative parts of the motor system can improve motor control instantaneously; these mechanisms are not involved in long-term motor learning.

#### 6.4.2.3 Storage of motor memory

A final consideration for why participants did not improve in this study is that long-term storage of motor memories is disrupted. ‘Storage’ is the neural representation of motor behaviour through changes at the synapse. Animal models of VOR show that motor memory is distributed throughout the cerebellum and cerebellar nuclei and in particular the vestibular nucleus (Yamazaki and Nagao, 2012). Within the cerebellum it has long been hypothesised that motor memory is stored in the synaptic interface of parallel fibres and Purkinje cells in the cortex (Strata, 2009; Ito, 1982).

Disruption to the cerebellar nuclei and/or their efferent/afferent pathways, or damage to the cerebellar cortex, inhibits the ability to form long-term motor memories. Results from this study could be explained in these terms. However, it is argued that storage of motor memory is not confined just to the cerebellum and its nuclei. Patterns of motor cortex excitability are one region where supposed ‘motor maps’ are represented in the brain (Hosp and Luft, 2011). It is not clear though, whether motor maps in this area are only formed under cerebellar influence. Data from this work suggests this may be the case. An alternative explanation is that motor patterns in M1 are already extant (from before disease onset) but they are crude and need cerebellar refinement to be executed properly (Daskalakis et al., 2004). However, the storage of motor memories occurs sequentially with first, motor adaption, secondly, consolidation and finally storage (Doyon, Penhune and Ungerleider, 2003). The data presented earlier does not adequately demonstrate that the first all parts of this sequence have transpired making it unlikely that the results found here are a problem of motor storage.

#### 6.4.3 *The effectiveness of the SGEP*

A difficulty for this study was to provide an exercise that suited the diverse range of behaviours found in this cohort. Whilst all participants demonstrated difficulties in ambulation, it is clear that a person walking unaided is not comparable to somebody in a wheelchair in a balance task. It is likely therefore, that for some participants, the sway exercises did not present a large enough challenge. In contrast swaying may have been too difficult for some (two participants were severely impaired standing

upright). Nevertheless, one of these participants showed an effect when imagining the guides suggesting that the task was not beyond the reach of others.

Whilst swaying certainly engages many aspects related to upright walking, it is not used as a clinical rehabilitation tool in isolation but rather in conjunction with other motor/balance exercises. It is a question therefore whether swaying in two axes provides enough stimulation to confer changes in balance behaviour. It is also an issue as to what amount of time is needed to confer changes. Whilst practicing for a minimum of fifteen minutes per day is a reasonable period of engagement, it is not known if more practice would have led to better results. As Shiel et al. (2001) have shown intensity is important in rehabilitation programmes. As previously mentioned, intensity must also be adapted to counter ceiling effects but it is not known if continued swaying provided this challenge.<sup>61</sup> A different issue was the duration of the sonic guides. Durations were based on the mean sway of a control individual. It is possible therefore that guides were either too long/short for participants idiosyncratic ways of swaying. Calculating mean sway durations for each participant and producing the range of sonic-guides based on individual body kinematics would have solved this issue. Monitoring the implementation of the programme was also difficult as it was performed at home. Participants were brought back every two weeks to check how exercises were being performed. It is not known if this was maintained during home practice. However, all participants completed the programme.

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<sup>61</sup> Participants were encouraged to continually challenge themselves when swaying i.e. to vary speeds, distances etc.

#### 6.4.4 *Limitations, implications and further directions*

There were a number of limitations to this part of the thesis. The most glaring omission is the lack of control group meaning that the effects of the auditory guides over two months were not directly tested. Logistical, financial and supervisory constraints meant that bringing back control participants was beyond the scope of this thesis. As a result, the minor improvements found within the group cannot be attributed to the sonic-guides as other factors are more likely to be the cause. One such factor is that for some participants (particularly those in wheelchairs or using walking aids), exercising at all was novel and would undoubtedly result in changes in lower body strength. Ilg et al. (2010) has shown exactly such effects in cerebellar disease from programmes of extended coordinative training. This study was also weakened by the small number of participants. Three people dropped out and unfortunately for the two month follow-up study, two had shown positive effects using the sonic guides in Experiment 2. However, as mentioned above, four out of the seven participants had shown an increase in movement smoothness when using the imagined guides meaning that over half the group instantaneous effects in at least one condition. Many of the issues discussed above again relate to heterogeneity problems within the cohort. Without having to cater for a diverse range of motor skills, a less general exercise could have been employed. It would be of interest therefore, for sonic guidance to be integrated into more established rehabilitation programmes (or experimental designs) to directly test their efficacy (i.e. work with a homogenous group, performing a specific exercise with a control group).

### 6.5 *Summary of results*

The findings from this part of the study do not advocate the use of sonic guidance to evoke long-term changes in motor behaviour in people with cerebellar disease. Nor do the results support using auditory imagery of sonic guides for long-term changes. The study provides evidence that the cerebellum is involved in motor learning, however, data presented here cannot discriminate between storage, consolidation or teaching. Nevertheless as these stages proceed in a linear fashion, it seems probable that cerebellar disease compromised the ability for motor adaption and therefore disrupted consolidation and storage.



## Chapter 7 – Conclusions

### *7.1 The problem revisited*

Damage to the cerebellum leads to difficulties controlling movement. A common and recognisable symptom of cerebellar damage is dysmetria. Dysmetric movement leads to a characteristic gait that consists of irregular foot placements and stride lengths leading to unsteadiness, falls and significantly impacts the quality of life. Despite important advancements in the understanding of neurorehabilitation mechanisms, treating people with cerebellar disease continues to provide a significant challenge. These challenges are rooted in the role the cerebellum plays in motor control which makes access to neurorehabilitative training problematic for this group. A potential cause of problems in cerebellar rehabilitation is a deficit in processing or acquiring sensory information which affects the cerebellum's ability to make predictions about the future.

### *7.2 Addressing the problem*

As understanding of cerebellar function has progressed, opportunities to focus on other neurorehabilitative techniques have emerged. One such technique is to supplement or substitute sensory information to compensate for shortfalls in acquiring and/or using sensory input. In recognition of this possibility, this thesis set out to determine if using on-going, prospective auditory stimuli to guide movement,

could improve motor control in people with cerebellar disease. The use of auditory stimuli in neurorehabilitation is not new. However, little attention has been paid to developing guides that are meaningful with regards to how movement is controlled or that take into account how people move within the environment. This work addressed this omission by taking an ecological approach, which advocates there is invariant structure in the external stimulus that is perceived and influences motor behaviour.

In this thesis, two strands of investigation were followed. First, motor control theory based in an ecological approach was used to develop auditory stimuli that could be understood as motion for guidance. The second part of this work tested these auditory guides in a population with cerebellar ataxia. Following this, the effects of practicing this balance exercise in a smoother and more coordinated manner over a longer time period were explored. It was reasoned that practicing destabilizing exercises with greater control would help to overcome some of the motor difficulties seen in cerebellar ataxia and have a secondary effect on locomotion.

In carrying out these experiments the thesis engaged with three central questions:

- 1) Can movement information be successfully embedded within auditory stimuli and used to influence movement behaviour in a predictable manner?
- 2) Can movement information embedded in auditory stimuli instantaneously improve motor behaviour in people with cerebellar disease? A second part to this question is whether mental rehearsal of movement-based auditory stimuli will have the same effect as listening to auditory guides?

- 3) Finally, does the use of auditory guidance over a prolonged period of time significantly alter performance on neurorehabilitation exercises and subsequently locomotion in people with cerebellar disease?

To conclude this work, each one of these questions is readdressed in light of the findings from the thesis.

### 7.3 Question one

That movement information can be successfully embedded within auditory stimuli is a robust finding in this work. Experiment 1 clearly shows that reaching behaviour can be influenced in a predictable manner using sound. Despite the ambiguity of the position of the peak velocity (PPV) (i.e. two of the guides produced unexpected scores), the accuracy in coordinating the hand with the end of the sonic guide, and the velocity of the reaches were adapted in line with the information within the guides. It is argued that these affects occur due to the properties of the auditory guides or more specifically, that movement information analogous to optic tau is sensed within the sounds and is used to control reaches. It is suggested that the spatio-temporal characteristics of auditory-tau simultaneously provide on-going and prospective information. Through a familiarity with looming information, ‘movement’ becomes salient within the guides and endpoints can be easily perceived to control reaches. This proposal is supported by the fact that participants *unconsciously* understood and adapted behaviour in-line with the information within the sounds.

### 7.3.1 Theoretical implications

That participants adapted reaches without instruction, fits with a broader theoretical construct where movement is embedded within a framework of perception-action coupling (as described by Lee, 2005). In the visual domain it is well understood how object properties influence movement. This study demonstrates how a similar effect occurs with auditory stimuli where invariant characteristics in the auditory array are recognised and used to control action. Where auditory-movement invariance was more consistent with the task, (i.e. where guides carried a  $k$ -value of 0.5) movement performance was increased. Recognition of preferred movement trajectories suggests a preference for first order variables in the environment and further frames this work in an ecological (perception-action) approach (e.g. Gibson, 1986; Lee, 2005). It is also hypothesised that because auditory guides are meaningful and representative of movement, multisensory/cross modal integration is enhanced. Faster and more accurate reaches for  $k=0.5$  guides supports this proposition and is consistent with research that shows congruent sensory input leads to increased neural activity in multisensory neurons/areas of the brain (Holmes and Spence, 2005; Foxe and Molholm, 2010).

Whilst the development of these guides builds on existing methods of sensory augmentation, such as bio-feedback or rhythmic cues, these guides improve on these techniques by combining on-going and prospective information. The delivery of this type of guidance is recognition of a perception-action approach to how movement is controlled. In taking this approach it is believed that a different range of motions can be targeted, including discrete actions, opening up different possibilities for auditory motor guidance.

### 7.3.2 Limitations of the study/ further directions

As mentioned, the results of the PPV data were ambiguous. This reality highlights a weakness in the study which was that visual, and to a lesser extent proprioceptive information, was likely to have been in conflict with the instructions within the sounds (i.e. visual information about the target, interfered with guiding information in the sounds). It is of interest therefore, to repeat this experiment whilst limiting vision and/or proprioception. An easy way to achieve this would be to perform reaches in a darkened room to a luminous target, thus excluding visual identification of the hand during the transport phase. It is expected that removal of vision would lead to greater reliance on the auditory guides and closer adherence to the PPV denoted by the  $k$  value. An investigation of this type would be of interest to further understand the auditory guidance of movement but also as a way of best determining how to apply auditory guides for use in neurorehabilitation. In line with the sensory reweighting hypothesis (Peterka, 2002) it may be preferential to obscure other sensory streams to maximise the effects of using the guides.

Using tau information for the gap between start point and target, solved a number of issues in this study regarding how to convey movement (i.e. the need for second order estimates was eliminated). Despite this, no other variables were tested so it is not known if there are more effective ways to program auditory guides. Sonification experiments have shown that position and velocity can successfully provide bio-feedback to improve movement in a range of motor-skills. It would be of interest therefore, how tau-based sounds would compare against sounds based on other variables.

A number of questions remain with regards to sound quality. Auditory guides were ‘artificially’ produced using a tone generator. Whilst this did not appear to hinder understanding of movement within the guides, it is not known if different types of auditory stimuli would increase the effect of auditory biological motion. It is suggested that natural sounds may prove to be more effective due to an innate preference for environmental auditory stimuli. A second question regarding sound quality is that this experiment did not explore the optimal techniques of presentation. It is possible however, that sounds could be further manipulated to enhance the effect of auditory-movement. Panning sounds between speakers for example, (based on the changing tau-margin) may increase movement understanding. Other sound features, such as loudness or intensity, could also be manipulated to convey tau. Explorations of this nature could further determine the most appropriate way to convey movement within sounds.

### *7.3.3 Clinical implications*

As many nervous system disorders result in impaired or absent sensory experience, guides that deliver an alternate source of sensory input containing the spatio-temporal characteristics of a specific action, could be of great benefit. Data from this study shows that the precise features of movement can be manipulated by adjusting how auditory stimuli change. By being able to manipulate periods of acceleration and deceleration, specific weaknesses in a person’s movement ability can be targeted. For example, if a person continually overreaches, guides could be altered so that movements with longer deceleration phases could be practiced. As the guides contain online and predictive information, use in neurological diseases where goal

identification, rhythm comprehension or degraded transport phases would be appropriate.

Sonic guides are easy to create and can be played through standard equipment and therefore, can be applied in numerous situations both within and outside the neurorehabilitation environment. As some of the equipment used in bio-feedback studies is cumbersome and expensive, movement-based auditory guides offer clinicians a low-cost and simple tool that can be easily distributed and used to enhance existing neurorehabilitation strategies.

## 7.4 Question two

The primary finding from this thesis is that on-going and dynamic auditory guides instantaneously improve motor behaviour in some cases of cerebellar disease. In addition it was found that mental rehearsal of movement-based auditory stimuli also improves movement smoothness. In both experiments it was implied that the presence of clear additional movement information reduced the necessity of the cerebellum to acquire sensory information. It was argued that the prospective nature of the sounds was key in reducing the cerebellum's burden. However, it could not be precisely determined how additional information was used by the nervous system. Whilst it is assumed that extra information contributed to the formation of predictive motor commands, it is not known if this was through direct stimulation of higher cortical structures (i.e. premotor cortex) or whether the output signal for the cerebellum was enhanced.



#### *7.4.1 Theoretical implications*

This study is the first to show that movement-based auditory stimuli can be used to improve movement smoothness in cerebellar ataxia. In doing so, it supports findings from Experiment 1 that suggested using a perception-action approach to auditory augmentation, facilitates understanding and guidance of motor acts. Whilst this experiment targeted people with cerebellar disease because of the well-known deficits in sensory processing, findings from this study are likely transferable to other rehabilitation in other neurological impairments.

This work also contributes to theoretical consideration of cerebellar function. Primarily evidence is provided that the cerebellum operates to acquire sensory information for use in other brain processes (Bower, 1997). It is argued that the main use for that information is to form internal models of future states. For motor control this means predictive motor commands however, this study adds to growing speculation for a general cerebellar function of expectant state estimates in multiple mental functions.

#### *7.4.2 Limitations of the study/ further directions*

There were a number of difficulties related to the swaying study. The main issue was the problem of recruiting participants with the same disease type, onset and motor skill. Recruitment problems were complicated by the low incidence of cerebellar ataxia in Scotland. As a consequence, inclusion criteria for the study were too broad and resulted in a diverse cohort with highly variable forms of cerebellar damage and symptoms. This variability introduces uncertainty into the results as it cannot be definitively excluded that improvements are related to idiosyncratic patterns of

cerebellar damage rather than an effect of the guides (however, control group findings do not support this suggestion).

A missed opportunity in this study was to explore the movement deficits in each individual separately. It is known that in ataxia movement problems are not stereotypical and that hypo- or hypermetria may be present. Nevertheless, in this study, guides were given that represented an idealised way of completing the action (i.e.  $k$  values of 0.5) that were maybe not ideal for individual body types. It would have been more appropriate therefore to tailor sounds to individual ways of moving. Time constraints meant that individual movement behaviours were not analysed, however, moving in authentic ways is central to the ecological approach and is potentially important for neurorehabilitation.

#### *7.4.3 Clinical implications*

The first swaying study added to a small but growing body of literature that shows physical rehabilitation is possible in people with cerebellar ataxia. In doing so it is one of a handful of studies to demonstrate additional sensory input has the potential to improve ataxic movement. This study therefore, broadens the possibilities for movement rehabilitation for the clinician. Importantly, a simple way to conduct rehabilitation within an individual's personal time and space was identified. The results of this thesis also raise the possibility of using these guides in other forms of neurological disorder. Huntington's disease for instance is characterised by poor online control, whereas Parkinsonian movement displays late initiation onset. In both of these examples movement based auditory guidance may prove to be beneficial.

### 7.5 *Question three*

The results from this study showed that using sonic guidance over an extended period of time, does not improve movement skill in the swaying exercise. Likewise there was no evidence that auditory imagery was automatically being used after two months of training or that it had an effect on motor behaviour. However, some positive changes were found in walking ability. Nevertheless, as findings from the swaying exercises were negative, it suggests that this variation was a product of being more active. It is more likely that improved step length was related to strength gains (probably at the ankles) and would have occurred regardless of the presence of auditory guides. The psychological impact of talking part in a study of this nature can also not be ignored. Many participants received no support or help for their condition. To be involved in experimentation the aim of which was to improve their quality of life provided significant motivation. Despite attempts to downplay outcomes, it is impossible to not raise expectations when carrying out work of this nature. In conclusion this part of the study provided no evidence for a beneficial effect of using movement-based auditory guidance in cerebellar disease.

#### 7.5.1 *Theoretical implications*

The failure to find positive changes in movement ability after the two month SGEP, suggests that the cerebellum is involved in long-term motor learning. Whilst it cannot be certain from this work how the cerebellum is involved in this process, as motor learning is procedural, it is suggested that it is unlikely that learning ever developed beyond motor adaption. The findings also suggest that for motor control to be improved requires that the sounds are available. This applies to the auditory imagery

results in the previous experiment which can be reinterpreted from this experiment, as being a result of auditory working memory, rather than generation of auditory imagery. However, these data could be interpreted as a cerebellar role in auditory imagery. This has not been tested before but it would complement studies that show motor imagery impairment in cerebellar patients. These findings do not preclude the use of auditory guidance in rehabilitation but suggest they should accompany other neurorehabilitation techniques rather than be rehabilitation tools in themselves.

### *7.5.2 Limitations of the study/further research*

There were a number of weaknesses in this study. Lack of a control group made it impossible to attribute the small effect specifically to the guides. The sample size was also small and suffered the same homogeneity problems seen in the previous experiment. Many participants were recruited from around the UK meaning return trips were not an option and this may have also introduced a bias. It is likely that individuals who were travelling large distances had high motivation and were also likely to be more able bodied (this was found in Table 5.1 but controls still produced greater jerk than the experimental group).

With regards to walking, an interesting further study would be to try and affect stepping directly rather than affect walking through improved core balance. Guides could be created for the duration of each step. Such a study would be interesting as direct comparisons could be made with rhythmic auditory stimuli studies (e.g. Thaut et al., 1996) to test between on-going and ‘empty’ guides.

### 7.5.3 Clinical implications

The immediate implications from this part of the study, is that movement-based auditory guidance is not an appropriate way to approach rehabilitation in cerebellar ataxia. However, questions regarding the experimental task, cohort and training techniques, suggest judgement should be reserved on this statement. Findings from Experiment 2 imply that movement-based auditory guidance could be used as a supplement to other training programmes. Alternatively guides could be used continuously (on MP3 devices etc.) which may be a preferred option if it meant long walks could be taken or stairs climbed without incident. Before such an option is available however, further development of auditory guides for action is needed.

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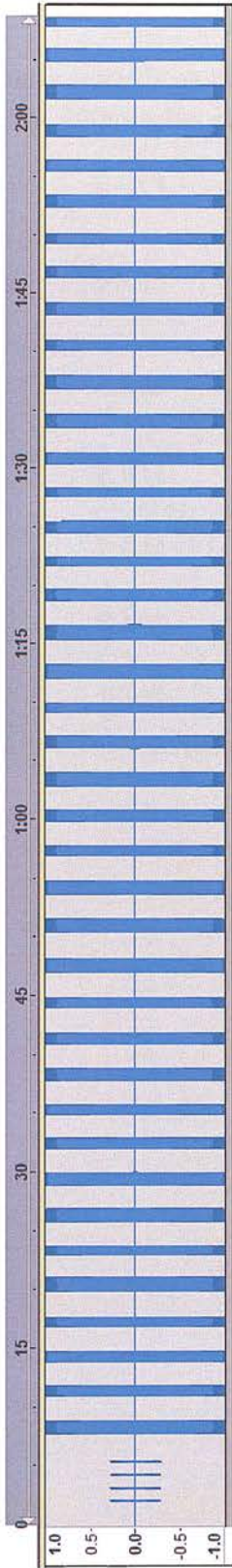


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APPENDIX A

The forty sonic guides in the reaching experiment displayed in Audacity software.



## APPENDIX B

Other variables produced by the tauG analysis on the R-trajectory of reaches. Mean and standard deviation are shown for 160 reaches per category of sound.

	<b>k=0.2</b>	<b>k=0.5</b>	<b>k=1.0</b>	<b>linear</b>
<b>Percentage coupling mean</b>	96.87	96.85	95.31	97.06
<b>Percentage coupling SD</b>	0.009	0.008	0.010	0.009
<b>r2 mean</b>	0.972	0.973	0.971	0.972
<b>r2 SD</b>	0.570	0.634	10.42	0.496
<b>k mean</b>	0.646	0.680	0.668	0.671
<b>SD k</b>	0.143	0.149	0.174	0.179

## APPENDIX C

### Items used from the Scale for the Assessment and Rating of Ataxia (SARA)

<b>1) Gait</b> Proband is asked (1) to walk at a safe distance parallel to a wall including a half-turn (turn around to face the opposite direction of gait) and (2) to walk in tandem (heels to toes) without support.  <div><div>0</div><div>Normal, no difficulties in walking, turning and walking tandem (up to one misstep allowed)</div></div> <div><div>1</div><div>Slight difficulties, only visible when walking 10 consecutive steps in tandem</div></div> <div><div>2</div><div>Clearly abnormal, tandem walking &gt;10 steps not possible</div></div> <div><div>3</div><div>Considerable staggering, difficulties in half-turn, but without support</div></div> <div><div>4</div><div>Marked staggering, intermittent support of the wall required</div></div> <div><div>5</div><div>Severe staggering, permanent support of one stick or light support by one arm required</div></div> <div><div>6</div><div>Walking &gt; 10 m only with strong support (two special sticks or stroller or accompanying person)</div></div> <div><div>7</div><div>Walking &lt; 10 m only with strong support (two special sticks or stroller or accompanying person)</div></div> <div><div>8</div><div>Unable to walk, even supported</div></div>		<b>2) Stance</b> Proband is asked to stand (1) in natural position, (2) with feet together in parallel (big toes touching each other) and (3) in tandem (both feet on one line, no space between heel and toe). Proband does not wear shoes, eyes are open. For each condition, three trials are allowed. Best trial is rated.  <div><div>0</div><div>Normal, able to stand in tandem for &gt; 10 s</div></div> <div><div>1</div><div>Able to stand with feet together without sway, but not in tandem for &gt; 10s</div></div> <div><div>2</div><div>Able to stand with feet together for &gt; 10 s, but only with sway</div></div> <div><div>3</div><div>Able to stand for &gt; 10 s without support in natural position, but not with feet together</div></div> <div><div>4</div><div>Able to stand for &gt;10 s in natural position only with intermittent support</div></div> <div><div>5</div><div>Able to stand &gt;10 s in natural position only with constant support of one arm</div></div> <div><div>6</div><div>Unable to stand for &gt;10 s even with constant support of one arm</div></div>	
Score		Score	
<b>3) Sitting</b> Proband is asked to sit on an examination bed without support of feet, eyes open and arms outstretched to the front.  <div><div>0</div><div>Normal, no difficulties sitting &gt;10 sec</div></div> <div><div>1</div><div>Slight difficulties, intermittent sway</div></div> <div><div>2</div><div>Constant sway, but able to sit &gt; 10 s without support</div></div> <div><div>3</div><div>Able to sit for &gt; 10 s only with intermittent support</div></div> <div><div>4</div><div>Unable to sit for &gt;10 s without continuous support</div></div>		<b>4) Speech disturbance</b> Speech is assessed during normal conversation.  <div><div>0</div><div>Normal</div></div> <div><div>1</div><div>Suggestion of speech disturbance</div></div> <div><div>2</div><div>Impaired speech, but easy to understand</div></div> <div><div>3</div><div>Occasional words difficult to understand</div></div> <div><div>4</div><div>Many words difficult to understand</div></div> <div><div>5</div><div>Only single words understandable</div></div> <div><div>6</div><div>Speech unintelligible / anarthria</div></div>	
Score		Score	

## APPENDIX D

### Case study number 1: AM (P1)

AM was 36 at the time of testing. AM's problems began at 14 years old with a series of crushing headaches that eventually led to a diagnosis. Before that AM experienced some 'clumsy' moments but these were not considered outside of normal for AM's age. Consultation revealed a cystic cerebellar tumour that was removed through surgery. The operation was a success with regards the tumour but AM was left temporarily paralysed from the neck down for six months. Unsurprisingly AM described this period as 'terrifying' but over the following years AM made considerable recovery. This recovery plateaued to some degree as adulthood arrived. AM still permanently uses a wheelchair and has not walked since surgery but upper body motoricity has returned albeit with some impairment.

At the first session, AM described various therapies undertaken to improve movement control such as conductive education, regular gym exercise and yoga. AM was convinced that these were of great benefit. AM was clearly highly motivated and continued to exercise regularly doing press ups and yoga.

Meeting AM, it was clear there was still motor dysfunction in the upper body. Reaching to targets caused intention tremor and movement was clearly dysmetric. Nystagmus was present and quite pronounced. Perhaps as part of AM's eye problems, or maybe related to tonic problems in the upper body, AM tilted the head back at all times to give the appearance of peering down. AM's handwriting was clear and this was regularly practiced. Dysarthria was present and combined with a strong regional accent, communication was sometimes difficult. At times AM would appear to stop mid-sentence as if trying to 'catch'

a train of thought. Despite the evident motor problems, AM was very agile at getting in and out of the wheelchair and could stand supported. At home AM had special wall bars to navigate around the house. AM spoke of just coming out of a period of depression but during all of our meetings AM seemed spirited, eager and was good company. AM would often make jokes of a general nature but also about having ataxia. Recreationally AM enjoyed working on a computer and mentioned more than once how difficult this had been at one point. AM liked to socialise and go to the pub, although small amounts of beer had a large effect. AM also took regular weekend breaks out of the city.

When attempting to stand upright in the early sessions, AM would require the support of both experimenters. After about 30 seconds, tremor would become extreme and AM would tire. It was noticeable in these sessions, that AM clung on to the experimenters' hands so tightly that a temporary mark would be left. Posture would also be compromised with the chest slumping forward slightly and as mentioned the head tilted back to focus on the pole placed to the front. During swaying AM would often verbalise a desire to stop but would rarely do so. In this regard AM was very determined and not put off by discomfort. At the third meeting a number of secondary consequences were described that AM attributed to practicing the swaying exercises. AM said that a feeling of well-being had arisen and that a 'buzzing' had been lifted. When asked to describe what was meant AM described a general cloudiness of thought that had been ameliorated.

In the laboratory it was noticeable that AM was 'braver' with the depth and speed of the swaying but that also tremor was appearing later and handgrip with the experimenters was lighter. AM also reported back that the guides were being used in a number of additional exercises around the home, for instance AM described swaying using the wall bars on the ramp that gave wheelchair access. By the fifth session AMs swaying had become much stronger. Periods of swaying had increased and AM would now need to be asked to stop.



Whilst no identifiable changes could be seen in behaviour such as speech or reaching it was clear that during swaying, AM was no longer 'holding' on but rather, using the experimenters' hands for guidance and support. Contact was much less heavy than the first sessions despite swaying with greater amplitude and velocity. This was reflected in AMs jerk score at two months compared to the imagined sound condition. However, despite these observable differences AM would still fall if support was withdrawn and remained dependent on the wheelchair.

It is difficult to say in AMs case how much the guides were of benefit. Whilst AM certainly got better at swaying whilst under the program it is difficult to assess how much of an impact this had on daily life. One aspect of AMs participation in the study was reports of elevated mood. This and a combination of AMs existing enthusiasm suggest this study helped in some way.

## Case study number 2: DD (P5)

DD was 72 at the time of testing. Problems started some three years previously. The first noticeable signs were encountered when bringing tea through from the living room to the kitchen. A couple of times this was spilled and DD began to question what was wrong. After a year DD was diagnosed with general cerebellar atrophy but was found negative on all known SCA types.

When DD first came to laboratory, walking was supported by the use of small cane. DD is small in stature but would walk with quick feet. DD explained that walking was generally fine but that some falls had occurred (perhaps four of five in the last few years) so the cane had become a 'safety' tool to improve confidence. DD also explained it was to let others know there was a problem. DD was a keen bowler so the cane was also important in stabilising balance when leaning forward to bowl. Recently DD had felt less inclined to bowl as fear of falls persisted. Generally when falls occurred they would happen in the frontal plane.

DD had individually sort out the research after seeing it discussed in an in-house journal. This is a measure of DD's diligence that became apparent over the next few months. DD had experienced some depression following diagnosis. This had been exacerbated by a feeling of little help or input from the medical profession. One place this was not the case was the ataxia centre in Sheffield that DD visited at 6 month intervals.

After meeting DD it was not immediately apparent there was anything wrong. Language was unimpaired other than the occasional slur on specific words. DD is witty, sharp and fun to be with and would engage in banter with the experimenters and DDs partner who was very supportive and always present.

On examination there were some motor signs. Mild nystagmus was present when following a finger and some dysmetria in the transport phase of the finger-nose test. However these conditions were mild at best. When standing, greater problems emerged. In static stance DD was quite stable with exaggerated sway but shutting the eyes immediately caused toppling. When walking without the cane DD moved very fast. It soon became clear that part of this was to generate inertia to counteract falling. This produced a lean into the direction of motion the outcome of which was overbalancing in the frontal plane. DD was aware of overbalance and would attempt to arrest this using the toes and ankles. The process of attempting to regain balance would often appear slow motion like. DDs body posture was also very 'tight' and there was little movement in the arms. When swaying a similar pattern of overbalancing would occur. It appeared as if sways were being mis-scaled and then the non-weight bearing leg would be lifted to try and equalise balance. There was also much rigidity in the body mainly as a result of tightening core body muscles to maintain balance. In the earlier sessions DD did not need assistance swaying but had to be 'caught' a couple of times per recording session due to overbalancing.

In the third session DD reported that a long walk had been taken without the use of the cane. Visibly delighted with this, DD was asked how that had been and to what degree this was attributable to the programme. DD reported a new sense of confidence that was described as 'being there' but could not honestly say if there was any effect of the sounds on their ataxia. The MP3 had been put on a Walkman and used as a 'primer' before walking started.

On the weight-shifting task DD had become much less ridged and the swaying was covering a larger area. From this point on DD did not have to be caught once. Walking had also become more fluid with less rigidity in the body, less lean into the direction of the walk and greater movement in the arms. An interesting aspect of this was DD reported being 'less engaged in walking' whereas before DD would pay attention to each step etc.,

now motor activity would be performed unconsciously. In this regard DD reported that sometimes it would only be noticed that a tray had been carried, or a distance walked without the cane, after the event had taken place. These improvements were noted by DD's partner who also suggested that DD had been in elevated mood since starting the programme.

By the final session DD was performing well on all given tests. DD was the most consistent performer in the group and changes in outcome measures confirmed what was observable in the laboratory. What was noticeable was that, such was DD's confidence, there was willingness to try activities outside of the programme. For example, as walking forwards had become stable, DD decided to try walking backwards; something that had not been attempted since long before diagnosis. Whilst tentative on this task it is testament to how empowered DD felt by the work that had been undertaken. Whilst it can never be certain which aspects of the intervention are attributable to DDs improvements, it is clear that the programme had positive physical and psychological effects.