Investigating motor preparation and the importance of external information in people with Parkinson's disease

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Abstract

There is overwhelming evidence that PD leads to impairments in *executing* voluntary movements. However, it is less clear whether it also leads to impairment in the *preparation* of movement. The current investigation first aims to further our understanding of motor preparation in people with PD.

Two techniques are commonly used to assess motor preparation. These are the manipulation of response complexity and cueing response-related information in advance of the imperative signal. They were both incorporated into a motor task in which participants performed two-movement sequences on a response board.

In Experiment 1, people with PD (comprising two groups – one on their anti-Parkinsonian medication, and the other following a delay in its normal administration) showed patterns in their motor performance that was similar to healthy age-matched adults. They showed lengthening in their reaction time (RT) with increased response complexity, indicating that the sequences were prepared before their initiation. In addition, both of the PD groups, as well as the healthy adult group, showed shorter RTs with valid cueing and longer RTs with invalid cueing relative to the neutral cue condition. In response to a part-invalid cue (with both valid and invalid information) all three groups had very similar RTs to that in the neutral cue condition. Taken together, the effects of increased response complexity and the effects of cueing can be taken to reflect intact preparation in people with PD.

The aim of Experiment 2 was to examine motor preparation in people with PD under reduced visual information. This was done in light of findings that the motor performance of people with PD improves with the presentation of relevant visual information and deteriorates with its removal. Experiment 2 presented a similar task to Experiment 1 but reduced the amount of relevant visual information provided about the sequence while it was being performed. The results of this experiment suggest that overall the motor performance of the PD group was very similar to the healthy adult group under conditions of reduced visual information. However, there was evidence that with this reduction of relevant visual information the PD group showed incomplete preparation in the part-invalid cue condition.

In Experiment 3, motor preparation was further examined by manipulating the time participants were required to maintain their response before executing it. The results of this experiment suggest that people with PD did not suffer a greater difficulty than healthy adults in maintaining their response.

The second aim of the current investigation was to better understand the influence of external information on motor preparation and execution in people with PD. Some research suggests that people with PD use external information strategically to compensate for their difficulties in the internal control of movement. Other research suggest that external information evokes a stronger obligatory response in people with PD. In order to test these two possibilities, in the third experiment, participants were first presented with a sequence to perform, and then, while initiating and executing that sequence, they were presented with a second sequence, providing either valid or invalid visual information about the two-movement sequence. It was expected that if invalid visual information evokes a stronger obligatory response in people with PD, then these participants would experience greater difficulties ignoring such information. This was not found to be the case. Rather the PD group showed a similar pattern of performance to the healthy adults. This indicates that they were able to ignore visual information when it was invalid and unhelpful, and so suggests that people with PD use external information strategically.

The results presented in this thesis suggest that motor preparation is largely intact in people with PD. Motor preparation may, however, be incomplete under reduced visual information. Furthermore, while visual information may be particularly important to people with PD, it does not seem to evoke a stronger obligatory response than in healthy adults. Rather, people with PD seem to use external information strategically.

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Statement of Candidate Contribution

In relation to regulation 2 and 3 of the *Regulations Governing Research Higher Degrees*, all experimental design, task development, participant recruitment and testing, data entry, analysis, interpretation, and preparation of manuscript (Appendix A) were conducted by the candidate.

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Chapter One: General Introduction

1.1 Introduction

Parkinson's disease (PD) is a disorder of movement with characteristic impairments including increased resting tremor, general muscle rigidity, bradykinesia – slowed motor execution – and akinesia – an overall poverty of spontaneous movement (Franz & Miller, 2002; Hocherman, Moont, & Schwartz, 2004; Jackson, Jackson, Harrison, Henderson, & Kennard, 1995a; Jahanshahi & Frith, 1998; Knight, 1992; Marsden, 1986; Reed & Franks, 1998). This thesis examines various aspects of motor preparation and execution.

There is overwhelming evidence that PD leads to impairments in *executing* voluntary movements, such as a general slowing, increased hesitations, and greater variability relative to age-matched healthy adults (Bherer, Belleville, & Gilbert, 2003; Desmurget et al., 2004; Goldman, Baty, Buckles, Sahrmann, & Morris, 1998; Kutukcu, Marks, Goodin, & Aminoff, 1998; Low, Miller, & Vierck, 2002; Monza et al., 1998; Müller et al., 1999; Onla-or & Winstein, 2001; Serrien, Steyvers, Debaere, Stelmach, & Swinnen, 2000). There are two main phases of movement execution – acceleration and deceleration. Acceleration begins at the initiation of the movement and ends at peak velocity, and comprises measures of peak acceleration, as well as the time and magnitude of peak velocity (Alberts, Tresilian, & Stelmach, 1998; Rand, Stelmach, & Bloedel, 2000; P. Weiss, Stelmach, Alder, & Waterman, 1996). People with PD show difficulties in this phase of motor execution, with reduced initial electromyographic activity (EMG), amplitude, peak acceleration, and velocity, as well as prolonged time to reach peak velocity (Bekkering et al., 2001; Berardelli, Accornero, Argenta, Meco, & Manfredi, 1986; Rand et al., 2000; Rand, Van Gemmert, & Stelmach, 2002; Reed & Franks, 1998; Stelmach, Teasdale, & Phillips, 1992; P. Weiss, Stelmach, & Hefter, 1997). The second phase of movement execution – deceleration – is marked by force reduction, which involves 'applying the brakes' to a movement and correcting errors that arise in the acceleration phase (Bonfiglioli, De Berti, Nichelli, Nicoletti, & Castiello, 1998; Rand et al., 2000). The ability to decelerate accurately and smoothly also appears to be impaired in people with PD (Reed & Franks, 1998; Sheridan, Flowers, & Hurrell, 1987; P. Weiss et al., 1996; P. H. Weiss, Stelmach, Chaiken, & Adler, 1999). This may involve excessive co-activation of agonist and

antagonist muscles resulting in jerky and uncoordinated movements (Rand et al., 2000; Reed & Franks, 1998; P. Weiss et al., 1997).

It is however uncertain whether PD also leads to impairment in the *preparation* of voluntary movement (Almeida, Wishart, & Lee, 2003; Bekkering et al., 2001; Gauntlett-Gilbert & Brown, 1998; Gueye, Viallet, Legallet, & Trouche, 1998; Reed & Franks, 1998; J. Wang, Thomas, & Stelmach, 1998). Motor preparation has been defined as "the selection, translation, and activation of various features of the movement, such as order of sequential elements, distance, direction, and velocity" (Smiley-Oyen & Worringham, 2001 p. 221). Shaffer (1991) argued that motor preparation allows the elements of a response to be combined in a way that allows their smooth and fluent execution. The motor program (the symbolic representation of motor preparation) has been defined as sequences of stored muscle commands (Keele, 1968), enabling an intended movement to be executed by the motor system (Shaffer, 1992).

There are a number of studies, including two meta-analyses (Wang, 1998 #250;Gauntlett-Gilbert, 1998 #74), which suggest that motor preparation is intact in people with PD (Bekkering et al., 2001; A. M. Johnson, Vernon, Almeida, Grantier, & Jog, 2003; Rand et al., 2000; P. Weiss et al., 1997). However there are also studies that suggest that people with PD do show impairments in motor preparation. There are a number of accounts of the nature of this impairment. Some argue that people with PD have a difficulty in the selection and construction of motor programs (Bloxham, Mindel, & Frith, 1984; Harrington & Haaland, 1991; Stelmach, Phillips, & Chau, 1989), or in combining different programs together, such as in the case where two movements are performed simultaneously (Alberts et al., 1998; Benecke, Rothwell, Dick, Day, & Marsden, 1986, 1987a). Others have found evidence of incomplete motor preparation in people with PD (Harrington & Haaland, 1991; Jennings, 1995), and a reduced ability to use relevant information to prepare a movement (Gueye et al., 1998; Wascher et al., 1997). Others still raise the possibility that people with PD suffer a disruption to the storage and maintenance of motor preparation, leading to a degradation of motor programs over time (Gentilucci & Negrotti, 1999b; Gueye et al., 1998; Negrottti, Secchi, & Gentilucci, 2005; Sheridan et al., 1987). Finally, there are suggestions that people with PD suffer a difficulty in releasing constructed motor programs (Berardelli et al., 1986; Bloxham et al., 1984; Jahanshahi, Brown, & Marsden, 1992a;

Kaneoke, Koike, Sakurai, Takahashi, & Watanabe, 1989; Kutukcu et al., 1998; Müller et al., 1999; Rafal, Inhoff, Friedman, & Bernstein, 1987; J. Wang et al., 1998; P. H. Weiss et al., 1999; Willingham, Koroshetz, Treadwell, & Bennett, 1995), or in switching between different sub-programs of a movement (Almeida et al., 2003; Benecke, Rothwell, Dick, Day, & Marsden, 1987b; Berardelli et al., 1986; Harrington & Haaland, 1991; Plotnik, Flash, Inzelberg, Schechtman, & Korczyn, 1998). The first aim of this investigation is to further examine motor preparation in people with PD. Section 1.3 discusses in more detail the aspects of motor preparation that are of interest.

The second aim of this thesis is to examine the role of external information in motor preparation and execution in people with PD. It has been found that when provided with external information that is relevant to the movement being performed, the preparation and execution of movement improves to a greater degree in people with PD than in healthy adults (Sheppard et al., 1996; Siegert, Harper, Cameron, & Abernethy, 2002). Further, there is evidence of greater deterioration in their movements when such information is removed (Cooke, Brown, & Brooks, 1978; Georgiou et al., 1994; Georgiou et al., 1993; Jones, Phillips, Bradshaw, Iansek, & Bradshaw, 1992; Kritikos et al., 1995). However it remains unclear how best to understand the importance of external information.

One suggestion is that people with PD use external information strategically as a compensatory strategy, to minimise the demands on the basal ganglia. In motor control there is a distinction between movements that are guided by internal control mechanisms and movements controlled by external information (Filoteo et al., 1997; Halsband, Matsuzaka, & Tanji, 1994; Oliveira, Gurd, Nixon, Marshall, & Passingham, 1997). The basal ganglia and the SMA are thought to play a greater role in the former (Cunnington, Bradshaw, & Iansek, 1996; Cunnington, Iansek, & Bradshaw, 1999a; Halsband et al., 1994; Hanakawa, Fukuyama, Katsumi, Honda, & Shibasaki, 1999; Mushiake & Strick, 1995), and so any dysfunction of the basal ganglia would be expected to lead to a specific difficulty in internally controlled movements (Cunnington et al., 1996; Georgiou et al., 1994; Hanakawa et al., 1999; Oliveira et al., 1997). Thus, people with PD might use external information to compensate for their difficulties in internally self-controlled movements by relying more heavily on alternate (and uncompromised) motor systems that use external information to

guide movement (Cunnington et al., 1996; Halsband et al., 1994; Hanakawa et al., 1999; Jahanshahi & Frith, 1998; Mushiake, Inase, & Tanji, 1991).

An alternative explanation of the role of external information in people with PD is that it evokes a stronger obligatory response than in healthy adults. It has been found that people with PD are more influenced by irrelevant visual information than healthy adults (Praamstra, Plat, Meyer, & Horstink, 1999; Praamstra, Stegeman, Cools, & Horstink, 1998). This suggests that PD may lead to a difficulty where visuospatial information more readily evokes movement-related activity in the motor cortex of people with PD (Praamstra & Plat, 2001). External information may then be important because it evokes a stronger obligatory response on people with PD, where they cannot help but respond to external information. Section 1.4 discusses this in more detail.

The basal ganglia and thought to be involved in both motor preparation and the internal control of movement. These are of particular interest to our understanding of PD because an abnormal loss of dopaminergic neurons in the substantia nigra, and a subsequent dysfunction of the basal ganglia, has been implicated as the cause of PD (Amirnovin, Williams, Cosgrove, & Eskandar, 2004; Bherer et al., 2003; Bradshaw & Mattingley, 1995; Crossman, 2000; Hankey & Wardlaw, 2002; Kandel, Schwartz, & Jessell, 2000; Knight, 1992; Mandir & Vaughan, 2000). A loss of normal basal ganglia functioning in people with PD would thus be expected to affect these two areas of motor control. To understand this relation further, Section 1.2 outlines the role of the basal ganglia in the control of movement under normal conditions.

1.2 The structure and function of the basal ganglia

The basal ganglia comprise four primary subcortical nuclei – the striatum (consisting of the caudate nucleus, the putamen, and the ventral striatum), the globus pallidus (separated into the internal and external segments – GPi and GPe, respectively), the substantia nigra, and the subthalamic nucleus (SThN). The striatum receives all input into the basal ganglia, predominantly from the cerebral cortex, but also from the thalamus and the substantia nigra (Aird, 2000; Crossman, 2000; Fitzgerald, 1996; Gazzaniga, Ivry, & Mangun, 1998;

Marsden, 1980, 1986; Mink, 1996; Pollack, 2001). It is thought that all cortical input travels through two major pathways of the basal ganglia after leaving the striatum (Bolam, Hanley, Booth, & Bevan, 2000; Contreras-Vidal, 1999; Smith, Bevan, Shink, & Bolam, 1998). The first, named the direct pathway, comprise a connection directly to the thalamus via the GPi (Crossman, 2000; Fitzgerald, 1996; Smith et al., 1998). The second, named the indirect pathway, passes through the GPe, the SThN, and the GPi before reaching the thalamus (Crossman, 2000; Smith et al., 1998). Figure 1.1 depicts the excitatory and inhibitory connections of these two pathways.

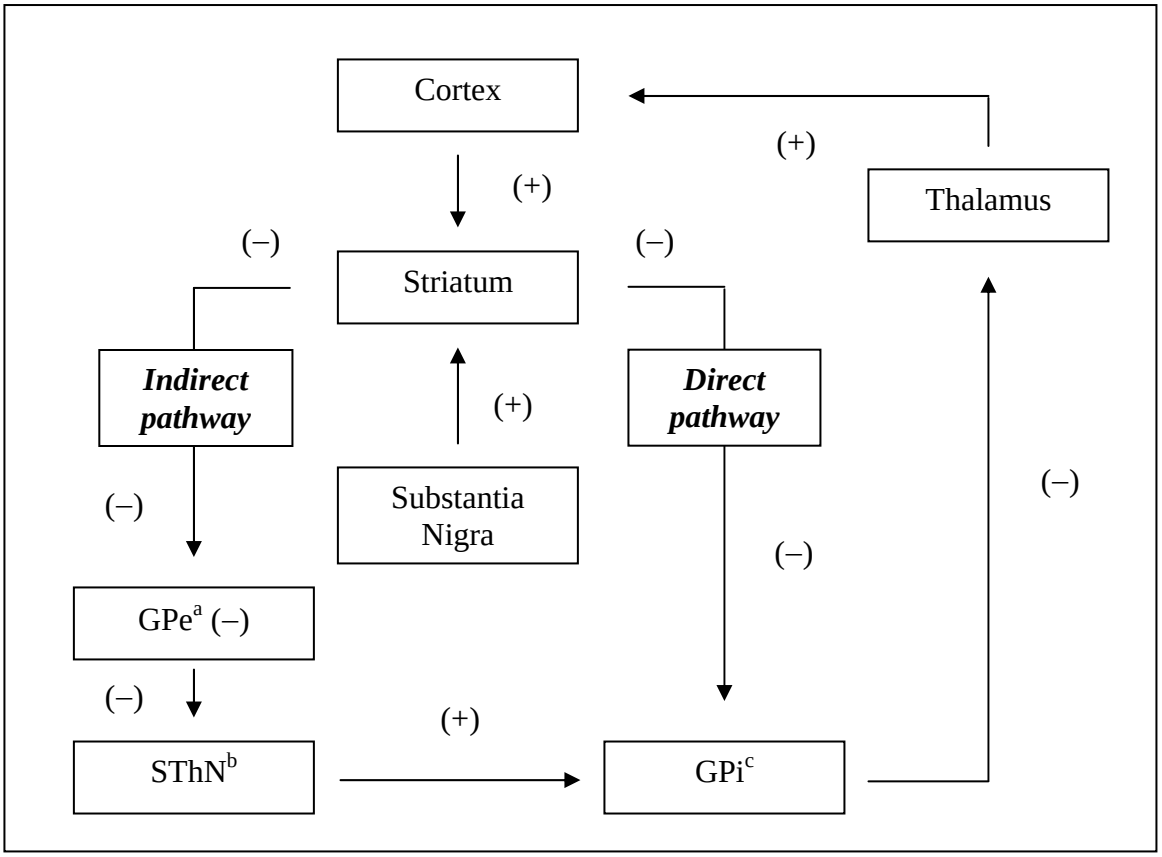

Figure 1.1 A schematic representation of the connections through the direct and the indirect pathways of the basal ganglia.

Note. Plus signs indicate excitatory connections, and minus signs indicate inhibitory connections. Various other connections between the nuclei of the basal ganglia also exist but will not be discussed in detail.

[a] refers to the external segment of the Globus Pallidus. [b] refers to the Subthalamic Nucleus. [c] refers to the internal segment of the Globus Pallidus.

These two pathways determine the amount of activation from the thalamus back to the cortex. Transmission through the direct pathway of the basal ganglia increases activation from the thalamus to the cortex because the GPi, which would usually inhibit the thalamus, is suppressed (Alexander, Crutcher, & DeLong, 1990; Contreras-Vidal, 1999; Smith et al., 1998; Wichmann & DeLong, 1996). In contrast, transmission through the indirect pathway decreases activation from the thalamus to the cortex. This is because the striatum suppresses the GPe, releasing the SThN to send its excitatory connection to the GPi, which subsequently inhibits the thalamus (Alexander et al., 1990; Bolam et al., 2000; Contreras-Vidal, 1999; Smith et al., 1998; Wichmann & DeLong, 1996).

The globus pallidus guides focused amplification and suppression of cortical activity (Mink & Thach, 1991). Because the GPi is common to both pathways, its level of activation can be taken to reflect the overall transmission from the basal ganglia to the thalamus. The decreased firing of some GPi neurons during movement is thought to facilitate relevant cortical activity (by increasing selected thalamocortical activation), while the increased activation of other GPi neurons suppresses antagonistic or unwanted cortical activation (Graybiel, Aosaki, Flaherty, & Kimura, 1994; Mink, 1996). It is thought that increases and decreases in thalamic output amplify and suppress cortical activity associated with a movement, resulting in the exclusive activation of elements of a movement, which enables it to be performed smoothly (Alexander et al., 1990; Bradshaw & Mattingley, 1995; Brooks, 2000; Brown & Marsden, 1998; Crossman, 2000; Graybiel, 2000; Marsden, 1980; Smith et al., 1998; Wichmann & DeLong, 1996; J. R. Wickens, 1993). That the inactivation of the globus pallidus leads to slowed movement execution due to an increased co-activation of different muscle groups also supports this suggestion (Mink & Thach, 1991).

1.2.1 The role of the basal ganglia in voluntary movement

There is evidence that the basal ganglia are involved both in motor preparation and the internal control of movement (Aldridge & Berridge, 1998; Bradshaw & Mattingley, 1995; Brown & Marsden, 1998; Graybiel, 2000; Jueptner & Weiller, 1998; Smith et al., 1998;

Wichmann & DeLong, 1996; J. Wickens, Hyland, & Anson, 1994; J. R. Wickens, 1993). Five partially-closed (and highly topographic) circuits involved in different aspects of motor control are believed to exist between the cortex and the basal ganglia (Alexander et al., 1990; Alexander, DeLong, & Strick, 1986; Bolam et al., 2000; Jahanshahi & Frith, 1998; Joel & Weiner, 1997). These circuits are collectively implicated in the intentional self-generation of purposeful complex behaviour (De Pisapia & Goddard, 2003; Jahanshahi & Frith, 1998; Rushworth, Walton, Kennerley, & Bannerman, 2004).

Three of these circuits are particularly important in understanding motor preparation and the internal control of movement, both in healthy adults and in people with PD. The motor circuit (between the basal ganglia and the SMA) is implicated both in the internal control of movement (Cunnington, Iansek, & Bradshaw, 1999b; Deiber, Honda, Ibañez, Sadato, & Hallett, 1999; Halsband et al., 1994; Jenkins, Jahanshahi, Jueptner, Passingham, & Brooks, 2000; Taniwaki et al., 2003), and in motor preparation (Alexander et al., 1990; Alexander et al., 1986; Catalan, Honda, Weeks, Cohen, & Hallett, 1998; Cunnington et al., 1996; Jahanshahi & Frith, 1998; Leuthold & Jentzsch, 2001; Mandir & Vaughan, 2000; Roland, Larsen, Lassen, & Skinhøj, 1980). The complex circuit (between the basal ganglia and the DPC) is linked to the planning of self-initiated movements (De Pisapia & Goddard, 2003; Jahanshahi & Frith, 1998; Luks, Simpson, Feiwell, & Miller, 2002; MacDonald, Cohen, Stenger, & Carter, 2000; Mandir & Vaughan, 2000; H.-C. Wang, Lees, & Brown, 1999), while the anterior cingulate circuit (between the basal ganglia and the ACC) is implicated in response selection, determining when to act, and the monitoring of the movement (Jahanshahi & Frith, 1998; Luks et al., 2002; MacDonald et al., 2000).

In addition to motoric processes, these frontostriatal circuits are also involved in non-motoric executive functions and attentional control. This is important as it is generally thought that the preparation of purposeful voluntary movements relies on processes such as executive functions and attention, and that these processes are internally controlled. To enable the efficient preparation of a response, one needs to allocate attention and maintain goal-relevant information in mind (Bunge, E., Scanlon, Rosen, & Gabrieli, 2002; De Pisapia & Goddard, 2003; MacDonald et al., 2000). When selecting among competing stimuli or responses, one needs to be able to inhibit irrelevant and inappropriate information (Bunge et al., 2002; Luks et al., 2002; Matsumoto, Suzuki, & Tanaka, 2003), and possibly

switch between different response options (Rushworth et al., 2004). Together, such executive control is thought to assist motor preparation by enhancing the representation of the desired response (Bunge et al., 2002).

1.2.1.1 Motor preparation

It has been suggested that the selective activation of the cortical, striatal, and pallidal neurons of different circuits reflects the involvement of these regions in motor preparation (Alexander, DeLong, & Crutcher, 1992; Alexander et al., 1986; Graybiel et al., 1994; Nambu, Yoshida, & Jinnai, 1990). Neurons in the striatum and the GPi, which receive input from the SMA, tend to fire consistently before the execution of a movement (Alexander et al., 1986). This is taken to reflect an involvement of the basal ganglia and the SMA in motor preparation, where different cortical activity associated with motor programs is either amplified or suppressed (Kandel et al., 2000; Montgomery & Buchholz, 1991; J. R. Wickens, 1993). Increased blood flow in the SMA has also been found during the preparation of complex movement sequences provides further support for this idea (Alexander et al., 1986; J. R. Wickens, 1993). The SMA contains two functionally separate regions – the caudal SMA proper and the rostral pre-SMA. The recording of event-related functional magnetic resonance imaging (fMRI) in the pre-SMA has been found to be elevated in response to the presentation of informative cues. This is taken to reflect the involvement of the pre-SMA in the selection and planning of motor responses (Luks et al., 2002; Rushworth et al., 2004). Thus, it is thought that the pre-SMA is more involved in aspects of motor preparation than the caudal SMA (Carbonnell, Hasbroucq, Grapperon, & Vidal, 2004; Halsband et al., 1994).

Both the complex circuit (between the basal ganglia and the DPC) and the anterior cingulate circuit (between the basal ganglia and the ACC) have also been implicated in aspects of motor preparation. Event-related fMRI has revealed greater activation of both cortical regions following the presentation of a cue informing participants of an upcoming motor response. This was taken to reflect the allocation of attention needed for motor preparation (Luks et al., 2002). Further, fMRI investigations have also highlighted the role of the DPC in selecting between competing responses (Bunge et al., 2002). The motor,

complex, and anterior cingulate circuits thus appear to play crucial roles in the preparation of movement, possibly by amplifying relevant cortical activity and inhibiting others (Alexander et al., 1990; Alexander et al., 1992; Carbonnell et al., 2004; Halsband et al., 1994; Jenkins et al., 2000; Reed & Franks, 1998).

1.2.1.2 The internal control of movement

The basal ganglia have also been implicated in the internal control of movement. Mushiake and Strick (1995) found one subclass of pallidal neurons that was active during movements that were internally controlled (self-initiated) and another subclass that was active during movements that were externally controlled (stimulus-driven). Findings from fMRI further suggest that the basal ganglia and the SMA may have a greater involvement in internally controlled than externally controlled movements (Cunnington et al., 1999b; Deiber et al., 1999; Halsband et al., 1994; Jenkins et al., 2000; Taniwaki et al., 2003). During the internal control of self-initiated finger movements, the brain regions of the motor circuit (the putamen, thalamus, SMA, sensorimotor cortex) are significantly activated (Taniwaki et al., 2003). Furthermore, during the internally controlled self-initiated movements, activity in one of these regions have also been found to be strongly correlated with activity in one or more of the other regions. In contrast, during the movements externally paced by a metronome, stronger activation has been found in other brain regions, such as the premotor and sensorimotor cortices (Taniwaki et al., 2003). Finally, path analysis calculations suggest strong positive interactions between these areas of the motor circuit during internally controlled movements. These results further support the suggestion that the motor circuit plays an important role in the internal control of movement (Jenkins et al., 2000; Taniwaki et al., 2003).

1.2.2 Understanding the pathology of PD

Abnormal loss of dopaminergic neurons in the substantia nigra is widely regarded as the core pathology of PD (Amirnovin et al., 2004; Bherer et al., 2003; Bradshaw & Mattingley, 1995; Crossman, 2000; Hankey & Wardlaw, 2002; Mandir & Vaughan, 2000).

Dopaminergic input from the substantia nigra to the striatum facilitates the direct pathway and inhibits the indirect pathway, and thus increases activation of the thalamus (Aird, 2000; Alexander et al., 1990; Brown & Marsden, 1998; Crossman, 2000; Groves, 1983; Marsden, 1980; Wichmann & DeLong, 1996). It is thought that dopamine has a gating function, where task-relevant activation through the frontostriatal circuits is facilitated and task-irrelevant activation (noise) is suppressed (Reed & Franks, 1998; Stern, Horvitz, Côté, & Mangels, 2005). Thus, dopaminergic depletion in people with PD is believed to affect both the motor control and executive functions associated with the frontostriatal circuits (Bekkering et al., 2001; Cools, Stefanova, Barker, Robbins, & Owen, 2002; Fama & Sullivan, 2002; Harrington & Haaland, 1991; Jahanshahi & Frith, 1998; Remy & Samson, 2003). While dopaminergic depletion in PD is believed to alter the balance of activation through the two pathways of the basal ganglia, there is disagreement how this specifically affects the frontostriatal circuits, and the different processes controlled by these circuits. There are four explanations of this.

First, some argue that dopaminergic depletion leads to an overall reduction in thalamic output to the cortex due to under-activation of the direct pathway and over-activation of the indirect pathway (Contreras-Vidal, 1999; Graybiel, 2000; Groves, 1983; Kandel et al., 2000; Wichmann & DeLong, 1996). This affects both the preparation and execution of movement in people with PD (Gentilucci & Negrotti, 1999b; Gueye et al., 1998; Lewis, Byblow, & Walt, 2000; Rand & Stelmach, 1999; Rand et al., 2002). Because the motor, complex, and anterior cingulate frontostriatal circuits have been implicated in aspects of motor preparation and the internal control of movement (Catalan et al., 1998; Jahanshahi & Frith, 1998; H.-C. Wang et al., 1999), underactivation of these circuits in people with PD (Sabatini et al., 2000) is thought to lead specifically to difficulties in these aspects of motor control (Alexander et al., 1990; Benecke, Dick, Rothwell, Day, & Marsden, 1985; Catalan et al., 1998; Cunnington et al., 1996; Jahanshahi & Frith, 1998; K. A. Johnson et al., 2001). This overall reduction in thalamic output in PD may affect the ability to select, implement, and regulate appropriate force parameters of a movement (as shown in abnormal initial agonist EMG activity) (Alberts et al., 1998; Franz & Miller, 2002; Jackson et al., 1995a; Rand et al., 2000; P. Weiss et al., 1996). Movement would be less smooth and accurate than in healthy adults, with more fragmented acceleration, a possible impairment in shifting from force production to force reduction, prolonged deceleration, and additional time

needed for more adjustments during movement execution (Benecke et al., 1986; Jahanshahi et al., 1992a; Rand et al., 2000; Scarpa & Castiello, 1994; P. Weiss et al., 1997; P. H. Weiss et al., 1999).

Second, underactivation of cortical brain regions linked to the basal ganglia (such as the SMA) might also interfere with the maintenance of motor programs that are stored in such regions (Gentilucci & Negrotti, 1999b; Gueye et al., 1998; Sheridan et al., 1987; J. R. Wickens, 1993). So people with PD may be able to initially prepare a movement but are unable to sustain this preparation over time.

Third, it has been suggested that this underactivation leads to an abnormal slowness in motor preparation and execution in people with PD. It has been suggested that people with PD require more time between a cue and an imperative signal to fully use advanced information, and more time to complete changes to incorrectly prepared movements (Jahanshahi et al., 1992a; A. M. Johnson et al., 2004; Scarpa & Castiello, 1994; P. H. Weiss et al., 1999).

Fourth, other investigators suggest that the loss of dopaminergic neurons and the related imbalance between the two main pathways of the basal ganglia decreases the efficiency of the motor system, increasing the system noise and variability in people with PD (Cunnington et al., 1996Wichmann, 1996 #135; Franz & Miller, 2002; Montgomery, Nuessen, & Gorman, 1991; Reed & Franks, 1998; Sheridan et al., 1987; P. Weiss et al., 1997). One of the roles of pallidal neurons in the indirect pathway of the basal ganglia is to terminate cortical activity in frontal brain regions (such as the SMA) to allow the release of relevant motor programs (Cunnington et al., 1996; Gentilucci & Negrotti, 1999a; Lang, Goldenberg, Podreka, Cheyne, & Deecke, 1990; Lewis et al., 2000; P. Weiss et al., 1997; Willingham et al., 1995). Thus, it has been suggested that abnormal basal ganglia output due to an imbalance between the two pathways would affect the termination of cortical activity, resulting in increased system noise and a slowness and variability in movement in people with PD (Cunnington et al., 1996Wichmann, 1996 #135; Franz & Miller, 2002; Montgomery et al., 1991; Reed & Franks, 1998; Sheridan et al., 1987; P. Weiss et al., 1997). It has in fact been suggested that dopaminergic medication alleviates some of the impairments in people with PD (including executive functions) by reducing the noise and increasing the efficiency in frontal brain regions such as the DPC (Cools, Barker, Sahakian,

& Robbins, 2001; Cools et al., 2002; Pillon, Czernecki, & Dubois, 2003; Remy & Samson, 2003).

1.2.3 Understanding the basal ganglia in relation to aspects of movement in people with PD

One of the aims of the current thesis is to assess which of the above four alternatives best accounts for the impairments of motor preparation in people with PD. Given the important of the basal ganglia in the internal control of movement, as discussed above, this thesis also investigates the role of external information in people with PD.

1.3 Motor preparation in people with PD

It is currently uncertain whether motor preparation is intact in people with PD. Some research suggests that motor preparation is intact (Bekkering et al., 2001; Gauntlett-Gilbert & Brown, 1998; Reed & Franks, 1998; J. Wang et al., 1998), while other research suggests difficulties relative to healthy adults (Gueye, 1998 #15;Almeida, 2003 #234; Jennings, 1995 #23). Before outlining this research further, it is important to describe two techniques that are regularly used to measure motor preparation – manipulating the complexity of a response and cueing relevant information about a response in advance.

Increasing the complexity of a response has been found to prolong the time healthy participants take to initiate that response (measured by their reaction time – RT). This is understood to reflect the additional time that is required to prepare the elements of a more complex movement before its execution (Henry & Rogers, 1960; Ketelaars, Garry, & Franks, 1997; Low et al., 2002; Rafal et al., 1987; Sidaway, 1991; Smiley-Oyen & Worringham, 1996, 2001; Stelmach & Worringham, 1988; Sternberg, Monsell, Knoll, & Wright, 1978; van Donkelaar & Franks, 1991a). There are a number of ways to manipulate the complexity of the response.

One way to manipulate the complexity of the response is to vary the number of movements to be performed in a sequence. Increasing the number of movements has been found to

prolong participants' RTs (Canic & Franks, 1989; Christina, Fischman, Lambert, & Moore, 1985; Christina & Rose, 1985; Franks & Van Donkelaar, 1990; Garcia-Colera & Semjen, 1988; Harrington et al., 2000; Henry & Rogers, 1960; Smiley-Oyen & Worringham, 2001), but not measures of motor execution. This is thought to reflect the greater amount of preparation undertaken before the initiation of the first movement in the sequence (Canic & Franks, 1989; Garcia-Colera & Semjen, 1988; Henry & Rogers, 1960; Smiley-Oyen & Worringham, 2001). In a series of studies assessing response preparation and sequence length, Smiley-Oyen and Worrington (2001) argued that because the preparation of a sequence takes place before executing the first movement in the sequence, increasing the number of movements to be performed will prolong RT. The premotor time (a component of RT) has been found to be longer when participants were required to perform two- or three-movement sequences than when they were required to perform a single movement. This is also taken to reflect the additional time needed to prepare the more complex sequences (Christina & Rose, 1985; Fischman, 1984).

A second way to manipulate the complexity of a response is to vary the accuracy required in a movement. Requiring participants to make contact with a smaller target has been found to prolong RT in healthy adults (Fitts, 1954; Haaland, Harrington, & Grice, 1993; Sidaway, 1991; Smiley-Oyen & Worringham, 1996). Sidaway (1991) argued that motor preparation is significantly affected by the level of accuracy demanded in a task. This is because greater accuracy places greater demands on the output of the motor system, and less accuracy places lower demands on the output of the motor system.

A third way to manipulate the complexity of a response is vary the directions of the motor sequence (Bekkering et al., 2001; van Donkelaar & Franks, 1991a). van Donkelaar and Franks (1991a) found that when tracing a pattern from memory, increasing the number of reversals (changes of direction) in the pattern prolonged participants' RTs. Bekkering et al. (2001) also found that participants' RT was significantly longer when performing a two-movement sequence that contained a change of direction than a two-movement sequence that followed the same trajectory.

So manipulating the complexity of a response can be used to examine the participants' motor preparation. It is generally accepted that increasing the complexity of a response will

prolong RT. Any of these methods of manipulating the complexity of a response can be used in experimental conditions to measure an individual's motor preparation.

The second method commonly used to measure motor preparation is cueing. In choice RT tasks, participants are presented with an imperative signal that indicates a response. They are required to replicate this response as quickly as possible after the imperative signal. At some point before the onset of this imperative signal, a cue is presented to participants providing information about the response to be made (Rosenbaum, 1980). This cue can be: a) valid – providing accurate information about the response; b) invalid – providing inaccurate information about the response; or c) neutral – providing no information about the response to be performed. Cueing valid information is found to shorten RT relative to the neutral cue condition (referred to as an RT benefit). This reflects the use of the cue in the preparation of the response (Goggin & Stelmach, 1990; Gueye et al., 1998; Larish & Frekany, 1985; Larish & Stelmach, 1982; Leuthold & Jentzsch, 2002a; Müller-Gethmann, Rinkenauer, Stahl, & Ulrich, 2000; Rosenbaum, 1980; P. H. Weiss et al., 1999; Zelaznik & Hahn, 1985). Cueing invalid information lengthens RT relative to the neutral cue condition (an RT cost). This RT cost is taken to reflect the time needed to suppress the response that was prepared with the invalid cue and re-prepare the response when the imperative signal is presented (Goggin, Stelmach, & Amrhein, 1989; Larish & Stelmach, 1982; Leuthold & Jentzsch, 2002a; Stelmach, Goggin, & Amrhein, 1988). These effects of cueing on RT (but not on measures of execution) can be taken as evidence that motor preparation generally occurs before the sequence is initiated (Amrhein, Stelmach, & Goggin, 1991; Amrhein, Von Dras, & Anderson, 1993; Larish & Frekany, 1985; Larish & Stelmach, 1982).

In Rosenbaum's (1980) seminal paper, participants were required to perform rapid aiming movements to one of eight target buttons. The participants used either their left or right index finger, moved either forward or back from the start button, and moved to either a near or distant target button. Before performing the response, participants were cued with information about the parameters of the movement. The cued information was fully informative (indicating which finger to use, which direction, and which distance); partially informative (providing information about one or two of these parameters); or non-informative (providing no information about any of the parameters of the movement). It was found that participants exhibited shorter RTs when provided with full advanced

information (about all three parameters), than with either partial information (one or two of the parameters) or no information. It was found that as the amount of advanced information increased, participants' RTs shortened, suggesting that they had utilised the information in the cue to prepare the movement in advance (Rosenbaum, 1980).

Jennings (1995) further examined motor preparation through cueing advance information. In this study, participants learnt different sequences of finger taps (using their index, middle, and ring fingers), where each sequence was designated with a particular letter of the alphabet (the imperative signal). When presented with one of these imperative signals, participants were required to perform the corresponding sequence as quickly and accurately as possible. Before being presented with one of these imperative signals, participants were shown a valid, invalid, or neutral cue. Valid cues presented the same letter to that which was subsequently presented in the imperative signal; invalid cues presented one of the alternate letters, and neutral cues presented a letter not associated with any of the sequences. Participants had shorter RTs when presented with valid cues, and longer RTs with invalid cues, relative to trials which presented a neutral cue. In both cases this was taken to reflect the advanced preparation of the sequence (Jennings, 1995). In addition, in a second study Jennings (1995) used a part-invalid cue condition, where the sequence indicated by the imperative signal differed from the cue only in the position of the second and third finger taps (leaving the first finger tap in the cue and the imperative signal the same). The partial validity of such cues was used to examine the preparation of each movement separately, revealing the extent of preparation undertaken. It was argued that any RT cost with this cue condition would show that participants had treated the three finger taps collectively within the same motor program. Because the cue provided invalid advance information about the sequence as a whole, this cost could be taken to reflect advance preparation of the entire sequence (Jennings, 1995). If participants had shown an RT benefit (shortening of their RT relative to the neutral cue condition), then it could be inferred that only the first finger tap (which was validly cued) had been prepared according to the cue. Jennings found that healthy adults again showed lengthened RTs relative to the neutral cue condition. This was taken to reflect advanced preparation of the entire sequence.

In summary, participant's RTs on trials with valid, part-invalid and full-invalid cueing can be compared to a neutral cue condition. An RT benefit is expected following valid cueing, and is taken to reflect the advanced preparation of the response according to the cue, where less time is needed following the imperative to initiate the prepared response. An RT cost following part-invalid or full-invalid cueing is also taken to reflect advance preparation. This lengthening of RT relative to a neutral cue condition is thought to reflect the additional time required to change or alter the prepared response following the presentation of the imperative signal indicating an alternate response. In addition, and in contrast to the RT cost outlined above, it has been suggested that part-invalid cueing may instead lead to an RT that is quite similar in length to a neutral cue condition (Haaland, personal communication, March 2001). This is still taken to reflect intact motor preparation, but where the effect of the valid and the invalid parts of the cue cancel each other out. Again, the use of cueing can be used in experimental conditions to assess motor preparation.

1.3.1 Evidence of intact motor preparation in people with PD

There are a number of studies, including two meta-analyses (Gauntlett-Gilbert & Brown, 1998; J. Wang et al., 1998), which have failed to find evidence of impairment in motor preparation in people with PD (Daum & Quinn, 1991; Scarpa & Castiello, 1994; Stelmach, Worringham, & Strand, 1986; P. Weiss et al., 1996; P. Weiss et al., 1997). Weiss et al. (1997) examined the effect of response complexity on people with PD and healthy age-matched adults. Participants were required to make one of three movement sequences – a single movement, a two-movement sequence, or the same two-movement sequence but with a smaller second target. The results indicate that both groups exhibited a similar lengthening of RTs with increased response complexity.

Bekkering et al. (2001) also assessed motor preparation in people with PD by varying response complexity. Participants tapped out different one- and two-movement sequences to target keys on a screen according to the illumination of light-emitting diodes (LEDs) positioned on the target keys. Response complexity was manipulated by altering sequence length, and, in the case of two movement sequences, the position of the second movement in the sequence. While the first movement was always either to the left or right key

adjacent to the start key, the second movement could be a short movement (in either direction) or a long movement (also in either direction). Longer movements and movements in the opposite direction to the first were taken to increase the complexity of the sequence. The results indicated that as the complexity of the sequence increased, both the healthy adult and the PD group showed similar lengthening of RTs. This again suggests intact preparation in the PD group.

In addition, there is evidence that people with PD do use advanced information for motor preparation (Gauntlett-Gilbert & Brown, 1998; Jordan, Sagar, & Cooper, 1992; Pollux & Robertson, 2001; Praamstra, Meyer, Cools, Horstink, & Stegeman, 1996; Stelmach et al., 1986; Stern et al., 2005; J. Wang et al., 1998; Willingham et al., 1995; Worringham & Stelmach, 1990). The more information provided about the movement in advance (such as which arm to use, the direction, and the distance of the movement), the shorter RTs for both people with PD and healthy adults, reflecting the benefit of advanced information in the selection and initiation of discrete movements (Stelmach et al., 1986). People with PD have also been found to show the expected RT benefits under simple RT cued tasks, where the cue always provides accurate information about the upcoming movement (Gueye et al., 1998; Jahanshahi et al., 1992a; Worringham & Stelmach, 1990).

Finally, in choice RT cue tasks where the cued information could be valid, invalid, or neutral, people with PD and healthy adults show similar effects of cueing. RT benefits with valid cueing (Hocherman et al., 2004; Hsieh, Lee, & Tai, 1995; Jahanshahi et al., 1992a; A. M. Johnson et al., 2003; Jordan et al., 1992; Pollux & Robertson, 2001; Stelmach et al., 1986; Willingham et al., 1995), and RT costs with invalid cueing (Hocherman et al., 2004) in both groups suggests intact motor preparation in people with PD. Johnson et al. (2003) had participants move to one of two target keys positioned on either side of a central start key. The presentation of an imperative signal indicated which target to reach towards. On some trials, participants were presented in advance with a visual cue (an arrow) indicating the target key that was required. Johnson et al. found that people with PD reduced their RTs to the same extent as healthy adults when presented with valid cueing. This suggests that they used relevant information in the same way as healthy adults to prepare the movement in advance.

1.3.2 Evidence of impaired motor preparation in people with PD

In contrast to these findings, there are numerous studies that have found differences to healthy age-matched adults. People with PD have been found to show greater difficulty in performing more complex movements than healthy adults, which may reflect a difficulty in preparing these movements (Agostino, Berardelli, Formica, Accornero, & Manfredi, 1992; Benecke et al., 1987b; Low et al., 2002; Rand & Stelmach, 1999; Rand et al., 2000; Rand et al., 2002; Roy, Saint-Cyr, Taylor, & Lang, 1993; Serrien et al., 2000; Stelmach et al., 1989; P. H. Weiss et al., 1999). People with PD have shown greater slowing than healthy adults when executing two movements simultaneously with the same arm (an elbow flexion and an isometric squeeze between thumb and finger) rather than either movement separately. This was interpreted as a difficulty in integrating different motor programs together (Benecke et al., 1986, 1987a) (see also Scarpa & Castiello, 1994). Greater variability in motor execution and decreased accuracy have also been found in people with PD when executing an in-phase bimanual task (two hands moving mirror image to each other at the same time) relative to healthy adults. These participants showed even greater difficulties when required to complete the more complex anti-phase task (two hands moving in unison in the same direction to each other) (Almeida et al., 2003). It was argued that the deterioration in performing bimanual tasks with added response complexity reflected a difficulty in combining different motor programs together (Alberts et al., 1998; Almeida et al., 2003).

In addition, people with PD have also failed to show the expected RT cost as the number of movements increased in sequences comprising different movements (Harrington & Haaland, 1991; Jennings, 1995). This was taken to reflect incomplete preparation in the participants with PD, with the more complex sequences being initiated before preparation was complete (Harrington & Haaland, 1991; Jennings, 1995). In support of this idea, in people with PD increasing response complexity has been found to prolong pause time (time spent between movements of a sequence) and change both the acceleration and deceleration phases of motor execution (Benecke et al., 1987b; Stelmach et al., 1989; P. H. Weiss et al., 1999). This was again interpreted as reflecting partial preparation of the sequence, with additional preparation occurring during the execution of the response (Stelmach et al., 1989; P. H. Weiss et al., 1999).

Consistent with these findings, people with PD have also shown compromised use of cued information. In some experiments, people with PD benefited less than healthy adults when presented with a central valid cue informing them of the target location relative to a neutral cue condition (Bloxham et al., 1984; Gueye et al., 1998). The reduced benefit in RT was taken to reflect a difficulty in the selection or initiation of the movement (Bloxham et al., 1984), or in maintaining a motor program in readiness when the response to be performed is not completely certain (Gueye et al., 1998). This latter interpretation is consistent with suggestions that people with PD may show a difficulty in maintaining their motor preparation over time (Gentilucci & Negrotti, 1999a; Gueye et al., 1998; Negrottti et al., 2005; Sheridan et al., 1987). Relative to healthy adults, people with PD have also shown exaggerated RT costs when presented with invalid information about which of two keys they were to respond towards (Wascher et al., 1997). Such exaggerated costs could reflect a difficulty in changing or modifying a prepared response when it is incorrect.

Finally, in the study done by Jennings (1995), as discussed earlier, participants were required to perform three-movement sequences. It was found that people with PD exhibited benefits with valid cueing and costs with invalid cueing. However, in performing the sequence, the RTs of the PD group were unexpectedly shorter and the execution of the second and third movements was prolonged relative to healthy age-matched adults. It was suggested that the latter movements were being prepared after the initiation of the sequence by the PD group, due to incomplete preparation of the sequence (Jennings, 1995). Moreover, when provided with part-invalid cueing (validly cueing the first movement of the sequence but invalidly cueing the second and third), people with PD showed a much-reduced cost to their RTs than the healthy adult group. Jennings concluded that the PD group may have been able to prepare the first movement in the sequence but may not have been able to prepare the second and third movements, reflecting impairment in the extent of their preparation (Jennings, 1995). These results suggest that people with PD may not prepare an entire sequence before its initiation, forcing them to rely on opportunities throughout the execution of the response to prepare the latter movements (Harrington & Haaland, 1991; Stelmach et al., 1989; P. H. Weiss et al., 1999).

1.3.3 A summary of motor preparation in people with PD

The literature on motor preparation in people with PD remains inconclusive. There are numerous studies, including the two meta-analyses, which fail to find evidence of impairment in motor preparation. However, differences to healthy adults were found in other studies, suggesting that people with PD may have difficulties in motor preparation.

There are a number of areas of motor preparation that are of interest in this thesis. First, whether motor preparation is impaired in people with PD. Second, whether people with PD suffer impaired motor preparation under conditions of reduced visual information. Third, whether people with PD are able to maintain their prepared response over time. As discussed previously, this thesis also investigates what the most plausible account is of how PD affects motor preparation.

1.4 The importance of external information in people with PD

The second area of interest in this thesis is the role of external information in the motor control of people with PD. There is significant evidence which suggests that the motor performance of people with PD is affected by the presence or absence of useful external information (Azulay et al., 1999; Behrman, Teitelbaum, & Cauraugh, 1998; Lewis et al., 2000; Majsak, Kaminski, Gentile, & Flanagan, 1998; McIntosh, Brown, Rice, & Thaut, 1997; Sheppard et al., 1996; Siegert et al., 2002). For example, lines painted on the floor underfoot have been found to improve both gait velocity and stride length in the quality of walking in people with PD (Hanakawa et al., 1999). It was argued that these lines compensated for the under-active SMA by acting as an external trigger for each upcoming step, providing external information to assist in the scaling of the stride length (Hanakawa et al., 1999). In addition, the sound of a metronome significantly improved the performance of people with PD on a sequential aiming movement task after visual information about the sequence had been removed (Georgiou et al., 1993). The sound of the metronome was thought to trigger each upcoming movement, thereby assisting the overall timing of the sequence (Georgiou et al., 1993). Finally, the presentation of visual cues (lines above and below the space for writing) and auditory cues (constant verbal reminders from the

researcher) were found to be effective in maintaining the amplitude of writing in people with PD, relative to an un-cued condition (Oliveira et al., 1997).

As well as the improvements found when useful external information is provided, there are numerous studies which indicate that removing such information increases motor impairment in people with PD (Cooke et al., 1978; Georgiou et al., 1994; Georgiou et al., 1993; Jones et al., 1992; Kritikos et al., 1995). In aimed movement tasks, when visual information about limb position was removed, people with PD produced slower and jerkier movements with less accurate trajectories and more errors than healthy adults (Romero, Van Gemmert, Adler, Bekkering, & Stelmach, 2003). In addition, longer execution and dwell times (time spent on each key between movements) have been found in PD groups when performing key press sequences under reduced external information (Georgiou et al., 1994; Georgiou et al., 1993; Jones et al., 1992; Kritikos et al., 1995). In one study, participants were required to tap out a series of button presses on a response board according to the illumination of light-emitting diodes (LEDs) placed on each button. People with PD showed significantly greater slowing than healthy adults at performing this task when the LEDs were turned off before initiating the first movement relative to when they remained illuminated throughout the execution of the response (Kritikos et al., 1995).

In a similar task, participants were again required to tap out a series of button presses, but this time under three levels of available visual information (Georgiou et al., 1994). In the first condition, the upcoming button's LED was turned off when participants released the previous target (low reduction of visual information). In the second condition, the upcoming button's LED was turned off when participants first made contact with the previous target (moderate reduction of visual information), and in the third condition, the LED was turned off when participants released the button previous to the last (high reduction of visual information). In contrast to the healthy adult group, the PD group was significantly slower in executing the task with the high reduction of visual information (Georgiou et al., 1994).

1.4.1 Understanding the influence of external information on people with PD

The improvements in motor performance with useful external information and the deterioration with its removal suggest that external information is particularly important for people with PD. This can again be understood in the context of the pathology of the disease. As mentioned previously, in motor control there is a distinction between internally controlled and externally controlled movement (Filoteo et al., 1997; Halsband et al., 1994; Oliveira et al., 1997). The basal ganglia and the SMA are thought to play a greater role in internally controlled movements (Cunnington et al., 1996; Cunnington et al., 1999a; Halsband et al., 1994; Hanakawa et al., 1999; Mushiake & Strick, 1995). Underactivation of the motor circuit between the basal ganglia and the SMA in people with PD (Sabatini et al., 2000) is thought to lead to a specific difficulty in the internal control of movement (Cunnington et al., 1996; Georgiou et al., 1994; Oliveira et al., 1997). External information may then be important to people with PD because movements that are guided by external information are controlled to a lesser extent by the faulty basal ganglia, and more by an alternate motor system, the lateral premotor system (Cunnington et al., 1996; Halsband et al., 1994; Hanakawa et al., 1999; Mushiake et al., 1991). There are two accounts of the role of external information in people with PD.

First, it has been argued that people with PD rely on external information as a compensatory strategy. Oliveira et al. (1997) suggested that people with PD can compensate for their underactive SMA and motor circuit by using external information to assist their movement. It may be that external information triggers upcoming elements of a movement by acting as a substitute for the basal ganglia that would normally be responsible for this internal triggering mechanism (Cunnington et al., 1996; Georgiou et al., 1994; Georgiou et al., 1993; Kritikos et al., 1995; McIntosh et al., 1997). A related idea is that the presence of external cues may facilitate the strategy used by people with PD to control their movement, by drawing attention to the requirements of the movement to be performed (Cunnington et al., 1999a; Jahanshahi & Frith, 1998; Oliveira et al., 1997). It is also possible that external information reduces the cognitive demands of the task by drawing attention to the requirements of the movement to be performed (Cunnington et al., 1999a; Jahanshahi & Frith, 1998; Oliveira et al., 1997). It is thought that by focusing attention in this way, there is less reliance on the motor circuit of the basal ganglia, which is linked

more strongly to automatic internal control mechanisms (Cunnington et al., 1999a; Morris, Iansek, Matyas, & Summers, 1996; Oliveira et al., 1997). On these accounts then, people with PD rely on external information as a compensatory strategy.

Second, it has recently been proposed that PD leads to abnormal processing of visual information in the motor cortex, where early visuomotor information more readily evokes movement-related activity in people with PD (Praamstra & Plat, 2001). It has been found that people with PD have shown greater RT slowing due to visual distractors around a target, suggesting that they are more influenced by irrelevant visual information than healthy adults (Praamstra et al., 1999; Praamstra et al., 1998). The measurement of lateralised readiness potentials (LRPs) also indicates that people with PD show a larger and earlier response to these visual distractors than healthy adults (Praamstra et al., 1999; Praamstra et al., 1998). It has been suggested that the LRP reflects the starting point of motor preparation (Van der Lubbe, Los, Jaskowski, & Verleger, 2004). Thus, the RT slowing coupled with the LRP results could be argued to reflect an abnormal influence of visual information on the motor cortex of people with PD (Praamstra et al., 1999; Praamstra & Plat, 2001; Praamstra et al., 1998). On this account then, external information evokes a stronger obligatory response in people with PD than in healthy adults (Praamstra & Plat, 2001).

Further, it is thought that the motor cortex is a crucial processing site for visuospatial information relevant to a motor task. As the SMA is believed to shape activity in the motor cortex by increasing and decreasing select cortical activity (Mandir & Vaughan, 2000), impaired basal ganglia output may lead to a disruption in this selective processing of such task-relevant information within the motor cortex (Praamstra & Plat, 2001). Through transcranial magnetic stimulation, inhibitory circuits within the motor cortex have been found to be reduced in people with PD, especially evident following a delay in the administration of anti-Parkinsonian medication (Ridding, Inzelberg, & Rothwell, 1995). This disruption to the inhibitory circuits is thought to make the motor cortex more susceptible to sensory input, leading to early visual information evoking a stronger response or influencing response-related neurons in the motor cortex of people with PD (Praamstra & Plat, 2001; Praamstra et al., 1998). Again then, external information may be important because it evokes a stronger obligatory response in people with PD.

1.4.2 A summary of the importance of external information in people with PD

External information has been found to be more important in the motor control of people with PD than in healthy adults. There are two accounts of this. First, people with PD may use external information strategically to compensate for difficulty in the internal control of movement. On this account, external information would be important because it would allow people with PD to partially by-pass their faulty basal ganglia (that has a greater involvement in internally self-controlled movement). Instead, they would rely more on alternate motor systems, where external information drives the movement. Second, people with PD may be less able to prevent early visual information from evoking movement-related activity in their motor cortex (Praamstra & Plat, 2001). If this were the case, external information would be important because it would exert a stronger obligatory response in people with PD. The second aim of this investigation is to clarify the importance of external information in the motor control of people with PD, by discussing which of these explanations is more plausible.

1.5 An overview of the thesis

The first aim of this investigation is to further our understanding of motor preparation in people with PD. The second aim is then to further understand the role of external information in terms of its effect on motor preparation and execution in people with PD. These two main aims were addressed across three experiments.

Experiments 1 and 2 assessed motor preparation in people with PD using both of the techniques outlined above – manipulating response complexity and cueing response-related information. This is an extension to the current literature as it combines these two different methods together in the one task. Participants were required to perform two-movement sequences on a response board. The effect of response complexity was examined by comparing the performance of uni-directional sequences (in which both movements are in the same direction) to bi-directional sequences (in which a change of direction is required for the second movement). By comparing motor initiation and execution times in people

with PD and healthy age-matched adults, inferences can be made regarding the preparation undertaken in both groups. If both groups require a similar amount of additional time to prepare the more complex bi-directional sequence before its initiation, this would suggest that preparation is intact in people with PD. On the other hand, there are two patterns that would suggest impaired motor preparation. First, disproportionate lengthening of RT in the PD group with added response complexity would suggest a greater difficulty in preparing the more complex sequences. Second, an absence of RT lengthening but prolonged motor execution relative to healthy age-matched adults would reflect incomplete preparation in the PD group, with additional preparation of the more complex bi-directional sequence occurring during its execution.

The effect of cueing response-related information was examined by providing valid, part-invalid, and full-invalid information. The cue sequence was presented initially, followed by a sequence in the imperative signal. In the valid cue condition, the sequence indicated by the cue was the same as that indicated by the imperative signal. In the full-invalid cue condition, the sequence indicated by the cue was entirely different to that indicated by the imperative signal. Finally, in the part-invalid cue condition the sequence indicated by the cue presented a sequence with the same first movement but a different second movement to that indicated by the imperative signal. These three cue conditions were compared to a neutral cue condition, in which no response-related information was presented in the cue.

If preparation is intact in people with PD, it was expected that they would show similar effects of cueing to healthy age-matched adults. There are several patterns that are generally expected in healthy adults. Valid cueing would generally result in an RT benefit, reflecting the advance preparation of the response according to the information in the valid cue. Full-invalid cueing would generally lead to an RT cost. This is also taken to reflect advanced preparation. The lengthening in RT here reflects the additional time needed to suppress the response that was prepared according to the cue and re-prepare the response according to the imperative signal (indicating a different sequence). Finally, part-invalid would lead either to an RT cost (similar to the effect of full-invalid cueing), or an RT similar in length to the neutral cue condition. Both would reflect advanced preparation. The RT cost would reflect the modification or re-preparation of the sequence with the presentation of the imperative signal (Jennings, 1995). Alternatively, an RT similar to the

neutral cue condition could also reflect advance preparation, but where the benefit of the valid part of the cue cancelled out the cost of the invalid part of the cue.

Possible difficulties in motor preparation would then be evident in a number of patterns in response to cueing. First, a reduction in the RT benefit with valid cueing, and a reduction in the RT cost of full-invalid cueing in the PD group, relative to healthy adults, would reflect a difficulty in using the information in the cue to prepare the sequence in advance. Second, exaggerated costs of part-invalid and full-invalid cueing, relative to healthy adults, could be taken to reflect a difficulty in changing or modifying the response with the presentation of the imperative signal. Finally, difficulties in motor preparation could also be inferred through an RT benefit with part-invalid cueing. This would reflect incomplete preparation of the sequence, where only the valid part of the cue (referring to the first movement in the sequence) was used to prepare the sequence in advance.

While both Experiments 1 and 2 investigated motor preparation in people with PD, they differed in the amount of visual information provided about the sequence. Experiment 1 provided ongoing visual information about the sequence during its initiation and execution. In contrast, in Experiment 2 the visual information about the sequence was turned off before they initiated the sequence. So in Experiment 2, participants performed the required sequence under reduced visual information. The effect of external information was studied by comparing the results of the two experiments.

Experiment 3 extended the investigation into both motor preparation and the effect of external information in people with PD. Participants were again required to perform two-movement sequences on the response board, with the presentation of a sequence in the cue and in the imperative signal. In Experiments 1 and 2, the sequence to be performed was determined by the imperative signal. However in Experiment 3, the sequence to be performed was determined by the cue, the first sequence shown, regardless of the sequence subsequently presented in the imperative signal. In Experiment 3, only valid and full-invalid cue conditions were used. Thus, the sequence indicated by the imperative signal provided either valid or full-invalid visual information relative to the previously presented cue, and remained visible while participants initiated and executed the sequence.

If people with PD use visual information strategically to compensate for their motor difficulties, it was expected that they would be able to ignore the information in the imperative signal when it was invalid. On the other hand, if visual information evokes a stronger obligatory response in people with PD, it was expected that the presence of invalid visual information in the imperative signal during the initiation and execution of the response would lead to more errors and slowing in the performance of the sequence.

In addition, having participants in Experiment 3 perform the sequence according to the previously presented cue implied that they were able to: (a) prepare the sequence according to the cue; and (b) maintain their prepared response until they were required to initiate it by the presentation of the imperative signal. There are suggestions that even if people with PD do show adequate advance preparation, they suffer a difficulty in maintaining their motor preparation over time due to an underactivation of relevant cortical regions (Gentilucci & Negrotti, 1999a; Negrottti et al., 2005; Sheridan et al., 1987). Attentional difficulties have been suggested to interfere with the preparation of movement in people with PD over longer foreperiods (Pollux & Robertson, 2001). Experiment 3 assessed this by using three different foreperiods between the cue and the imperative signal. If people with PD suffer difficulties in maintaining a prepared response (possibly due to attentional difficulties), it was expected that with a lengthening of foreperiod they would be more affected than healthy adults.

In conclusion, three experiments were conducted as part of this investigation. All three aimed to further our understanding of motor preparation and the importance of external information in people with PD. Chapter Two describes the general methodology. The method and results of the three experiments will be detailed separately in Chapters Three to Five. Because all three experiments address related aspects of these two areas of motor control in people with PD, the detailed implications of each of the experiments will be discussed together in Chapter Six.

Chapter Two – General Methodology

2.1 Overview

This thesis aims to further our understanding of motor preparation and the importance of visual information in people with PD. The three experiments comprising the investigation were preceded by a pilot study aimed to establish methodology (Thomson, Hammond, & Anderson, 2005), which is presented in Appendix A. The participants in the three experiments included a group of people with PD, a group of healthy age-matched adults, and a group of healthy young adults. The two older groups participated in all three experiments, while the healthy young adult group only participated in Experiments 2 and 3. In Experiment 1, the participants with PD were separated into two groups – one group completed the testing session on their normal anti-Parkinsonian medication, and the other completed the testing session following a mean delay of 11 hours in the administration of their normal anti-Parkinsonian medication. For both Experiments 2 and 3, all of the participants with PD performed the testing session on their normal medication.

All participants in the PD and healthy age-matched adult groups were administered the Cambridge Cognitive Examination (CAMCOG-R) (Roth, Huppert, Mountjoy, & Tym, 1999; Roth et al., 1986) in Experiment 1 to screen for dementia. All participants in the PD group were also administered the Unified Parkinson's Disease Rating Scale (UPDRS) (Fahn, Elton, & Committee, 1987) in Experiments 2 and 3 to assess the severity and progression of their PD symptoms over the duration of the investigation.

Testing for each of the experiments was carried out at a venue most convenient to the participant, often at their own home. Each of the three experiments took approximately one and half hours to complete (comprising the motor task in each experiment and the additional tests mentioned above). All participants gave informed consent to the investigation, which was approved by the Human Research Ethics Committee of Sir Charles Gairdner Hospital (Perth, Western Australia). Appendix B presents the Information and Consent form for Experiment 1 (those used in Experiments 2 and 3 were very similar and will not be presented). One participant in the PD group failed to complete the first experiment due to the severity of his symptoms, and chose to withdraw from the remainder

of the investigation. An additional participant in the PD group was excluded from the analysis in the third experiment because he did not grasp the requirements of the task, making in excess of 30% errors. Four other participants from the PD group, five from the healthy old adult group, and three from the healthy young adult group withdrew participation over the investigation, mostly citing time and family pressures. There were no adverse events during this investigation.

2.2 Participants

The PD group comprised 24 individuals with idiopathic PD. They were recruited through Sir Charles Gairdner Hospital (Perth, Western Australia) and a local PD support network. The group ranged in age between 53 and 83 years (with a mean age of 67 years), and comprised 16 men and eight women. Disease duration ranged between one and 17 years (with a mean duration of six years), and all but one was taking anti-Parkinsonian medication for their symptoms (see Appendix C for details).

Twenty-three healthy age-matched individuals were recruited for the Old Adult group. This group comprised 10 men and 13 women, and ranged in age between 45 and 86 years (with a mean age of 67 years). Finally, the Young Adult group comprised 20 healthy young adults, including 10 men and 10 women, and aged between 22 and 28 years (with a mean age of 26 years).

2.3 The Motor Tasks

2.3.1 Apparatus for the motor tasks

In all three experiments, participants were required to perform different two-movement sequences with their index finger on a response board, which was adapted from a study by Bekkering et al. (2001). The response board was 330 mm long and 100 mm wide, with a rise of 60 mm at the back, and 30 mm at the front, from table surface. The five target keys (20 mm long x 15 mm wide) were arranged horizontally, and equally spaced 60 mm apart

(from centre to centre) on the response board. Two LEDs (one green and one red) were positioned vertically above each key (see Figure 2.1). The participants' wrists were supported between trials by a soft rectangular cushion positioned in front of the response board.

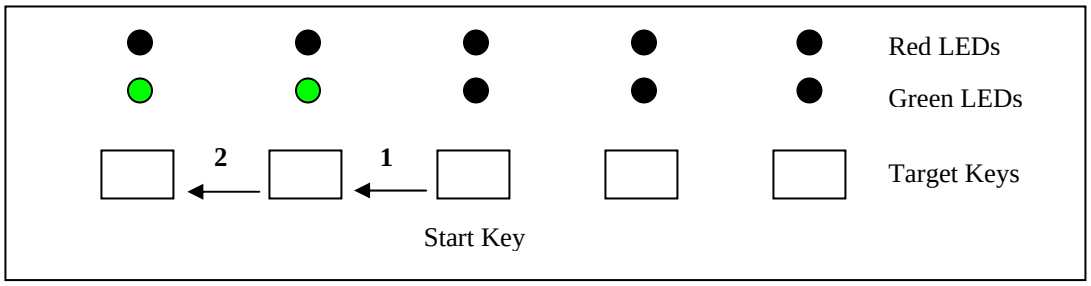

Figure 2.1 A schematic representation of the response board showing the upper two rows of light-emitting diodes (LEDs) and the lower row of target keys. The two illuminated green LEDs indicate the sequence to be performed

Note. The LEDs shown depict a uni-directional sequence. A bi-directional sequence would have been depicted with the second green LED positioned above the start key.

On each trial, participants were required to make two movements, determined by the illumination of two of five light-emitting diodes (LEDs). The first movement was always to one of the two target keys immediately adjacent to the central start key. The second movement was either to the outermost target key on that side of the response board for a uni-directional sequence, or was a return movement back to the start key for a bi-directional sequence (see Figure 2.1 for an example of the former). Both movements were always the same distance.

Trials in all three experiments began with the red and green LEDs above the central start key flashing on and off until the start key was depressed with the participant's index finger for 2000 ms. A sequence was then cued through the illumination of red LEDs for 750 ms. Following a foreperiod during which time all LEDs were turned off, a sequence was indicated by the illumination of two green LEDs, being the imperative signal. In all three

experiments, there was an inter-trial interval in which all LEDs were turned off before the commencement of the next trial.

The three experiments varied slightly across this general design. There were differences in: (a) the duration of the foreperiod; (b) the duration of the imperative signal; (c) the exact point in time when participants were instructed to initiate their response; (d) whether the participant was required to replicate the sequence in the cue or the sequence in the imperative signal; and (e) the number of cue conditions presented. The specific design of each experiment is outlined in detail in Chapters Three to Five.

2.3.2 Dependent measures

For each experiment, four dependent measures were taken on each trial. Reaction time (RT) was measured as the time (in ms) taken to lift the finger from the start key. The way RT was measured in each experiment varied slightly, and is described further in the relevant chapters. The other three dependent measures were recorded in the same way in each experiment. The first movement time (MT1) was the time (in ms) taken to reach the first target key after the participant had lifted their finger from the start key. Dwell time (DT) was the time (in ms) spent on the first target key. The second movement time (MT2) was the time (in ms) taken to move from the first to the second target key. Median times (in ms) of the four dependent measures were taken for each participant on each experimental condition. The mean of these median times was calculated for each group. The experimental conditions of each of the experiments, as well as an overview of the analyses undertaken are discussed in detail in the three experimental chapters to follow.

2.4 The Cambridge Cognitive Examination-R (CAMCOG-R)

All participants in the PD and Old Adult groups were screened for dementia. This was particularly important as the prevalence of dementia is found to be significantly higher (approximately 40% higher) in people with PD than in the general population (Hobson & Meara, 1999; Marsden, 1986). The CAMCOG-R (from the Cambridge Examination for

Mental Disorders of the Elderly (CAMDEX-R) is a brief neuropsychological measure designed to assess cognitive impairment in elderly people (Hobson & Meara, 1999; Huppert, Brayne, Gill, Paykel, & Beardsall, 1995; Lindeboom, Ter Horst, Hooyer, Dinkgreve, & Jonker, 1993; Roth et al., 1999; Roth et al., 1986). It is widely used as a screener for dementia in both clinical and epidemiological studies, including in groups of people with PD (Hobson & Meara, 1999; Williams, Huppert, Matthews, Nickson, & CFAS, 2003).

The CAMCOG-R measures a broad range of cognitive domains including: memory; language; attention and concentration; praxis; orientation; abstract thinking; perception; and executive functions. Both the global score and each of the subscale scores (the memory, attention, and executive functions subscales, in particular) have been found to be significantly different between groups of mildly demented and groups of non-demented elderly adults (Fountoulakis, Tsolaki, & Kazis, 2001; Hobson & Meara, 1999; Huppert et al., 1996; Williams et al., 2003).

Unlike other brief cognitive assessment tools, the CAMCOG-R was designed with a wide range of item difficulty, to minimise floor and ceiling effects (Huppert et al., 1995; Williams et al., 2003). It is therefore able to differentiate scores even at higher levels of cognitive functioning, and so is generally regarded to be a sensitive and specific measure of cognitive impairment (Hobson & Meara, 1999; Huppert et al., 1995; Huppert et al., 1996; Williams et al., 2003). The combined brevity and breadth of detail made the CAMCOG-R an ideal choice as a screener for dementia in the current investigation.

Each participant was assessed individually on the CAMCOG-R, which included both paper and pencil and verbal response tasks. Administration took approximately 30 minutes, and produced summary scores of each of the main cognitive domains as well as a global score of cognitive functioning.

2.5 The Unified Parkinson's Disease Rating Scale

The Unified Parkinson's Disease Rating Scale (UPDRS) is probably the most widely used clinical scale for PD (Clarke & Moore, 2004; Goetz et al., 2003; Langston et al., 1992;

Martignoni, Franchignoni, Pasetti, Ferriero, & Picco, 2003). The scale covers the core disabilities and impairments of the disease within four sections: Part I – Mentation, Behavior and Mood; Part II – Activities of Daily Living; Part III – Motor; and Part IV – Complications (Goetz et al., 2003; Samuel, 2005).

Part I Mentation, Behavior and Mood assesses changes in the individual's thinking and mood as a result of the disease, including intellectual impairment, thought disorder, motivation and initiative, and depression (Samuel, 2005).

Part II Activities of Daily Living examines the impact of the disease on the individual's life. This section covers all major areas of activities of daily living including speech, salivation, swallowing, handwriting, the ability to use utensils and cut up food, self-hygiene, ambulation, dressing, the ability to turn in bed and adjust bed clothes, falling (unrelated to freezing), freezing while walking, tremor, and any sensory complaints due to PD (Samuel, 2005).

Part III Motor comprises the formal motor examination. This includes an assessment of the quality of speech, facial expression, presence of resting tremor, presence of action or postural tremor, rigidity of muscles, quality of repetitive finger tapping, quality of hand movements, rapid alternating movements, leg agility, ability to rise from a chair unaided, general posture, quality of gait, postural stability, body bradykinesia, and hypokinesia. On the relevant items, an assessment is made for each limb separately (Samuel, 2005).

Part IV Complications[1] examines the presence of complications as a result of treatment. This includes the presence of dyskinesia and fluctuations in symptom severity with the effectiveness of medication (Samuel, 2005).

All four sections have shown good reliability and validity (Goetz et al., 2003; Samuel, 2005). To date, the UPDRS remains the gold standard of assessment tools for the clinical symptoms and impairments of PD (Goetz et al., 2003). It is thus the most appropriate measure for the current investigation.

[1] This section was not used in the current investigation, resulting in a modified total UPDRS score for participants that comprised Parts I, II, and III.

2.6 The Hoehn and Yahr Scale

In addition to scores on the individual sections and the total UPDRS score, a modified Hoehn and Yahr staging scale can be derived following the administration of the UPDRS.

Hoehn and Yahr Staging of Parkinson's Disease comprises:

Stage One: a) Signs and symptoms on one side of the body only; b) Symptoms mild; c) Symptoms inconvenient but not disabling; d) Usually presents with tremor of one limb; e) Friends have noticed changes in posture, locomotion and facial expression.

Stage Two: a) Symptoms are bilateral; b) Minimal disability; c) Posture and gait affected.

Stage Three: a) Significant slowing of body movements; b) Early impairment of equilibrium on walking or standing; c) Generalised dysfunction that is moderately severe

Stage Four: a) Severe symptoms; b) Can still walk to a limited extent; c) Rigidity and bradykinesia; d) No longer able to live alone; e) Tremor may be less than earlier stages

Stage Five: a) Cachectic stage; b) Invalidism complete; c) Cannot stand or walk; d) Requires constant nursing care

2.7 Summary

All three experiments in this investigation aimed to assess motor preparation and the importance of external information in the motor control of people with PD. In each experiment, participants performed a motor task comprising two-movement sequences on a response board, and the additional tests described above. However, there were important differences in the motor task in each experiment. The design of each motor task is described in more detail in the following three chapters.

Chapter Three: Examining motor preparation in people with PD

3.1 Introduction: An overview of Experiment 1

The aim of Experiment 1 was to assess motor preparation in people with PD. As previously discussed, some authors have found no evidence of compromised motor preparation relative to healthy age-matched adults (Bekkering et al., 2001; Gauntlett-Gilbert & Brown, 1998; A. M. Johnson et al., 2003; Stelmach et al., 1986; J. Wang et al., 1998). On the other hand, others have found differences to healthy adults that may reflect impaired motor preparation (Alberts et al., 1998; Almeida et al., 2003; Gueye et al., 1998; Harrington & Haaland, 1991; Jennings, 1995; Wascher et al., 1997; P. H. Weiss et al., 1999).

There are two methods that are commonly used to assess motor preparation. First, motor preparation can be measured by manipulating the complexity of a response. Any lengthening of RT with increased response complexity is taken to reflect the greater time needed to prepare the more complex response before its initiation (Harrington et al., 2000; Klapp, Wyatt, & Lingo, 1974; Smiley-Oyen & Worringham, 2001).

Second, motor preparation can be measured by cueing information about the response to be made before it is performed (Rosenbaum, 1980). Cued information can be valid, full-invalid, part-invalid, or neutral. The RT benefit found with valid cueing relative to a neutral cue condition is taken to reflect the advance preparation of the response according to the information in the valid cue (Goggin & Stelmach, 1990; Gueye et al., 1998; Jennings, 1995; Larish & Frekany, 1985; Larish & Stelmach, 1982; Müller-Gethmann et al., 2000; Rosenbaum, 1980; P. H. Weiss et al., 1999; Zelaznik & Hahn, 1985). Conversely, the RT cost associated with a full-invalid cue relative to a neutral cue condition is taken to reflect the additional time needed to suppress the response that was prepared according to the cue and re-prepare according to the imperative signal indicating a different response (Goggin et al., 1989; Larish & Stelmach, 1982; Leuthold & Jentzsch, 2002b; Stelmach et al., 1988).

The final type of cue that can be used to assess motor preparation is part-invalid cueing; where part-valid and part-invalid information is provided about the movement. In a multi-movement sequence this may validly cue the position of the first movement, but invalidly cue the position of the remaining movements in the sequence (Jennings, 1995). This type of

cue can be used to examine the preparation of each movement separately, revealing the extent of preparation undertaken. Part-invalid cueing has previously been found to result in an RT cost relative to a neutral cue condition. This is taken to demonstrate that participants had treated the movements in the sequence collectively, and prepared them together according to the cue (Jennings, 1995). It is also possible that a part-invalid cue could lead to an RT that is quite similar to a neutral cue condition. This initially seems counter-intuitive, as similar RTs to a neutral cue condition are generally taken to reflect difficulties in preparing the response according to the cue. However, in the case where the cue contains both valid and invalid response-related information, the effect of one may cancel out the effect of the other (Haaland, personal communication, March 2001).

The current experiment utilised both of these methods. Participants were required to perform two-movement sequences on a response board in which both the complexity of the sequence was manipulated, and in which valid, part-invalid, and full-invalid information was cued to participants.

There were three groups in this experiment. The first comprised people with PD who were on their normal anti-Parkinsonian medication (termed the PD ON group). The second group comprised people with PD who performed the experiment following a delay in taking their anti-Parkinsonian medication (termed the PD OFF group). These two groups were compared to a group of healthy age-matched adults to determine if PD affected motor preparation, and what effect, if any, that anti-Parkinsonian medication had on this.

It was expected that the PD groups would perform the task more slowly. In addition, if the PD groups suffered a difficulty in motor preparation, they would be differentially affected by the manipulation of response complexity and in their use of cued information. Significantly greater slowing of RT in the PD groups, relative to age-matched adults, following an increase in response complexity would reflect a difficulty in preparing the more complex sequences. Significantly greater slowing on measures of execution (without necessarily any slowing of RT) with added response complexity would also reflect difficulties in the motor preparation of people with PD. Here though, lengthening in motor execution would suggest that the preparation of the more complex sequences was incomplete and continued after the initiation of the response.

Different effects of cueing in the PD groups relative to the healthy adult group could also be taken to reflect difficulties in motor preparation. An overall reduction in the benefits and costs of valid, part-invalid and full-invalid cueing relative to the neutral cue condition would reflect a difficulty in fully using the information in the cue to prepare the response in advance. Exaggerated costs of part-invalid and full-invalid cueing would suggest that the cue was used in the advance preparation of the response, but that participants experienced difficulties in changing or modifying their response when finding out that the cue was invalid. Both of these patterns have previously been taken as evidence for difficulties in motor preparation (Bloxham et al., 1984; Gueye et al., 1998; Wascher et al., 1997). Finally, a significant benefit of part-invalid cueing would show that preparation was incomplete, with the valid part of the cue having a stronger influence on motor preparation than the latter invalid part of the cue.

Exploratory correlation analyses were used to identify the factors that influenced task performance in the three experimental groups. It was expected that disease duration (years since diagnosis) in the two PD groups would positively correlate with overall time taken on the four dependent measures, indicating that the progression of the disease led to greater motor slowing. In addition, if the PD group did show difficulties in motor preparation, it was expected that this would be reflected in correlations between disease duration and their response to manipulations of response complexity and cueing advance information.

3.2 Method

3.2.1 Participants

Three of the twenty-four participants with idiopathic PD recruited for the current investigation were excluded from Experiment 1. Two were *de novo* (not yet taking anti-Parkinsonian medication) and one failed to complete the task due to the severity of his symptoms. The remaining 21 participants were randomly allocated to one of two groups distinguished by medication status. The PD ON group consisted of eleven participants (8:3 M:F, aged between 60 and 83 years, with a mean age of 72 years) who completed the testing session while on their normal anti-Parkinsonian medication. The PD OFF group

consisted of ten participants (6:4 M:F, aged between 53 and 77 years, with a mean age of 65 years) who delayed taking their anti-Parkinsonian medication leading up to and including the testing session. The delay ranged from five to 17 hours, with a mean delay of 11 hours. The mean disease duration of the two groups was not significantly different (F (1, 20) = .13, p = .72). Disease duration in the PD ON group ranged between one and 17 years (with a mean duration of six years), and in the PD OFF group ranged between one and 12 years (with a mean duration of seven years). Twenty-three healthy age-matched adults (10:13 M:F, aged between 45 and 86 years, with a mean age of 67 years) were recruited for the Old Adult group. Age was not significantly different between the groups (F (2, 43) = 1.66, p = .20). All participants gave informed consent to the experiment, which was approved by the Human Research Ethics Committee of Sir Charles Gairdner Hospital.

3.2.2 Tests Administered

In addition to the motor task, participants were administered the Cambridge Cognitive Examination (CAMCOG-R), which is part of the Cambridge Examination for Mental Disorders of the Elderly (CAMDEX-R) (Roth et al., 1999; Roth et al., 1986), to screen for the presence of dementia.

3.2.2.1 The Motor Task: Design and Procedure

Participants were required to perform two-movement sequences on a response board according to the illumination of two of five light-emitting diodes (LEDs). The LEDs were positioned above corresponding target keys (see Figure 2.1 in Chapter Two). The first movement was always to one of the two target keys immediately adjacent to the central start key, and the second movement was either to the outermost target key on that side of the response board for a uni-directional sequence, or was a return movement back to the start key for a bi-directional sequence. Both movements were always the same distance.

Each trial began with the red and green LEDs above the central start key flashing on and off until that key was depressed with the participant's index finger for 2000 ms (termed the

trial warning). A sequence was then presented through the illumination of red LEDs for 750 ms (the cue). Following a 450-ms foreperiod, during which time all LEDs were turned off, two green LEDs were illuminated as the imperative signal, indicating the sequence to be performed. Participants were instructed to make the movements indicated by the imperative signal as quickly and accurately as possible after its onset. The two green LEDs of the imperative signal remained illuminated for the duration of the initiation and execution of the sequence. After both movements had been made, the green LEDs were then turned off for a 2000–ms inter-trial interval. Figure 3.1 depicts the time frame of a trial.

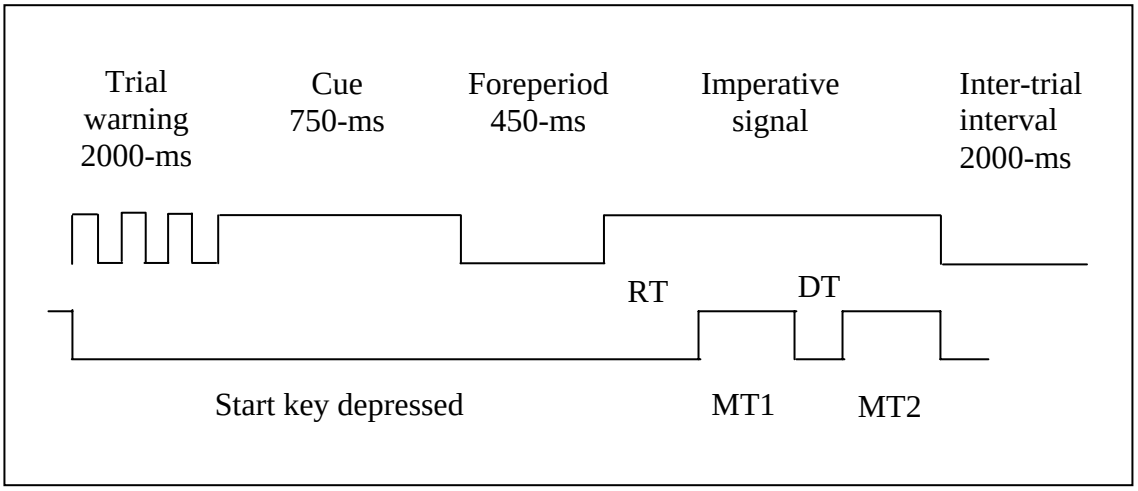

Figure 3.1 A diagrammatical representation of a typical trial in Experiment 1.
Note. This figure indicates the phases in which the LEDs were illuminated and turned off, and when participants were instructed to depress the start key and perform the sequence.

There were five cue conditions: (a) valid; (b) part-invalid; (c) full-invalid; (d) neutral; and (e) catch trials. On valid cue trials, the illuminated red LEDs of the cue matched the green LEDs of the imperative signal. In this case, the sequence of the cue fully reflected the required sequence, as determined by the imperative signal. On part-invalid cue trials, the sequence indicated by the cue differed from the imperative signal only in the position of the second green LED (at either of the outermost keys or the central key). On these part-invalid trials, the illuminated LEDs in the cue and the imperative signal indicated the same target key for the first movement, but indicated a different target key for the second movement.

On full-invalid cue trials, the sequence indicated by the cue differed from the imperative signal in the position of both LEDs. On these trials, the illuminated red LEDs in the cue indicated two different target keys to that in the imperative signal. On neutral trials, the cue consisted of the illumination of all five red LEDs, giving no information about the response to be made on that trial. Finally, on catch trials, while the cue was presented in the same way as in the other conditions, it was not followed by an imperative signal. On these trials, participants were required to continue depressing the start key until the beginning of the next trial. Catch trials were included to discourage participants anticipating the onset of the imperative signal.

These experimental trials consisted of six blocks of 44 trials. There were 24 (55%) valid trials, eight (18%) neutral trials, and four (9%) trials in each of the part-invalid, full-invalid, and catch cue conditions. The order in which the five cue conditions were presented was randomised. The six blocks followed a practice session of 14 trials, in which each cue condition was presented at least once. Participants performed three blocks with their dominant hand and three with their non-dominant hand, alternating over the six blocks (the order was counter-balanced across participants).

3.2.2.2 The Cambridge Cognitive Examination (CAMCOG-R)

The CAMCOG-R was administered individually to each participant, taking approximately half an hour to complete. The CAMCOG-R assesses a range of cognitive functions, such as orientation to time and place, language abilities, memory, attention and concentration, praxis, abstract thinking, perception, and executive functions. For each participant, a score for each section as well as a global CAMCOG-R score were calculated.

3.3 Data Analysis

Median times (in ms) were taken for each participant on the four dependent measures across the conditions. Reaction time (RT) was measured as the time from the onset of the imperative signal to when participants lifted their finger from the start key. Movement time

one (MT1) was the time that participants took to reach the first target key after lifting their finger from the start key. Dwell time (DT) was taken as the time spent on the first target key. Movement time two (MT2) was the time taken to move from the first to the second target key. Mean median times were calculated for each group.

To establish if the two PD groups (on and off their anti-Parkinsonian medication) were slower than the Old Adult group, the mean median times of the three experimental groups were compared on the four dependent measures. This was done using the neutral cue condition only (with the uni-directional and bi-directional sequences averaged together). This cue condition was taken as the baseline condition of the experiment to identify any differences between the three groups on the dependent measures without the influence of cueing.

To establish if people with PD suffered any difficulties in their motor preparation, the effect on each group of manipulating response complexity and varying the cue condition was compared. The effects of response complexity and of cueing response-related information will be outlined separately[2]. To examine the effect of response complexity on the three groups, the neutral cue condition was again used in isolation. Mean median times for uni-directional and bi-directional sequences were compared through a repeated measures analysis of variance for the four dependent measures.

To examine the effect of cueing, the mean median times of the four dependent measures under the main cue conditions (valid, neutral, part-invalid, and full-invalid) were entered into repeated measures analysis of variances. The mean median times for the valid, neutral, and part-invalid cue conditions were averaged across the uni-directional and bi-directional sequences. The mean median times for the full-invalid cue condition comprised only uni-directional sequences, as bi-directional sequences were not included in this cue condition[3]. To accurately establish the effect of full-invalid cueing relative to the neutral cue condition through post hoc analyses, the mean median time for the neutral cue condition using only uni-directional sequences was also calculated.

[2] Because the full-invalid cue condition comprised only uni-directional sequences, a complete assessment of any interaction between response complexity and cueing was not possible. Full-invalid bi-directional sequences were introduced in Experiment 2 to allow this comparison.

[3] While this produced a potential confound, the difference between conditions only underestimated any cost that may be present in full-invalid cueing. This is because the more complex (and presumably slower) bi-directional sequences did not contribute to the mean median time for full-invalid cueing.

To further explore the effect of cueing on the three experimental groups, benefits and costs of cueing (valid, part-invalid, and full-invalid) relative to the neutral cue condition were calculated for each participant. These calculations were used to: (a) depict the benefits and costs of cueing graphically; and (b) to be used in exploratory correlation analyses. This was done by subtracting the median RT in the neutral cue condition from one of the other conditions (valid, part-invalid, or full-invalid); dividing this number by the median RT in the neutral condition; and multiplying the result by 100. For example: $((RT_{valid} - RT_{neutral})/ RT_{neutral}) \times 100$. Negative values represented RT benefits and positive values represented RT costs relative to the neutral cue condition. To assess the effect of full-invalid cueing, the neutral cue condition in this specific calculation comprised only uni-directional sequences.

To identify the factors that contributed to each of the participant's performance on the motor task, exploratory correlation analyses were undertaken for each group. There were three main relationships that were investigated. First, disease duration was correlated with the four dependent measures in both of the PD. Second, scores on each of the sections, as well as the global score, of the CAMCOG-R were used in correlations with the four dependent measures to assess the influence of cognitive functioning on task performance of the three groups. Finally, the frequency of errors was correlated with the four dependent measures for each of the three groups. These errors comprised incorrect responses (making contact with the wrong target key) and responding before the presentation of the imperative signal. In each of these three relationships, the correlations were initially made separately by cue condition. The correlations were then made separately for each combination of cue condition and response complexity, as well as by the relative effects of cueing. These were used to highlight any specific relationships that may relate to motor preparation in the three groups.

3.4 Results

The results of this experiment will be outlined in five main sections. Section 3.4.1 presents the results from the CAMCOG-R for each of the three groups. Section 3.4.2 outlines the screening of the data, including the frequency of errors made by the three groups, the variability on the four dependent measures, the effect of handedness, and the effect of

practice on the task. Section 3.4.3 outlines the differences between the experimental groups on the baseline neutral cue condition over the four dependent measures. Section 3.4.4 outlines the results relating to motor preparation in the three experimental groups. This section addresses the influence of response complexity and cueing separately. Section 3.4.5 presents the exploratory correlation analyses.

3.4.1 Cognitive screening – CAMCOG-R

There were no participants whose score fell below the cut-off of 80 points on the global CAMCOG-R that would suggest cognitive impairment (Hobson & Meara, 1999). The three groups' global score was not significantly different from each other (F (2, 43) = 3.13, p = .054). The Old Adult group obtained a mean global score of 96.52 out of a possible 105 (SEM = 0.94), the PD ON group obtained a mean global score of 91.73 (SEM = 2.26), and the PD OFF group obtained a mean global score of 95.70 (SEM = 1.26). The only scale in which the three groups' scores were significantly different was on the Attention scale (F (2, 43) = 4.93, $p < .05$). The PD ON group's mean score of 7.36 (SEM = 0.31) out of a possible 9.00, was significantly lower than the PD OFF group (t (19) = 2.67, $p < .05$), whose mean score was 8.00 (SEM = 0.22). This was also significantly lower than the Old Adult group (t (32) = 2.83, $p < .01$), whose mean score was 8.43 (SEM = 0.22). However, again none of the group's scores were low enough to suggest any concern about their cognitive functioning (Hobson & Meara, 1999; Williams et al., 2003).

3.4.2 Motor task: Data screening and preliminary analyses

3.4.2.1 The frequency of errors

Incorrect responses (making contact with the wrong key) and any responses that were made before the imperative signal was presented were coded as errors and removed from analysis[4]. An average of 2% of trials was removed for all participants. The three groups

[4] Due to the way the data was processed, incorrect responses and responding before the imperative signal could not be examined separately.

were not significantly different in the number of errors made, with an average of 2% total errors in the Old Adult group (SEM = 0.2), 3% in the PD ON group (SEM = 0.7), and 3% in the PD OFF group (SEM = 1.2).

3.4.2.2 Variability on the four dependent measures

The variability of each participant was calculated in two ways. The standard deviation for each of the four dependent measures was calculated for each participant. This was to examine overall variability in motor preparation and execution. The coefficient of variation was also calculated for each participant. This involved dividing the standard deviation by the mean on each of the four dependent measures for each participant. This was to assess variability without the influence of differences between the groups in overall mean latencies on the dependent measures. Both the standard deviation and the coefficient of variation were separated into: (a) the neutral cue condition; and (b) all three remaining cueing conditions combined together. The conditions were separated in this way to examine variability both with and without the effects of cueing. Averages for each group were then taken for the four dependent measures.

3.4.2.2.1 Variability using standard deviations

There was a significant difference in the standard deviation of RT between the groups, both on the neutral cue condition (F (2, 43) = 4.17, p < .05) and on the combined cueing conditions (F (2, 43) = 4.79, p < .05). Post hoc analyses revealed that the PD ON group were significantly more variable than the Old Adult group on both (t (32) = 2.29, p < .05 and t (32) = 2.59, p < .05, respectively). There was also a significant difference in the standard deviation of MT1 between the groups on the combined cueing conditions (F (2, 43) = 8.15, p < .01), where both the PD ON (t (32) = 4.19, p < .001) and the PD OFF (t (31) = 2.24, p < .05) groups showed greater variability than the Old Adult group. There was a significant difference in the standard deviation of DT (F (2, 43) = 3.24, p < .05) and of MT2 (F (2, 43) = 8.56, p < .01) between the groups on the combined cueing conditions. Post hoc analyses reveal that the PD ON group was significantly more variable than the Old

Adult group on both DT (t (32) = 2.43, p < .05) and MT2 (t (32) = 3.83, p < .01), and the PD OFF group was significantly more variable than the Old Adult group on MT2 (t (31) = 3.14, p < .01).

3.4.2.2.2 Variability using the coefficient of variation

There was a significant difference in the coefficient of variation of RT between the groups, both on the neutral cue condition (F (2, 43) = 4.48, p < .05) and on the combined cueing conditions (F (2, 43) = 7.86, p < .01). Post hoc analyses revealed that the PD ON group were significantly more variable than the Old Adult group on the neutral cue condition (t (32) = 2.41, p < .05) and the combined cueing conditions (t (32) = 3.13, p < .01), and was also significantly more variable than the PD OFF group on both (t (19) = 2.28, p < .05 and t (19) = 2.64, p < .05, respectively). The PD OFF group was no more variable than the Old Adult group on the neutral cue condition or the remaining combined cueing condition. There were no significant group differences in the coefficient of variation on any of the three measures of execution. Taken together, these results show that while participants in the PD groups were more variable on the four dependent measures than the participants in the Old Adult group (as shown by the standard deviations), most of these differences disappeared when controlling for the mean time taken by the groups on the four dependent measures (through the coefficient of variation).

3.4.2.3 The effect of handedness on the performance of the motor task

While the task was generally performed faster with the participants' dominant hand, there were no significant main effects or interactions relating to hand dominance, and so blocks were collapsed for the overall analysis.

3.4.2.4 The effect of practice on the performance of the motor task

There was a significant main effect of Block on all four dependent measures – RT (F (5, 205) = 39.27, p < .001); MT1 (F (5, 205) = 6.03, p < .001); DT (F (5, 205) = 2.28, p < .05); and MT2 (F (5, 205) = 2.93, p < .05). Participants were faster on all four dependent measures in the later blocks (19% faster on RT, 7% on MT1, 6% faster on DT, and 3% faster on MT2), suggesting a practice effect. There were no significant interactions between Group and Block on any of the four dependent measures, nor was there any interaction between Group, Cue Condition, and Block, indicating that the three groups experienced similar practice effects over the duration of the task.

3.4.3 Group differences on the baseline neutral cue condition

The first aim of this experiment was to determine if the three groups differed in the time taken to perform the task. The neutral cue condition was regarded as the baseline measure in this experiment and was used to assess performance times without the influence of the other cue conditions. It was expected that both PD groups would be significant slower on the three measures of execution than the Old Adult group. Due to the uncertainty in the literature, it was unclear whether they would also be significant slower on RT. Also, it was expected that the delay in the administration of participants' normal anti-Parkinsonian medication in the PD OFF group would mean that that group would be slower than the PD ON group on the four dependent measures.

The mean median times on the four dependent measures on the neutral baseline cue condition for each group are shown in Table 1. There was a significant main effect of Group on both MT1 (F (2, 43) = 10.24, p < .001) and MT2 (F (2, 43) = 11.83, p < .001), but the three groups were not significantly different to each other on RT or DT. Post-hoc analyses suggest that both the PD ON and the PD OFF groups were significantly slower than the Old Adult group on both movement time measures. For MT1, the PD ON group was 99 ms slower than the Old Adult group (t (32) = 4.46, p < .001), and the PD OFF group was 66 ms slower (t (31) = 3.52, p < .005). In contrast, the 33-ms slowing in the PD ON group relative to the PD OFF group on MT1 did not reach significance (t (19) = .90, p =

.38). For MT2, post hoc analyses again suggest that the two PD groups were significantly slower than the Old Adult group. The PD ON group was 89 ms slower than the Old Adult group (t (32) = 4.58, p < .001), and the PD OFF group was 48 ms slower (t (31) = 3.45, p < .005). As was the case for MT1, the 41-ms slowing on MT2 in the PD ON group relative to the PD OFF group was not significant (t (19) = 1.43, p = .17). Thus, both of the two PD groups were significantly slower than the Old Adult group on the movement time measures, but not on RT or DT. In addition, the two PD groups were not significantly different to each other on any of the four dependent measures.

Table 1 Mean median times of the four dependent measures by experimental group using the neutral cue condition only (SEM presented in parentheses).

	Old Adult		PD ON		PD OFF		Row Means	
RT	561	(16)	609	(41)	547	(28)	570	(15)
MT1	227	(8)	326	(28)	293	(23)	266	(11)
DT	135	(8)	172	(13)	147	(14)	147	(6)
MT2	181	(7)	270	(24)	229	(14)	215	(9)
Total	1104	(25)	1377	(85)	1215	(63)		

3.4.4 Motor preparation in people with PD and healthy adults

The second main aim of this experiment was to determine if people with PD (on or off their anti-Parkinsonian medication) showed difficulties in motor preparation relative to the healthy old adult group. It was expected that if people with PD did not have difficulties in motor preparation, very similar patterns to the healthy old adult group would be found following the manipulations of response complexity and the cueing of response-related information. In contrast, it was expected that if people with PD did suffer difficulties in motor preparation under these conditions, then differences with the Old Adult group would be found.

The effect of response complexity was investigated across the four dependent measures using only the neutral cue condition. The effect of cueing response-related information to

participants was then investigated, separated into reaction time (RT) and measures of execution (MT1, DT, and MT2). The effect of cueing was addressed both in terms of overall time taken on the four cue conditions, and in the effect of valid, part-invalid, and full-invalid cueing relative to the neutral cue condition.

There are four patterns that would indicate difficulties in motor preparation. First, with added response complexity, greater slowing of RT or increased slowing of measures of execution would reflect a difficulty in the motor preparation of the more complex sequences by the PD groups. Second, reduced benefits and costs of all cueing relative to the neutral cue condition would reflect a difficulty in using the cue to prepare the sequence in advance. Third, increased costs of part-invalid and full-invalid cueing would reflect a difficulty in modifying or changing the response prepared according to the cue, with the presentation of the imperative signal. The final pattern that may indicate a difficulty in motor preparation would be a benefit of part-invalid cueing, which would indicate incomplete preparation of the sequence.

3.4.4.1 The effect of response complexity

Table 2 shows the four dependent measures separated by response complexity in the three groups. There was a significant main effect of Response Complexity on RT (F (1, 41) = 44.57, $p < .001$, $\eta^2 = 0.52$), with participants showing a 58-ms lengthening of RT on bi-directional sequences relative to uni-directional sequences. In addition, both MT1 (11 ms) and DT (5 ms) were lengthened on bi-directional sequences relative to uni-directional sequences. Of the three measures of execution, there was a significant main effect of Response Complexity only on MT1 (F (1, 41) = 4.27, $p < .05$, $\eta^2 = 0.09$).

There were no significant interactions between Group and Response Complexity on RT, MT1, or DT, suggesting that all three groups were similarly affected on these measures by this manipulation (see Table 2). There was, however, a significant interaction between Group and Response Complexity on MT2 (F (2, 41) = 7.64, $p < .005$, $\eta^2 = 0.27$). Bi-directional sequences were performed slower than uni-directional sequences in both the Old Adult group (13 ms) and the PD ON group (15 ms) on MT2 (t (22) = 3.64, $p < .005$ and t

(10) = 2.78, p < .05, respectively). In contrast, the PD OFF group showed a non-significant 13-ms shortening of MT2 on bi-directional sequences (Table 2). While this latter interaction in MT2 is difficult to explain, the overall pattern suggests that all three groups were affected similarly by manipulating response complexity. In particular, the significant lengthening of RT with the more complex bi-directional sequences in all three groups suggests that they had prepared their response before its initiation, with more time required to prepare a sequence with a change of direction than a sequence that did not require a change of direction.

Table 2 Mean median times (in ms) of the four dependent measures on neutral trials separated by experimental group and response complexity (SEM presented in parentheses).

		Old Adult		PD ON		PD OFF		Row means	
RT	Uni	539	(20)	569	(29)	523	(30)	543	(16)
	Bi	583	(21)	649	(31)	571	(32)	601	(17)
MT1	Uni	228	(12)	319	(18)	282	(18)	276	(9)
	Bi	225	(15)	332	(22)	303	(23)	287	(12)
DT	Uni	133	(9)	171	(13)	143	(13)	149	(7)
	Bi	138	(9)	173	(12)	150	(13)	154	(7)
MT2	Uni	175	(11)	263	(15)	236	(16)	225	(8)
	Bi	188	(11)	278	(16)	223	(17)	230	(9)

3.4.4.2 The effect of cueing response-related information

3.4.4.2.1 Measure of motor initiation – RT

Table 3 shows RT separated by the four cue conditions for the three experimental groups. There was a significant main effect of Cue Condition on RT (F (3, 123) = 102.49, $p < .001$, $\eta^2 = 0.71$). All three groups experienced shorter RTs on the valid cue condition than on the neutral cue condition (see Table 3). After applying Bonferroni corrections, all three groups showed a shortening of RT in the valid cue condition relative to the neutral cue condition.

The Old Adult group showed a 135-ms shortening (t (22) = 9.07, p < .003), the PD ON group showed a 132 ms shortening (t (10) = 11.09, p < .003), and the PD OFF group showed an 88 ms shortening (t (9) = 7.23, p < .003).

Table 3 Mean median times of RT (in ms) by experimental group and cue condition (SEM presented in parentheses).

		Old Adult		PD ON		PD OFF		Row means	
Valid	Uni/Bi	426	(18)	477	(26)	459	(27)	454	(14)
Neutral	Uni/Bi	561	(20)	609	(29)	547	(30)	572	(15)
	Uni	539	(16)	569	(38)	523	(31)	543	(14)
Part-Invalid	Uni/Bi	576	(20)	597	(29)	559	(30)	577	(15)
Full-Invalid	Uni	561	(20)	583	(29)	573	(30)	572	(15)

Note. Uni/Bi indicates conditions in which uni-directional and bi-directional sequences were averaged together. Uni only indicate conditions which comprised only uni-directional sequences

In contrast, the full-invalid cue condition did not result in significantly longer times on the dependent measures than the neutral cue condition in any of the three groups. However, because the full-invalid cue condition comprised only uni-directional sequences, while the neutral cue condition was an average of the uni-directional and bi-directional sequences, post hoc analyses was also made with the neutral cue condition comprising only uni-directional sequences. It was found that the full-invalid cue condition lengthened RT in all three groups relative to the neutral cue condition for uni-directional sequences (see Table 3). While the 14-ms cost in the PD ON group did not reach significance (t (10) = 1.32, p = .22), a within-subjects Cohen's *d* effect size was calculated as 0.55. In addition, after applying Bonferroni corrections, the 22-ms cost in the Old Adult group narrowly failed to reach significance (t (22) = 2.31, p = .03), and the 50-ms cost in the PD OFF group was significant (t (9) = 3.26, p < .02). Finally, part-invalid cueing was not significantly lengthened or shortened relative to the neutral cue condition in any of the groups on RT (see Table 3).

Figure 3.2 depicts the effects of the valid, part-invalid, and full-invalid cue conditions relative to the neutral cue condition on RT. It shows that while all three groups showed benefits of valid cueing, costs of full-invalid cueing, and only a small effect of part-invalid cueing, there was some difference between the groups. Although the interaction between Group and Cue Condition on RT was not significant (F (6, 123) = 2.14, p = .054, η^2 = 0.09), Figure 3.2 suggests that the PD OFF group had a reduced benefit of valid cueing relative to both other groups (indicated by the less negative value). Post-hoc tests supports this observation, showing that the PD OFF group did exhibit slightly reduced benefits of valid cueing compared to both the Old Adult group (t (31) = 2.19, p < .05) and the PD ON group (t (19) = 2.53, p < .05). The PD OFF group also had a greater cost of full-invalid cueing than the PD ON group (with a Cohen's *d* effect size of 0.89) and the Old Adult group (with a Cohen's *d* effect size of 0.59), but neither of these reached significance (t (19) = 2.03, p = .057 and t (31) = 1.60, p = .12, respectively).

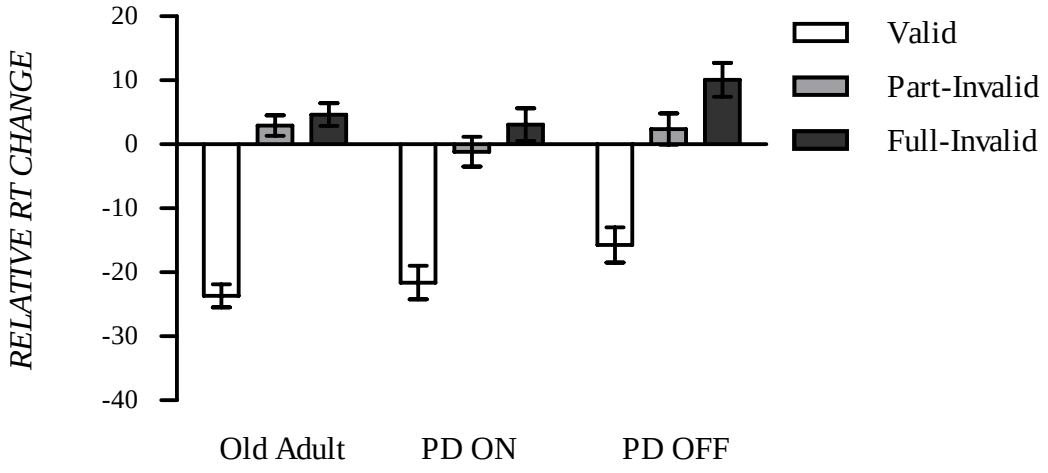

Figure 3.2 The effect of cue condition on RT in the three experimental groups (error bars represent ± 1 SEM). Negative values indicate an RT benefit, whereas positive values indicate an RT cost relative to the neutral cue condition.

Note. The calculation for full-invalid cueing used the mean median neutral RT using uni-directional sequences only.

3.4.4.2.2 Measures of motor execution – MT1, DT, MT2

Table 4 shows the three measures of execution for the experimental groups, separated by the four cue conditions. Differences between the effects of cue conditions on all three measures of execution were much smaller than on RT. There was a significant main effect of Cue Condition on MT1 (F (3, 123) = 4.88, p < .01, η^2 = 0.11), but the greatest difference was only a 9-ms cost of part-invalid cueing relative to the neutral cue condition (t (43) = 4.00, p < .01), and was likely to be due, in part, to the large observed power of 0.90. There was no significant main effect of Cue Condition on DT, with the largest difference between the cue conditions being only 2 ms. While there was a significant main effect of Cue Condition on MT2 (F (3, 123) = 6.54, p < .001, η^2 = 0.14), this was qualified by a significant interaction between Group and Cue Condition on MT2 (F (3, 123) = 2.62, p < .05, η^2 = 0.11). Following Bonferroni corrections, while the full-invalid and neutral cue conditions were not significantly different to each other in the PD OFF group, the full-invalid cue condition was significantly shorter than the neutral cue condition in both other groups. The Old Adult group showed a 4 ms benefit on MT2 (t (22) = 2.79, p < .03), while the PD ON group showed a 14 ms benefit (t (10) = 4.83, p < .03). However, these benefits are likely to be due to the fact that full-invalid cueing comprised only uni-directional sequences while the neutral cue condition comprised both uni-directional and bi-directional sequences. Accordingly, these benefits on MT2 in both groups were much smaller when the full-invalid cue condition was compared to the neutral cue condition on only uni-directional sequences. Only the PD ON group continued to show a significant 7-ms benefit following this comparison (t (10) = 2.91, p < .03). Taken together, while cueing did significantly affect the measures of execution (though this is likely to be the result of the very large observed power), differences in all three experimental groups were small. This suggests that the cue had been predominantly used for motor preparation before the execution of the sequence.

Table 4 Mean median times of the three measures of execution (in ms) by experimental group and cue condition (SEM presented in parentheses).

	Cue		Old Adult		PD ON		PD OFF		Row means	
MT1	V[a]	Uni/Bi	231	(13)	327	(19)	292	(20)	283	(10)
	N[b]	Uni/Bi	227	(13)	326	(19)	293	(20)	282	(10)
		Uni	228	(8)	319	(27)	282	(17)	263	(10)
	PI[c]	Uni/Bi	237	(13)	338	(19)	298	(20)	291	(10)
	FI[d]	Uni	233	(13)	325	(18)	289	(19)	283	(10)
DT	V	Uni/Bi	137	(9)	171	(12)	148	(13)	152	(7)
	N	Uni/Bi	135	(9)	172	(12)	147	(13)	151	(7)
		Uni	133	(8)	171	(13)	143	(15)	145	(7)
	PI	Uni/Bi	135	(8)	171	(12)	148	(13)	151	(6)
	FI	Uni	132	(9)	171	(12)	144	(13)	149	(7)
MT2	V	Uni/Bi	184	(11)	269	(15)	231	(16)	228	(8)
	N	Uni/Bi	181	(11)	270	(15)	229	(16)	227	(8)
		Uni	175	(6)	263	(24)	236	(15)	211	(10)
	PI	Uni/Bi	183	(10)	268	(15)	227	(15)	226	(8)
	FI	Uni	177	(11)	256	(15)	230	(16)	221	(8)

Note. Uni/Bi: indicate conditions in which uni-directional and bi-directional sequences were averaged together. Uni only: indicate conditions that comprised only uni-directional sequences.

[a] denotes the valid cue condition. [b] denotes the neutral cue condition. [c] denotes the part-invalid cue condition. [d] denotes the full-invalid cue condition.

3.4.5 Exploratory correlation analyses

This final section outlines the correlations that were found in the three groups. This section is separated into: (a) the relationship between disease duration and task performance in the two PD groups; (b) the relationship between cognitive functioning (the CAMCOG-R) and

performance on the motor task in all three groups; and (c) the relationship between the frequency of errors and performance on the task in the three groups. These are addressed in terms of the overall time taken on the dependent measures, the influence of response complexity, and the relative effect of cueing. Correlations were made only after errors were removed from the data. While the three experimental groups produced only a small number of errors in total, these were still deemed to be a useful measure in light of an examination of the corresponding scatter diagrams. Additional correlations are also presented that show the relationships that disease duration, cognitive functioning, and errors had with each other in the three experimental groups. These are included to clarify the meaning of the exploratory correlations that were found.

It was expected that in both PD groups, disease duration would be positively correlated with the four dependent measures, indicating that those participants who had had the disease longer were also the slower participants on the motor task. It was also expected that the correlations between disease duration and the four dependent measures separated by response complexity would be stronger on the bi-directional sequences, showing that the progression of the disease is related to greater slowing on the more complex sequences. Finally, if the progression of the disease leads to difficulties in motor preparation, correlations were also expected between disease duration and the relative effect of cueing in both PD groups.

In examining the role of cognitive functioning, it was expected that the participants in all three groups who scored highest on the CAMCOG-R would also be the participants who were both faster and who made fewer errors on the motor task. Because all participants demonstrated normal cognitive performance on the CAMCOG-R, differences between the groups in these correlations were not expected to be large. Finally, even in the absence of a significantly greater number of errors in the PD groups, positive correlations between errors and the dependent measures in either or both groups would show that those participants who were slower on the four dependent measures were also those who made more errors. In addition, these correlations were expected to be stronger when assessing the specific influence of response complexity and cueing on the four dependent measures.

3.4.5.1 The relationship between disease duration and task performance in the two PD groups

Table 5 shows the relationship between disease duration, participants' age, frequency of errors on the task, and scores on the CAMCOG-R in the two PD groups. Disease duration was weakly correlated with age in both PD groups, showing that the participants with PD who had had the disease longer were not necessarily the older participants. Furthermore, disease duration was weakly correlated both with the frequency of errors on the motor task and with scores on the CAMCOG-R. This indicates that the time since diagnosis in both PD groups did not predict the number of errors made on the motor task or with cognitive functioning on the sections of the CAMCOG-R.

Table 5 Pearson's correlation coefficients between disease duration and: (a) age; (b) errors (responding before the imperative signal and incorrect responses); and (c) scores on the sections of the CAMCOG-R in the two PD groups.

	PD ON	PD OFF
Age	-.25	-.04
Errors	.34	-.35
Section 1: Executive Function	-.12	.40
Section 2: Language	-.19	.17
Section 3: Memory	-.42	-.37
Section 4: Attention	.05	.28
Section 5: Abstract Thinking	-.47	.11
Global CAMCOG-R	-.31	.09

Pearson's correlation coefficients were then calculated between disease duration in the two PD groups and the four dependent measures. Table 6 shows that disease duration was moderately to strongly positive correlated with all four dependent measures in the PD OFF group (most strongly with RT). In contrast, disease duration was not correlated with any of the four dependent measures in the PD ON group (which was confirmed in corresponding scatter diagrams). This pattern shows that while the time since diagnosis predicted slowness in motor initiation and execution in people with PD when they were off their anti-Parkinsonian medication, this relationship disappeared when these people took the normal

administration of their anti-Parkinsonian medication. Furthermore, although not presented, these correlations were found to be very similar across uni-directional and bi-directional sequences. This indicates that, while disease duration predicted slowing on the four dependent measures in the PD OFF group, this was not affected by the complexity of the response being performed. Finally, correlations were also calculated between disease duration and the relative effect of cueing on the four dependent measures, but they were small and non-significant. Thus, the time since diagnosis did not predict how participants used (or were affected by) the cued response-related information relative to the neutral cue condition.

Table 6 Pearson's correlation coefficients between disease duration in the two PD groups and the four dependent measures, by cue condition.

	Cue Condition	PD ON	PD OFF
RT	Valid	.22	.75*
	Neutral	.07	.69*
	Part-Invalid	.21	.61
	Full-Invalid	.12	.65*
MT1	Valid	-.26	.62
	Neutral	-.25	.58
	Part-Invalid	-.29	.58
	Full-Invalid	-.24	.56
DT	Valid	-.08	.47
	Neutral	-.03	.53
	Part-Invalid	-.09	.52
	Full-Invalid	.02	.53
MT2	Valid	-.30	.50
	Neutral	-.26	.49
	Part-Invalid	-.37	.52
	Full-Invalid	-.29	.56

* Indicates significance at the .05 level (2-tailed)

3.4.5.2 The relationship between cognitive functioning and task performance in the three experimental groups

The second relationship that was examined was the influence of cognitive functioning on the four dependent measures. Table 7 shows the Pearson's correlation coefficients between each of the sections of the CAMCOG-R (as well as the global score) and RT for the three experimental groups. (The correlations with the other three dependent measures were weak and will not be presented.) Both the Old Adult and PD ON groups showed moderate to strong negative correlations between the CAMCOG-R sections and RT, although they did show some variation between the sections. For the Old Adult group, the Executive Function, Language, and Abstract Thinking sections of the CAMCOG-R produced the strongest relationship with RT. In the PD ON group, the strongest relationships were with the Memory, Attention, and Abstract Thinking sections (see Table 7). These indicate that those participants in both of these groups who showed higher cognitive functioning on the CAMCOG-R were also those who were faster on RT across the cue conditions. In contrast, participants in the PD OFF group showed moderate to strong positive correlations between the CAMCOG-R sections and RT. This relationship was found to be strongest with the Executive Function and the Attention scales of the CAMCOG-R (see Table 7). This pattern contrasts directly with the two other groups, and suggests that those participants in the PD OFF group who showed the highest cognitive functioning (on the two scales mentioned in particular) were also those who were slower on RT across the cue conditions. This contrasting pattern suggests that cognitive functioning had a different influence on the motor control of people with PD, depending on whether they were on and off their anti-Parkinsonian medication. This will be elaborated on in the discussion.

While a number of these correlations were found to be slightly stronger when participants performed bi-directional sequences as opposed to uni-directional sequences, this was not consistently found across all correlations and will not be discussed in detail. In addition, the correlations between the CAMCOG-R sections and the relative effect of cue condition on the four dependent measures were small in all groups.

Table 7 Pearson's correlation coefficients between CAMCOG-R sections and RT by experimental group and cue condition.

	Cue Condition	Old Adult	PD ON	PD OFF
Executive Function	Valid	-.23	-.37	.71*
	Neutral	-.58**	-.33	.76*
	Part-Invalid	-.44*	-.54	.78*
	Full-Invalid	-.52*	-.34	.66*
Language	Valid	-.34	-.25	.46
	Neutral	-.44*	-.28	.57
	Part-Invalid	-.32	-.49	.60
	Full-Invalid	-.28	-.32	.41
Memory	Valid	-.27	-.48	-.07
	Neutral	-.08	-.47	.08
	Part-Invalid	.01	-.70*	.09
	Full-Invalid	-.05	-.63*	-.17
Attention	Valid	-.03	-.38	.64*
	Neutral	.08	-.46	.68*
	Part-Invalid	.07	-.62*	.70*
	Full-Invalid	.15	-.56	.70*
Abstract Thinking	Valid	-.06	-.56	.29
	Neutral	-.56**	-.52	.44
	Part-Invalid	-.44*	-.71*	.42
	Full-Invalid	-.56**	-.53	.50
Global CAMCOG-R	Valid	-.21	-.40	.52
	Neutral	-.30	-.40	.58
	Part-Invalid	-.20	-.67*	.69*
	Full-Invalid	-.23	-.48	.55

* Indicates significant at the .05 level (2-tailed); ** Indicates significant at the .01 level (2-tailed)

3.4.5.3 The relationship between the frequency of errors, CAMCOG-R scores and performance on the motor task in the three experimental groups

The relationship between the frequency of errors, CAMCOG-R scores and performance on the motor task was the final area of interest to determine if cognitive functioning also influenced accuracy and the use of cueing on the motor task. Table 8 show the correlations between the frequency of errors and CAMCOG-R scores in each group. The Old Adult and PD ON groups had only weak to moderate negative correlations between the frequency of errors and CAMCOG-R scores. In contrast, the PD OFF group showed stronger negative correlations, especially on the Executive Function and Attention scales of the CAMCOG-R. This shows that those participants in all groups, but particularly in the PD OFF group, who showed higher cognitive functioning on the CAMCOG-R were also those who made fewer errors on the motor task.

Table 8 Pearson's correlation coefficients between the frequency of errors on the motor task and CAMCOG-R sections for the three experimental groups.

	Old Adult	PD ON	PD OFF
Executive Function	-.22	-.28	-.61
Language	.11	-.32	-.25
Memory	.06	-.35	-.30
Attention	-.14	-.36	-.64*
Abstract Thinking	-.44*	-.19	-.29
Global CAMCOG-R	-.09	-.36	-.72*

* Indicates significant at the .05 level (2-tailed).

Table 9 presents the correlations between the frequency of errors and the four dependent measures in the three experimental groups. While the PD OFF group appears to show moderate to strong negative correlations between the frequency of errors and RT, an examination of scatter diagrams suggest that outliers inflated these correlations. In contrast, the moderate positive correlations found in the Old Adult group were supported through scatter diagrams, showing that those who made more errors on the motor task were also the

slower on RT, especially on the part-invalid and full-invalid cue conditions. Only weak correlations were found across the other three dependent measures for each of the experimental groups. An examination into the relationship between the frequency of errors and response complexity failed to show any differences between uni-directional and bi-directional sequences. Finally, the relationship between the frequency of errors and the relative effect of cueing on the four dependent measures also produced only weak correlations for all three experimental groups. This shows that the number of errors was not related to either the complexity of the response or the use of the cued information for any of the groups.

Table 9 Pearson's correlation coefficients between the frequency of errors and the four dependent measures by experimental group and cue condition.

	Cue Condition	Old Adult	PD ON	PD OFF
RT	Valid	.23	.10	-.72*
	Neutral	.36	-.01	-.58
	Part-Invalid	.50*	.04	-.76*
	Full-Invalid	.46*	-.02	-.60
MT1	Valid	-.22	.34	-.09
	Neutral	-.24	.42	-.16
	Part-Invalid	-.21	.36	-.07
	Full-Invalid	-.20	.36	.04
DT	Valid	-.16	.01	-.21
	Neutral	-.16	.05	-.18
	Part-Invalid	-.17	.01	-.20
	Full-Invalid	-.19	.05	-.08
MT2	Valid	-.11	.23	-.09
	Neutral	-.14	.26	-.09
	Part-Invalid	-.15	.24	-.20
	Full-Invalid	-.19	.21	-.02

* Indicates significant at the .05 level (2-tailed)

3.5 Discussion

The aim of this experiment was to examine motor preparation in people with PD (both on and off their anti-Parkinsonian medication). This was done by assessing the effects of manipulating the complexity of the sequences, and cueing response-related information to participants. The central findings from this experiment are outlined in the two main sections below. The first section discusses the performance of the PD groups and the Old Adult group on the neutral cue condition. This is addressed in terms of the overall time taken on the four dependent measures, as well as the influence of various factors on task performance in the three experimental groups. The second section discusses the main findings that relate to motor preparation in people with PD and healthy adults. This comprises the influence of response complexity and the effect of cueing response-related information on the three groups.

3.5.1 Slowing of motor initiation and execution in people with PD

The two PD groups were significant slower than the Old Adult group on both MT1 and MT2, but not on RT or DT. Such slowing on motor execution in people with PD relative to healthy age-matched adults is consistent with the literature (Jahanshahi et al., 1992a; Reed & Franks, 1998; Stelmach et al., 1992; P. Weiss et al., 1996). While the PD groups were slower than the Old Adult group on DT, this failed to reach significance. This was somewhat surprising, as most evidence suggests that people with PD do show significantly prolonged DT relative to healthy adults in tasks similar to the one used in the current experiment (Harrington & Haaland, 1991; Rand & Stelmach, 1999; Rand et al., 2002; Roy et al., 1993; Stelmach et al., 1989; P. Weiss et al., 1997).

Past studies have been inconclusive on the issue of whether RT is slowed in people with PD. This disagreement may reflect the suggestion that movement execution is a more sensitive indicator than RT of overall impairments in people with PD (Evarts, Teräväinen, & Calne, 1981; Georgiou et al., 1994; Georgiou et al., 1993). Some studies have found significant RT slowing (Desmurget et al., 2004; Müller et al., 1999; Pollux & Robertson, 2001; Russ & Seger, 1995; J. Wang et al., 1998), while others have found roughly

equivalent RTs relative to healthy age-matched adults (Bekkering et al., 2001; Gentilucci & Negrotti, 1999a, 1999b; Harrington & Haaland, 1991; Plotnik et al., 1998; P. Weiss et al., 1997). The RT results in this experiment are consistent with the latter findings.

The similar times taken by the two PD groups on the four dependent measures is consistent with results from Jahanshahi et al. (1992b). Thus, the reduction of anti-Parkinsonian medication did not have a significant impact on motor preparation or execution in people with PD. It has been suggested that dopamine depletion will be seen first at the level of clinical deficits, followed by the presence of slowing of motor execution, and finally by a slowing of RT (Gauntlett-Gilbert & Brown, 1998). However, it has also been argued that a more complete withdrawal of anti-Parkinsonian medication, as opposed to the delay that was used in the current experiment, is required to find significant deterioration in motor performance in people with PD (Gauntlett-Gilbert & Brown, 1998). Thus, it is possible that the delay in the normal administration of anti-Parkinsonian medication in the current experiment was insufficient to produce significant slowing in motor initiation and execution in people with PD off their medication.

The exploratory correlation analyses between disease duration and the four dependent measures in the two PD groups does, however, point to a subtle effect of anti-Parkinsonian medication. While the PD OFF group showed progressive slowing on the four dependent measures as disease duration lengthened (especially on RT), the PD ON group failed to show this relationship. Thus, when off their anti-Parkinsonian medication, participants who had been diagnosed with PD for a longer period of time experienced greater slowing than participants with a more recent diagnosis. In contrast, when participants received their normal administration of anti-Parkinsonian medication (the PD ON group), this pattern failed to emerge. This suggests that anti-Parkinsonian medication may mask some of the normal slowing of motor performance that is associated with disease progression, even when there are no noticeable group differences between people with PD on and off their anti-Parkinsonian medication.

There was also evidence through the exploratory correlation analyses that anti-Parkinsonian medication may influence the effect of cognitive functioning on the motor control of people with PD. Moderate to strong negative correlations were found between cognitive functioning (CAMCOG-R scores) and RT on the four cue conditions in the Old Adult and

PD ON groups. This shows that those participants who scored higher on tests of cognitive functioning were also those who were faster at initiating their response on the motor task. Furthermore, participants in the Old Adult and PD ON groups who showed higher cognitive functioning were also those who made fewer errors on the task. Taken together, these correlations are likely to reflect the overall relationship between cognitive functioning and motor functioning, where those who show higher functioning on one domain will show higher functioning on the other (Krampe, 2002; Salthouse & Somberg, 1982).

In contrast to both the Old Adult and PD ON groups, moderate to strong *positive* correlations were found between cognitive functioning and RT in the PD OFF group. CAMCOG-R scores were negatively correlated with errors in the PD OFF group and in the two other experimental groups. Thus, rather than interpreting the faster RTs as reflecting better performance in the PD OFF group (as was done for the other two groups), it is more likely that the participants who scored higher on tests of cognitive functioning may have slowed their RT to improve the accuracy and control of their response. Importantly, these correlations between CAMCOG-R scores, RT, and errors in the PD OFF group were found predominantly with the Executive Function and Attention scales of the CAMCOG-R. Those participants who scored higher on the tests of attention and executive functions were more able to slow their RT to reduce their errors and maintain control over their response than those who scored lower on these tests. Attentional and executive functions influence aspects of motor preparation such as the decision of what response to make, the inhibition of alternate responses, and the ability to direct and sustain attention towards relevant task-related information (Bunge et al., 2002; Luks et al., 2002; Matsumoto et al., 2003). Thus, the strong positive correlations between attention and executive functions and RT in the PD OFF group are likely to reflect the influence of these cognitive processes on motor preparation.

The fact that, of the two PD groups, only the PD OFF group showed this particular pattern may reflect the influence of anti-Parkinsonian medication on cognitive functioning in people with PD. There is evidence that the administration of anti-Parkinsonian medication improves aspects of cognitive functioning, such as attention and executive functions (Pillon et al., 2003), and that the reduction of anti-Parkinsonian medication leads to a deterioration in these processes (Cools et al., 2001). Anti-Parkinsonian medication may act by increasing

the efficiency of activation in the prefrontal cortex – raising the signal-to-noise ratio (Cools et al., 2002; Remy & Samson, 2003). The positive correlations between RT and attention and executive functions were particularly evident in the PD OFF group. This may be because the reduction of anti-Parkinsonian medication unmasks the genuine capabilities of the participants, and thus better differentiates these processes within the PD OFF group. The two PD groups did not differ in their performance on the Attention and Executive Function scales of the CAMCOG, and were not significantly worse than the Old Adult group. However these positive correlations between RT and attention and executive functions in the PD OFF group suggest that these cognitive processes affect motor control differently in people with PD, depending on whether they are on or off their anti-Parkinsonian medication.

3.5.2 Motor preparation in people with PD

The main aim of this experiment was to determine if people with PD (on or off their anti-Parkinsonian medication) showed difficulties in motor preparation. The manipulation of response complexity (a change of direction) was found to affect both of the PD groups and the Old Adult group in a similar way. In particular, all three groups experienced significant slowing of RT with bi-directional sequences relative to uni-directional sequences. That RT increased in all three groups with the more complex sequences suggests that motor preparation is intact in people with PD (Bekkering et al., 2001; Reed & Franks, 1998). Furthermore, the fact that response complexity did not affect the execution of the sequence to a greater extent in either of the PD groups, relative to the Old Adult group, provides further support for intact preparation. If the more complex bi-directional sequence lengthened motor execution significantly more in people with PD, it could be suggested that additional preparation of the more complex sequence was continuing after the initiation of the response (Jennings, 1995; Stelmach et al., 1989; P. H. Weiss et al., 1999). This was not found. The similar lengthening of RT with added response complexity, and the absence of significantly greater slowing on measures of execution, can be taken to reflect intact preparation in people with PD (both on and off their anti-Parkinsonian medication).

The patterns that were found across the experimental groups with the manipulation of cue condition also support the idea that motor preparation is intact in people with PD. The significant RT benefits, found in all groups, when presented with valid cueing relative to the neutral cue condition show that participants had used the response-related information in the cue to prepare the sequence before the presentation of the imperative signal. Similarly, the RT costs of full-invalid cueing, again found in all groups, suggest that participants had prepared the sequence according to the cue. On these trials, the lengthened RT is believed to reflect the time needed to modify or change their response with the presentation of the imperative signal. Furthermore, the very similar RTs in the part-invalid and neutral cue conditions in all three groups can also be taken as evidence for intact motor preparation in people with PD. This result is consistent with the expectation that the valid and the invalid parts of the cue effectively cancelled each other out.

Significant lengthening of measures of motor execution with cueing in people with PD relative to healthy adults has previously been taken to reflect incomplete preparation of the sequence (Jennings, 1995). In Experiment 1, cueing had a very small effect on the measures of execution in all three groups. This suggests that preparation of the response was effectively completed during RT, with no additional on-line preparation of the response.

Taken together, these results suggest that people with PD (both on and off their anti-Parkinsonian medication), as well as healthy old adults, had used the cues to prepare the response prior to the imperative signal. This implies that motor preparation is intact in people with PD.

While the main results described above suggest that preparation was intact in both PD groups, there was some evidence of subtle difficulties in motor preparation in the two PD groups. The PD OFF group showed a significantly reduced benefit of valid cueing on RT relative to both other groups. With moderate to strong effect sizes, this group also showed an increased cost of full-invalid cueing relative to the two other groups. However this was not supported statistically through independent t-tests. In addition, while both the PD OFF group and the Old Adult group showed a significant cost of full-invalid cueing relative to the neutral cue condition, the cost in the PD ON group did not reach significance.

Linking these results back to the pathology of the disease, there are four main explanations of how PD affects motor preparation. First, it has been suggested that the dysfunction of the basal ganglia in PD leads to a direct deficit in the selection and construction of motor programs (Bloxham et al., 1984; Harrington & Haaland, 1991; Stelmach et al., 1989). However, a direct deficit in motor preparation would: (a) lead to an overall reduction in the effect of all cue conditions relative to the neutral cue condition, and (b) disrupt the ability to prepare more complex sequences. There are two relevant findings in this experiment that are inconsistent with this proposal. First, the two PD groups and the Old Adult group showed similar benefits and costs of cueing on RT. Second, the manipulation of response complexity had a similar affect on RT in all three groups. Both suggest that the selection and construction of motor programs is not impaired in people with PD.

Second, it has been suggested that people with PD suffer a disruption in the storage and maintenance of motor preparation (Gentilucci & Negrotti, 1999b; Gueye et al., 1998; Lewis et al., 2000; Sheridan et al., 1987). The reduced benefit of valid cueing in the PD OFF group and the reduced cost of full-invalid cueing in the PD ON group could be taken to reflect this difficulty, where the response prepared by the participants with PD was maintained less strongly. Again, however, it would be expected that a difficulty in the maintenance of motor preparation would lead to an overall reduction in the effect of cueing across all cue conditions. The PD OFF group would have been expected to also show a reduced cost of invalid cueing. This was not found, with some evidence of increased, rather than decreased, costs of full-invalid cueing (see Figure 3.2). Furthermore, the PD ON group would also have been expected to show reduced benefits of valid cueing, where again their response would be less strongly maintained. Again, this was not found, with similar significant benefits of valid cueing to the Old Adult group. Taken together, these results suggest that people with PD do not suffer a difficulty in the storage and maintenance of their motor programs.

Third, it has been suggested that PD instead disrupts the activation of motor cortical regions, leading to an abnormal slowness in motor preparation and execution. If this were the case, people with PD would require more time between a cue and an imperative signal to fully use advanced information, and more time to complete changes to incorrectly prepared movements (Jahanshahi et al., 1992a; A. M. Johnson et al., 2004; Scarpa &

Castiello, 1994; P. H. Weiss et al., 1999). The reduced benefit of valid cueing in the PD OFF group and the reduced cost of full-invalid cueing in the PD ON group may reflect a reduced information processing and a slowness in organising the response. However, if people with PD were abnormally slow in using the cues, a reduced effect of cueing would have been found across all cueing conditions. This was not found to be the case. Thus, the results from the current investigation are also not consistent with this explanation.

Finally, it has been suggested that people with PD suffer decreased efficiency and added noise in the PD motor system, resulting in variability in both motor preparation and execution (Montgomery et al., 1991; Reed & Franks, 1998; Sheridan et al., 1987; P. Weiss et al., 1997). The reduced benefit of valid cueing in the PD OFF group and the reduced cost of full-invalid cueing in the PD ON group, in the absence of a more systematic pattern, may reflect this additional noise in the PD motor system. As discussed above, a more consistent pattern of deficits with the manipulation of response complexity and across the cueing conditions would have been expected if people with PD suffer either a direct deficit in motor preparation or in maintaining their prepared response. The greater variability on the four dependent measures (as measured by the standard deviation) in participants in the PD groups, relative to participants in the Old Adult group, is also consistent with this interpretation of increased noise in the PD motor system. Much of this variability disappeared when using the coefficient of variation. This suggests that the variability is no greater than the variability that was found to be proportionate to the mean latencies in the healthy adult group. Thus, the underlying pathology of PD leads to both slowed motor performance and increased variability, but that the latter is no greater than would be expected according to their slowed motor performance. The results of this experiment suggest that PD affects motor preparation by decreasing the efficiency of, and introducing noise to, the motor system. This will be discussed in greater detail in Chapter Six.

3.5.3 Conclusions and future directions

The results from this experiment strong suggest that motor preparation is intact in people with PD (both on and off their anti-Parkinsonian medication). The comparable lengthening of RT with added response complexity in all groups suggests that people with PD and

healthy adult were similarly affected by the increase in sequence complexity when preparing their response. Furthermore, the broadly similar benefits and costs with valid and invalid cueing provide evidence that people with PD were able to use the information in the cue to prepare the response in advance, in a similar way to healthy adults. There were some subtle differences in the effect of cueing between the groups. However, these were not significant enough to contradict this general finding.

Delaying the administration of anti-Parkinsonian medication did affect the motor control of people with PD. While the time taken to perform the task did not vary significantly between the two PD groups, there was evidence through correlation analyses that suggest important differences. Disease duration predicted motor slowing in the PD OFF group, but not in the PD ON group, raising the possibility that anti-Parkinsonian medication may mask the normal slowing that is associated with the progression of the disease. Furthermore, a delay in anti-Parkinsonian medication also appeared to influence the underlying control of movement in people with PD. Participants in the PD ON group showed a similar relationship between cognitive functioning and performance on the task to the Old Adult group, where higher cognitive functioning was associated with shorter RTs and fewer errors. In contrast, participants in the PD OFF group showed a very different pattern. Higher cognitive functioning, specifically on the Executive Function and Attention scales of the CAMCOG-R, was associated with slower RTs and fewer errors on the motor task. Thus, it appears that those participants with the greater executive and attentional control in the PD OFF group were better able to maintain control of their movement, by slowing their RTs to improve their accuracy. This highlights the importance of attention and executive functions in motor preparation, and the different effect of these processes on people with PD, depending on whether they are on or off their anti-Parkinsonian medication.

There is one factor, however, that may have influenced the motor performance of the PD groups, and is yet to be addressed. There is evidence that the presence of relevant external information about a movement is particularly important for people with PD. It appears that the motor performance of people with PD improves when relevant external information about the movement is provided (Hanakawa et al., 1999; Oliveira et al., 1997), and deteriorates when such information is removed (Georgiou et al., 1994; Kritikos et al., 1995; Verschueren, Swinnen, Dom, & De Weerdt, 1997). Thus, it is possible that the ongoing

visual information provided in the imperative signal may have masked any difficulties in either the preparation or execution of the sequences in people with PD. Experiment 2 continued the examination of motor preparation in people with PD by investigating this possibility. Experiment 2 used a similar motor task to Experiment 1, however the imperative signal was presented for only a short period of time before being turned off. This reduced the amount of visual information provided to participants as they performed the sequence. Doing this enabled an examination of the role of visual information in the preparation and execution of motor sequences in people with PD.

Chapter Four: Motor preparation in people with PD under reduced visual information

4.1 Introduction

4.1.1 A summary of Experiment 1

There were four main findings from Experiment 1 that suggest that advance preparation had taken place in people with PD (both on and off their anti-Parkinsonian medication). First, increasing the complexity of the response by requiring a change of direction between movements lengthened RT in all three experimental groups. Second, the cueing of valid information about the upcoming sequence led to a significant RT benefit in all three groups. Third, the cueing of full-invalid information prolonged RT in all three groups, a slowing that reached significance in the Old Adult and the PD OFF groups. Finally, there was no RT benefit or cost of part-invalid cueing relative to the neutral cue condition. This finding might best be viewed as reflecting a cancelling out effect of the valid and invalid parts of the cue. Taken together, the results from Experiment 1 suggest that both the healthy adults and people with PD (both on and off their anti-Parkinsonian medication) had utilised the response-related information in the cue to prepare the sequence in advance. This supports the suggestion that motor preparation is fundamentally intact in PD (Bekkering et al., 2001; Gauntlett-Gilbert & Brown, 1998; Hocherman et al., 2004; A. M. Johnson et al., 2003; Reed & Franks, 1998; J. Wang et al., 1998).

4.1.2 An overview of Experiment 2

The aim of Experiment 2 was to further examine motor preparation in people with PD, but under conditions of reduced visual information. There have been suggestions that the motor performance of people with PD improves when provided with relevant external information about the movement (Hanakawa et al., 1999; Oliveira et al., 1997; Sheppard et al., 1996; Siegert et al., 2002), and deteriorates with its removal (Cooke et al., 1978; Georgiou et al., 1994; Georgiou et al., 1993; Jones et al., 1992; Kritikos et al., 1995). If this is the case, the illuminated LEDs of the imperative signal presented throughout the initiation and execution

of the response in Experiment 1 may have masked any difficulties that people with PD have in motor preparation.

In Experiment 1, the imperative signal remaining illuminated throughout the initiation and execution of the motor sequence. In Experiment 2, the imperative signal was presented only briefly, and participants were required to perform the same motor sequences only after the imperative signal was turned off. By reducing the amount of relevant visual information in this way, Experiment 2 aimed to assess if there were difficulties in motor preparation that had been masked by the presence of relevant external information in Experiment 1.

The four original areas of interest from Experiment 1 remained in Experiment 2. These were: (a) overall group differences on the four dependent measures (using neutral trials only); (b) the effect of response complexity on motor preparation and execution; (c) the effect of cued response-related information on the advanced preparation of the sequence; and (d) the exploratory correlation analyses to highlight what factors influenced motor performance in the experimental groups.

There were two extensions to Experiment 1. First, it was important to separate the slower performance in people with PD, relative to healthy age-matched adults, due to any overall impairment in motor performance (as evaluated in Experiment 1), from slowing specifically due to the reduction of visual information. Additional slowing due to the reduction of visual information can be isolated by comparing results of the two experiments. It was predicted that the extent to which the PD group was slower than the old adult group would be greater in the current experiment than in Experiment 1. This would reflect the additional difficulty experienced by participants with PD in movements under reduced relevant visual information.

Second, measures of disease severity were introduced into the exploratory correlation analyses of Experiment 2. It was expected that measures of disease severity in the participants with PD would predict both slowing on the motor task and the number of errors made. This would indicate that as the disease progressed and symptoms worsened, the participants with PD would show greater difficulty on the motor task. In addition, it was expected that if the participants with PD experienced a difficulty in motor preparation due to the reduction of visual information, disease severity would also correlate with the

relative effects of cueing (particularly on RT). This would indicate the influence of disease progression on the use of cued information.

It was decided that the influence of medication would not be followed up in Experiment 2. While Experiment 1 did find differences in people with PD on and off their anti-Parkinsonian medication, group differences with the manipulation of response complexity and cueing were not large. This is consistent with previous research that suggests that the withdrawal of anti-Parkinsonian medication only begins to have a significant effect on motor performance following a more complete removal from the participant's system over a period of days, rather than hours as was used in Experiment 1 (Gauntlett-Gilbert & Brown, 1998; Jahanshahi et al., 1992a). Finally, while the primary comparison was between the PD group and the Old Adult group, a group of healthy young adults also participated in Experiment 2. This is consistent with the design of previous studies that included a group of healthy young adults but did not discuss the results relating to that group in detail (Hocherman et al., 2004; Stern et al., 2005; P. Weiss et al., 1996).

4.2 Method

4.2.1 Participants

Twenty-one individuals with idiopathic PD participated in this experiment (14:7 M:F), all of whom had participated in the previous experiment. The participants in this group were aged between 54 and 84 years, with a mean of 69 years. Disease duration ranged between one and 17 years, with a mean of six years (SEM = 1.0). In contrast to Experiment 1, all participants were tested under the influence of their normal anti-Parkinsonian medication. As well as 19 of the original healthy age-matched old adults (8:11 M:F, aged between 46 and 87 years, with a mean of 67 years), 20 healthy young adults also took part in this experiment (10:10 M:F, aged between 22 and 28 years, with a mean of 26 years). There was no significance difference between the mean age of the two older groups (t (38) = .63, p = .53). The time between the conduct of Experiments 1 and 2 was approximately six months.

4.2.2 Tests Administered

All three groups were administered the motor task. All participants in the PD group were also administered the first three sections of the Unified Parkinson's disease Rating Scale (UPDRS) (Fahn et al., 1987) to assess the severity of their symptoms.

4.2.2.1 The Motor Task: Design and Procedure

The design of the motor task was the same as Experiment 1 with two exceptions: (a) the timing within the task (the duration of the foreperiod and the inter-trial interval); and (b) the way the imperative signal was presented. The duration of the foreperiod and inter-trial interval were deemed unnecessarily long for participants in all groups in Experiment 1, and were thus shortened to allow a briefer task to be presented to participants in Experiment 2.

As in Experiment 1, each trial began with the red and green LEDs above the central start key flashing on and off until the participant had depressed that key with their index finger for 2000 ms (the trial warning). The sequence in the cue was then presented for 750 ms, followed by a 250-ms foreperiod during which time all LEDs were turned off (this foreperiod was slightly shorter than that used in Experiment 1). Following this foreperiod, the two green LEDs of the imperative signal were then illuminated indicating the sequence to be performed. In Experiment 1 the onset of the LEDs signalled to participants to initiate the sequence and remained illuminated until both movements had been performed. In Experiment 2 however the imperative signal was illuminated for only 250 ms. Participants were instructed to make the movements to the appropriate target keys as quickly and accurately as possible after the imperative signal was turned off. In light of the results of Experiment 1 that show that all three groups took over 400 ms to initiate their response on any of the cue conditions, this 250-ms presentation was selected to be too brief for participants to prepare their response entirely during the presentation of the imperative signal. Once the second movement had been performed, all LEDs remained off for a further 1500 ms until the beginning of the next trial. This inter-trial interval was also slightly shorter than the 2000 ms in Experiment 1. Figure 4.1 depicts the time frame of a trial.

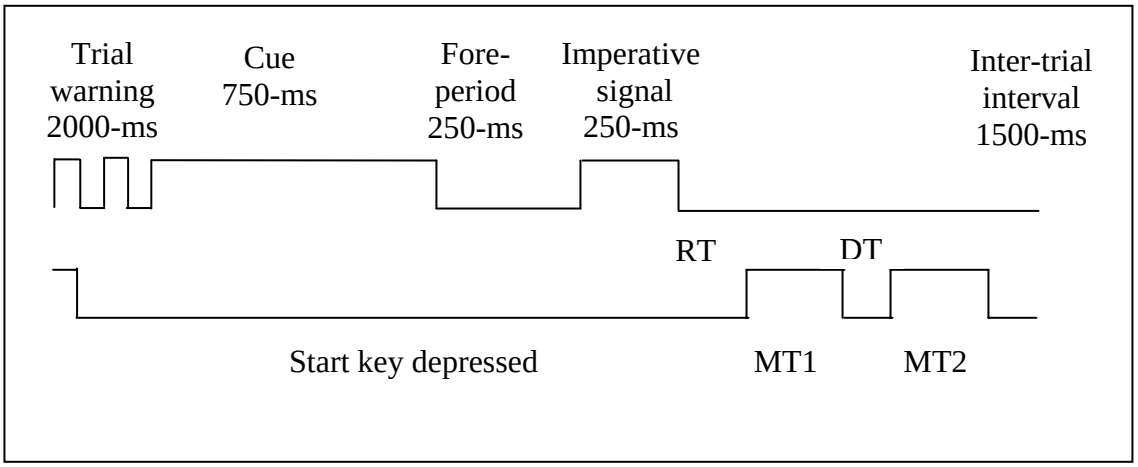

Figure 4.1 A diagrammatical representation of a typical trial in Experiment 2.
Note. It indicates the phases in which the LEDs were illuminated and turned off, and when participants were instructed to depress the start key and perform the sequence.

The five cue conditions that were used in Experiment 1 were also used in the current experiment – valid, neutral, part-invalid, full-invalid, and catch trials. One further modification in Experiment 2 was the inclusion of bi-directional full-invalid trials. This allowed a full examination into any interactions that may exist between the cue conditions and response complexity. Following a practice session of 14 trials in which each cue condition was presented at least once, participants again performed six randomised blocks of 44 experimental trials, with the same proportion of each cue condition as in Experiment 1. Three of the blocks were performed with their dominant hand, and three with their non-dominant hand (again counter-balanced across participants).

4.2.2.2 The Unified Parkinson's Disease Rating Scale (UPDRS) and the Hoehn and Yahr scale

The first three sections of the UPDRS were administered to the participants in the PD group to assess the severity of their symptoms. Part I assessed aspects of participants mental functioning, behaviour and mood. Part II assessed how PD has affected aspects of the participants' activity of daily living, and Part III comprised the motor examination of the participant. A modified global score consisting of these three sections was calculated for

each participant. In addition, a modified Hoehn and Yahr score was obtained from the administration of the UPDRS.

4.3 Data Analysis

Mean median times were again taken for the various response complexity and cue conditions over the four dependent measures. These were reaction time (RT), the first movement time (MT1), dwell time (DT), and the second movement time (MT2). In contrast to Experiment 1, where RT was taken from the onset of the imperative signal, RT in Experiment 2 was measured from when the imperative signal was turned off. The three measures of execution were taken in the same way as in Experiment 1. To establish if there was any general slowing in the PD group relative to the Old Adult group, mean median times for the four dependent measures were examined on the neutral cue condition. This was regarded as the baseline condition in the task, without the influence of cueing. In addition, the time taken by the PD group on the four neutral dependent measures was calculated relative to the Old Adult group in Experiments 1 and 2 to examine if there was any slowing on this baseline condition in the PD group that was specific to the reduction of visual information. This was done using the following formula: $((RT_{PD} - RT_{Old\ adult})/ RT_{Old\ adult}) \times 100$. This provides a measure of the magnitude of the slowing experienced by the PD group relative to the Old Adult group. The relative slowing in this experiment and in Experiment 1 was then compared to determine whether any greater slowing was found in either of the experiments.

To investigate motor preparation in the three experimental groups, all conditions (the four cue conditions and the two levels of response complexity) were entered into a repeated measures analysis of variance for each of the four dependent measures. The effects of response complexity and cueing will be outlined separately, followed by the interactions between the two. In addition to the presentation of inferential statistics, the effect of cueing for the valid, part-invalid and full-invalid cue conditions were calculated relative to the neutral cue condition (as they were in Experiment 1). This was done to graphically depict the benefits and costs of cueing and for use in exploratory correlation analyses. As in

Experiment 1, a negative score would reflect a cueing benefit, and a positive score would reflect a cueing cost.

Finally, exploratory correlation analyses were undertaken to establish what factors contributed to task performance in the three groups. There were three main relationships that were investigated. First, for the PD group, disease duration and measures of disease severity (both the UPDRS and the Hoehn and Yahr scale) were correlated with the four dependent measures. Second, in each of the three groups, the frequency of *errors* (making contact with the wrong target key and responding before the presentation of the imperative signal) was correlated with the four dependent measures. Finally, in Experiment 2 a second type of mistake was introduced. *Anticipations* were defined as those trials in which participants incorrectly initiated the sequence by lifting their finger from the start key while the imperative signal was still illuminated. The frequency of anticipations was also examined in each group. Both errors and anticipations were used in correlations with the four dependent measures to establish if there were any differences between the experimental groups in how they performed the task.

4.4 Results

The results of this experiment will be outlined in five main sections. Section 4.4.1 outlines the results of the two measures of disease severity in the PD group. Section 4.4.2 presents the screening of the data from the motor task. Section 4.4.3 outlines the main differences between the experimental groups on the four dependent measures under the baseline neutral cue condition, and compares the findings in Experiment 1 and 2. Section 4.4.4 addresses motor preparation in the three groups. This includes the effect of response complexity, the effect of cueing response-related information, and any possible interaction between response complexity and cueing. Section 4.4.5 outlines the exploratory correlation analyses. These correlations were made only after errors and anticipations were removed from the data.

4.4.1 Disease severity of the PD group: The UPDRS and the Hoehn and Yahr scale

The PD group obtained a mean global score of 38 (SEM = 3.0) out of a possible 176 on the modified UPDRS, and a mean stage of 2.5 (SEM = 0.1, and ranged from 1.5 to 4.0) out of 5.0 on the modified Hoehn and Yahr scale. In each, higher scores represented greater disability.

4.4.2 Motor task: Data screening and preliminary analyses

4.4.2.1 The frequency of errors

Responses that were initiated before the presentation of the imperative signal and incorrect responses (making contact with the wrong key) were coded as errors. They were removed in the same way as in Experiment 1. There was a group difference in the number of errors made (F (2, 59) = 4.87, $p < .05$), with both the Young and Old Adult groups making an average of 1% errors (SEM = 0.2 and 0.3, respectively), while the PD group made an average of 4% (SEM = 1.1).

4.4.2.2 The frequency of anticipations

Anticipations (responding while the imperative signal was still illuminated) were coded separately to errors and were also removed from the analysis. Anticipations were regarded as being different in nature to the errors in which participants responded before the imperative signal. The latter represents responses that were made before the participant even knew the correct sequence. In contrast, anticipations represented responses where the participant knew the correct sequence, but were unable to withhold their response until the imperative signal had been turned off. Groups did not differ in the number of these anticipations (F (2, 59) = 1.66, $p = .20$), with both the Young and Old Adult groups making an average of 1% anticipations, while the PD group made an average of 2%. Overall, 60% of the participants in the Young Adult (SEM = 0.11), 68% in the Old Adult (SEM = 0.11), and 71% in the PD (SEM = 0.10) groups anticipated at least once over the session.

4.4.2.3 Variability on the four dependent measures

In a similar way to Experiment 1, variability on the four dependent measures was analysed according to the standard deviations and the coefficient of variation. To assess variability both with and without the effects of cueing, the cue conditions were again separated into: (a) the neutral cue condition; and (b) the combined cueing conditions (valid, part-invalid and full-invalid). On the neutral cue condition, there were significant differences in the standard deviations of MT1 (F (2, 59) = 5.15, $p < .005$) and DT (F (2, 59) = 6.69, $p < .01$) between the groups. On the combined cueing conditions, there were significant differences in the standard deviations of RT (F (2, 59) = 5.78, $p < .01$), MT1 (F (2, 59) = 13.46, $p < .001$), and MT2 (F (2, 59) = 17.33, $p < .001$) between the groups. Importantly, it was found through post hoc analyses that the participants in the PD group were significantly more variable than the participants in the Old Adult group on MT2 on the neutral cue condition (t (38) = 2.16, $p < .05$), and both MT1 (t (38) = 2.77, $p < .01$) and MT2 (t (38) = 3.45, $p < .01$) on the combined cueing conditions. There were, however, no group differences on the four dependent measures using the coefficient of variation. This suggests that, while the PD group did show increased variability (according to their standard deviations), this was not disproportionate to the slowing in mean latencies on the four dependent measures relative to the healthy adult groups.

4.4.2.4 The effect of handedness on performance of the motor task

While performance of the task was generally faster with participants' dominant hand, there were no significant main effects or interactions relating to hand dominance. So trials on both hands were collapsed together for the overall analysis.

4.4.2.5 The effect of practice on performance of the motor task

There was a significant main effect of Block only on RT (F (5, 285) = 3.58, $p < .005$). Participants showed progressive shortening in their RT over the six blocks (the mean median being 11% faster in the sixth than in the first block). This suggests the presence of a practice effect. There was also a significant interaction between Group and Block on RT (F (10, 285) = 2.38, $p < .05$), where the Old Adult and the PD groups showed this practice effect on RT, but the Young Adult group did not. There were no main effects or interactions of Block on any of the other dependent measures, indicating that the three groups performed in a similar way on the measures of execution over the duration of the task. Finally, there were no three-way interactions between Block, Cue Condition, and Group on any of the four dependent measures, indicating that the three groups' use of cueing did not change over the six blocks.

4.4.3 Group differences on the baseline neutral cue condition

The neutral cue condition was taken as the baseline measure, and was used to assess the time taken by the three groups on the four dependent measures without the influence of cueing. It was expected that the PD group would be slower on the three measures of execution, consistent with established research. However, it was unclear whether they would also perform slower on RT since, as previously discussed, the established research has not demonstrated whether RT is also significantly affected by PD. In addition to the overall group differences, it was important to determine if, relative to the finding in Experiment 1, the reduction of visual information in Experiment 2 resulted in specific slowing in the PD group. It was expected that the PD group would show this additional slowing.

4.4.3.1 Mean median times on the measures of response initiation and execution

The mean median times of each group on the four baseline dependent measures (neutral trials only) are shown on Table 10. There was a significant main effect of Group on all four dependent measures – RT (F (2, 57) = 7.28, $p < .005$, $\eta^2 = 0.20$); MT1 (F (2, 57) = 31.19, $p < .001$, $\eta^2 = 0.52$); DT (F (2, 57) = 17.85, $p < .001$, $\eta^2 = 0.39$); and MT2 (F (2, 57) = 28.90, $p < .001$, $\eta^2 = 0.50$). Post hoc analyses revealed that the Old Adult group was significantly slower than the Young Adult group on all four dependent measures. They took 51 ms longer on RT (t (37) = 2.42, $p < .05$), 64 ms longer on MT1 (t (37) = 4.97, $p < .001$), 32 ms longer on DT (t (37) = 3.71, $p < .005$) and 40 ms longer on MT2 (t (37) = 4.00, $p < .001$) than the Young Adult group (see Table 10).

The results also reveal that the PD group was slower than the Old Adult group on all four dependent measures (see Table 10). As expected, and consistent with Experiment 1, the PD group was significantly slower than the Old Adult group on both measures of movement time. They were 92 ms slower on MT1 (t (38) = 3.92, $p < .001$) and 85 ms slower on MT2 (t (38) = 4.23, $p < .001$). In addition, the 27 ms slowing of the PD group on DT was also significant (t (38) = 2.38, $p < .05$). While the 65 ms slowing in RT did not reach significance (t (38) = 1.94, $p = .06$), it was calculated as a moderate effect size through Cohen's *d* (0.65).

Table 10 Mean median times of the four baseline dependent measures (in ms) by experimental group (SEM presented in parentheses).

	Young Adult		Old Adult		PD		Row Means	
RT	243	(22)	294	(22)	357	(21)	299	(13)
MT1	160	(14)	224	(15)	316	(14)	233	(8)
DT	92	(7)	124	(7)	151	(7)	122	(4)
MT2	132	(12)	172	(12)	257	(12)	187	(7)
Total	627	(25)	814	(23)	1083	(56)		

4.4.3.2 Examining the slowing of the PD group relative to the Old Adult group

Figure 4.2 shows the relative slowing of the PD group to the healthy Old Adult group on the four dependent measures in Experiments 1 and 2. On all four dependent measures, and in each experiment, a positive relative score was obtained. This indicates that the PD group was consistently slower than the Old Adult group. Figure 4.2 also shows that the relative slowing of the PD group was very similar across experiments on MT1, DT, and MT2. This suggests that the relative slowing of the PD group to the Old Adult group on measures of execution was no greater in Experiment 2 than in Experiment 1. This implies that the reduction of visual information did not cause any additional slowing in motor execution in the PD group. In contrast, the relative slowing of the PD group on RT was greater in this experiment than in Experiment 1. This indicates the presence of additional slowing on RT in the PD group with the reduction of visual information.

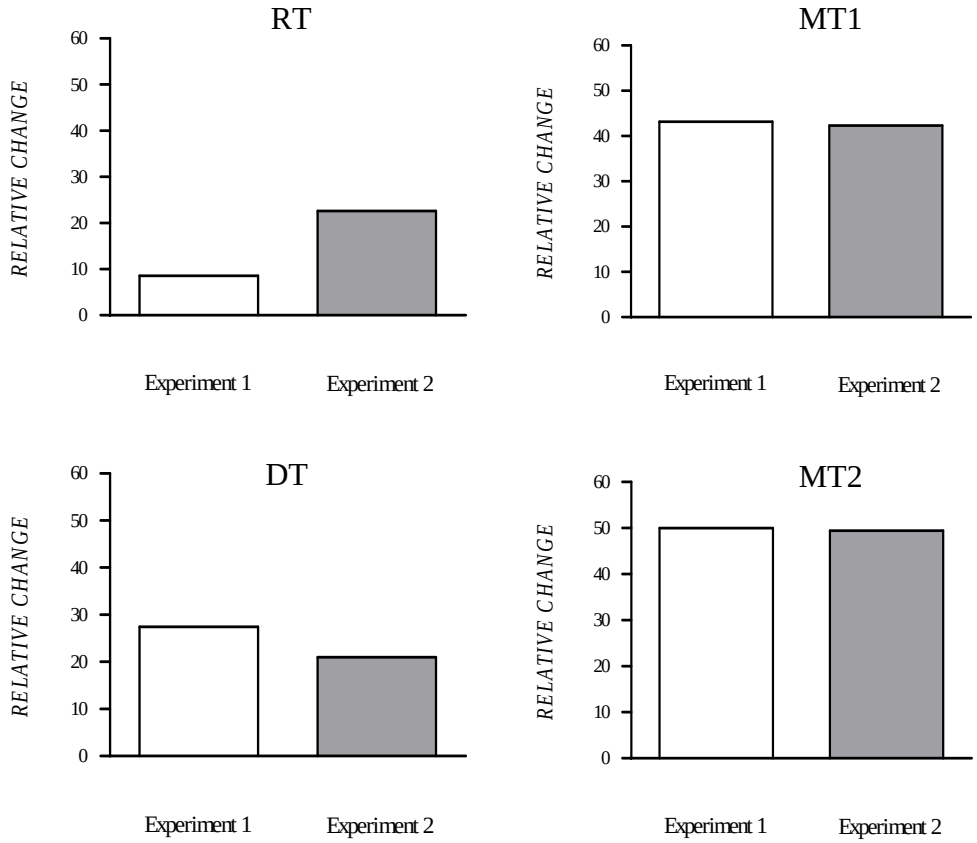

Figure 4.2 The relative slowing of the PD group to the Old Adult group on the four dependent measures in Experiments 1 and 2.

Note. SEMs cannot be calculated because the relative scores were taken on the group level. Only the PD ON group in Experiment 1 was used in this comparison.

4.4.4 Motor preparation in people with PD and healthy adults

The main aim of this experiment was to examine motor preparation in people with PD under reduced visual information. If the experiment were to reveal similar patterns between the PD group and the Old Adult group across the manipulations of response complexity and the cueing of response-related information, it would suggest that people with PD do not have difficulties in motor preparation. Conversely, significant group differences would suggest that people with PD do suffer difficulties in motor preparation with a reduction in the amount of visual information.

4.4.4.1 The effect of response complexity

Table 11 shows the effect on the four dependent measures of varying response complexity. As was found in Experiment 1, there was a significant main effect of Response Complexity on RT (F (1, 57) = 34.96, $p < .001$, $\eta^2 = 0.38$), with RTs in bi-directional sequences being 26 ms longer than RTs in uni-directional sequences. There was no interaction between Group and Response Complexity, with all three groups experiencing costs with bi-directional sequences. Table 11 shows that the Young Adult group was 15 ms slower in their RTs on bi-directional than on uni-directional sequences (t (19) = 2.89, $p < .01$), the Old Adult group was 25 ms slower (t (18) = 3.33, $p < .005$), and the PD group was 36 ms slower (t (20) = 4.06, $p < .005$).

While there was no effect of Response Complexity on MT1, there was on DT (F (1, 57) = 36.01, $p < .001$, $\eta^2 = 0.47$). There was also a significant interaction between Group and Response Complexity on DT (F (2, 57) = 5.36, $p < .01$, $\eta^2 = 0.13$). However the difference was only between the Young Adult group and the two older groups, and is not of central importance to this investigation. While the Young Adult group performed bi-directional sequences only 2 ms slower than uni-directional sequences, both the Old Adult and the PD groups experienced significantly greater costs. The Old Adult group experienced a 10-ms cost (t (18) = 5.95, $p < .001$), and the PD group an 11-ms cost (t (20) = 3.63, $p < .005$) when performing bi-directional sequences.

Table 11 Mean median times of the four dependent measures (in ms) by experimental group and response complexity (SEM presented in parentheses).

		Young Adult		Old Adult		PD		Row means	
RT	Uni	240	(23)	287	(23)	341	(22)	290	(13)
	Bi	246	(22)	301	(23)	376	(21)	308	(13)
MT1	Uni	159	(15)	230	(15)	318	(14)	236	(8)
	Bi	161	(14)	217	(15)	315	(14)	231	(8)
DT	Uni	91	(7)	119	(7)	145	(7)	119	(4)
	Bi	93	(7)	129	(7)	156	(7)	126	(4)
MT2	Uni	126	(12)	167	(12)	250	(11)	181	(7)
	Bi	139	(13)	178	(13)	265	(13)	194	(7)

Finally, there was a significant main effect of Response Complexity on MT2 (F (1, 57) = 31.00, $p < .001$, $\eta^2 = 0.38$), with all three groups showing similar costs of bi-directional sequences (see Table 11). Taken together, these results suggest that the PD group responded to the increased complexity of the bi-directional sequences in the same way as the Old Adult group. This suggests that the preparation for, and the execution of, the response by the PD group was not differentially affected by response complexity.

4.4.4.2 The effect of cueing response-related information

4.4.4.2.1 Measure of motor initiation – RT

Table 12 shows RT separated by the four cue conditions for the three experimental groups. As was found in Experiment 1, there was a significant main effect of Cue Condition on RT (F (3, 171) = 126.27, $p < .001$, $\eta^2 = 0.69$). Due to the number of post hoc comparisons made, Bonferroni corrections were applied. All three groups showed significantly shorter RTs with valid cueing. The RT of the Young Adult group was 78-ms shorter in the valid

cue condition than in the neutral cue condition (t (19) = 11.03, p < .006), the Old Adult group's RT was 100-ms shorter (t (18) = 7.50, p < .006), and the PD group's RT was 105-ms shorter (t (20) = 9.45, p < .006). These results show that all three groups had used the valid cue to prepare the sequence in advance. In contrast, RT under the full-invalid cue condition, relative to the neutral cue condition, was not significantly lengthened in any of the groups. The Young Adult group suffered only a 5-ms cost, the Old Adult group a 22-ms cost, and the PD group a 12-ms cost of full-invalid cueing relative to the neutral cue condition.

Finally, the effect of part-invalid cueing relative to the neutral cue condition did vary between the three groups. There was a significant interaction between Group and Cue Condition on RT (F (6, 171) = 2.61, p < .05, η^2 = 0.08). The RT of both the Young and Old Adult groups under part-invalid cueing was not significantly different to that under the neutral cue condition (12-ms and 8-ms shorter than the neutral cue condition, respectively). In Contrast, the PD group's RT was 42-ms shorter in the part-invalid cue condition than in the neutral cue condition, and this reached significance (t (20) = 3.95, p < .006).

Table 12 Mean median times of RT (in ms) by experimental group and cue condition (SEM presented in parentheses).

	Young Adult		Old Adult		PD		Row means	
Valid	165	(18)	194	(19)	254	(18)	205	(11)
Neutral	243	(22)	294	(22)	359	(21)	299	(13)
Part-Invalid	231	(19)	286	(19)	317	(18)	278	(11)
Full-Invalid	248	(22)	316	(23)	371	(21)	312	(13)
Total	222	(19)	273	(20)	325	(19)		

Note. Uni-directional and bi-directional sequences are averaged together.

Figure 4.3 depicts the benefits and costs of valid, part-invalid and full-invalid cueing relative to the neutral cue condition. All three experimental groups were found to benefit from valid cueing (as shown by the negative RT change), but show only a small effect of full-invalid cueing relative to the neutral cue condition. Figure 4.3 also shows that, in contrast to both healthy adult groups who showed only a small effect of part-invalid cueing, the PD group showed a benefit of part-invalid cueing.

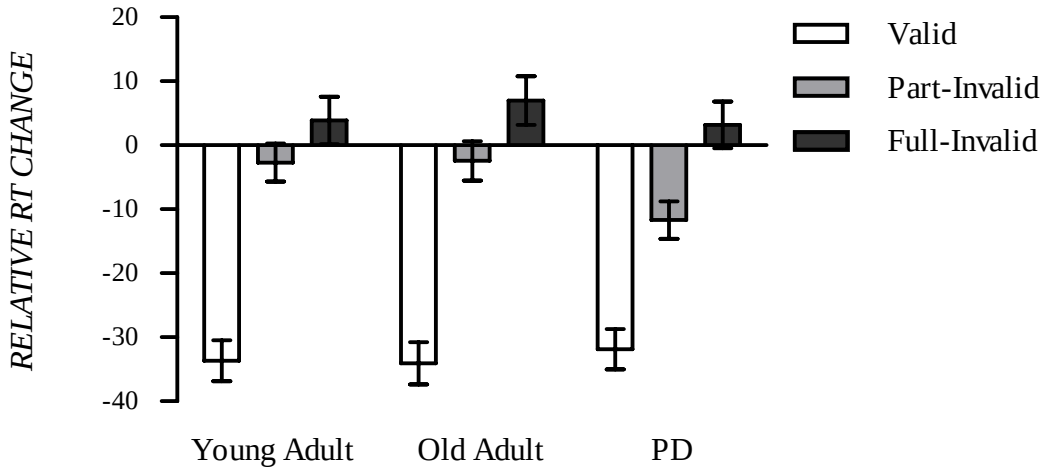

Figure 4.3 The effect of cue condition on RT in the experimental three groups (error bars represent ± 1 SEM).

Note. Negative values indicate an RT benefit, whereas positive values indicate an RT cost relative to the neutral cue condition.

4.4.4.2.2 Measures of motor execution – MT1, DT, MT2

Table 13 shows the three measures of execution separated by the four cue conditions in the three groups. Overall, the effect of cueing was smaller on measures of execution than it was on RT. There was a significant main effect of Cue Condition on MT1 (F (3, 171) = 4.42, p < .01, η^2 = 0.07) and DT (F (3, 171) = 3.84, p < .05, η^2 = 0.06). However the greatest difference from the neutral cue condition on MT1 was with full-invalid cueing (t (59) = 2.59, p < .05), which resulted in only a 7-ms lengthening. In DT, the differences between cue conditions were even smaller, with the greatest difference being a 3ms lengthening in

the valid cue condition (t (59) = 2.43, p < .05). In MT2, there was no significant main effect of Cue Condition (F (3, 171) = 1.22, p = .30) with the largest differences being only 2 ms. Furthermore, there was no interaction between Group and Cue Condition on any of these dependent measures, suggesting that on measures of execution, all three groups reacted to cueing in the same way. Again, the statistical significance found with such small differences in these measures of execution is likely to be a result of the strong observed power (0.87 for MT1 and 0.81 for DT). These results within the measures of execution are consistent with that of Experiment 1, and suggest that the influence of cued information is almost entirely contained to RT.

Table 13 Mean median times of the three measures of execution (in ms) by experimental group and cue condition (SEM presented in parentheses).

		Young Adult		Old Adult		PD		Row Means	
MT1	Valid	160	(15)	220	(15)	319	(14)	233	(8)
	Neutral	160	(14)	224	(15)	316	(14)	233	(8)
	PI[a]	163	(14)	227	(15)	319	(14)	236	(8)
	FI[b]	167	(15)	230	(16)	323	(15)	240	(9)
DT	Valid	94	(7)	127	(7)	153	(7)	125	(4)
	Neutral	92	(7)	124	(7)	151	(7)	122	(4)
	PI	93	(7)	126	(7)	151	(7)	123	(4)
	FI	92	(7)	124	(7)	149	(7)	122	(4)
MT2	Valid	133	(12)	175	(13)	258	(12)	189	(7)
	Neutral	132	(12)	172	(12)	257	(12)	187	(7)
	PI	133	(12)	175	(12)	258	(12)	189	(7)
	FI	134	(12)	173	(12)	258	(12)	188	(7)

[a] Denotes Part-Invalid. [b] Denotes Full-Invalid

4.4.4.3 The relationship between response complexity and cueing

The effect of cueing on the four dependent measures did not vary greatly in any of the three experimental groups by manipulating response complexity. First, there was no interaction between Response Complexity and Cue Condition on RT, nor was there any significant three-way interaction between Response Complexity, Cue Condition, and Group on RT. Second, while there were significant interactions between Response Complexity and Cue Condition on all other dependent measures (MT1, $\underline{F}$ (3, 171) = 4.61, $\underline{p} < .005$, $\underline{\eta}^2 = 0.08$; DT, $\underline{F}$ (3, 171) = 3.19, $\underline{p} < .05$, $\underline{\eta}^2 = 0.05$; and MT2, $\underline{F}$ (3, 171) = 2.96, $\underline{p} < .05$, $\underline{\eta}^2 = 0.05$), differences were not large enough to be theoretically important (with the large observed power again likely to be contributing to these results – 0.88, 0.73, 0.69, respectively). Finally, while there was a three-way interaction between Group, Cue Condition, and Response Complexity on MT2 ($\underline{F}$ (6, 171) = 2.55, $\underline{p} < .05$, $\underline{\eta}^2 = 0.08$), differences were again small, with the greatest difference in any of the groups being only 5 ms. This three way interaction is once again likely to be due mostly to the large observed power (0.84). Overall, these results suggest that the PD group was no more affected than the healthy adult groups in their use of cueing as response complexity varied.

4.4.5 Exploratory correlation analyses

This section outlines the important correlations that were found in the task performance of the three groups. In light of the results from the PD ON group in Experiment 1, it was expected that the measures of disease severity, but not disease duration, would predict slowing on the task in the PD group. In addition, it was also expected that positive correlations would be found between: (a) the measures of disease severity and variability on the four dependent measures; (b) the measures of disease severity and the frequency of errors and anticipations; and (c) the frequency of errors and anticipations and the four dependent measures. Thus, those participants in the PD group who showed the greater symptom severity would also show the greater motor slowing, greater variability, and would produce the greater number of errors and anticipations. This would reflect the greater difficulty in performing the task by the participants in the PD group with the more severe

symptoms. Furthermore, even stronger correlations would be expected when participants perform the more complex bi-directional sequences, due to the task being more difficult with added response complexity. Finally, it was expected that the progression of the disease would also affect the way that participants in the PD group used the cue conditions to prepare their response. Because of the significant RT benefit of part-invalid cueing in the PD group, it was predicted that the measures of disease severity would negatively correlate with the relative effect of part-invalid cueing on RT. This would show that those participants in the PD group with the more severe symptoms also showed the greater benefits of part-invalid cueing.

4.4.5.1 The relationship between disease duration and disease severity in the PD group and task performance

Pearson's correlation coefficients were calculated between disease duration, measures of disease severity and performance on the motor task in the PD group. Table 14 shows the relationship between these measures, as well as participants' age and accuracy on the task (errors and anticipations). A strong positive correlation was found between errors and anticipations, showing that the participants in the PD group who made more errors (incorrect responses and responses before the presentation of the imperative signal) also made more anticipations (responding while the imperative signal was presented). Furthermore, both measures of disease severity (the UPDRS and Hoehn and Yahr scale) were moderately to strongly positively correlated with errors and anticipations. In contrast, the measure of disease duration was weakly correlated both with measures of disease severity, and with errors and anticipations. This shows that when participants are on anti-Parkinsonian medication the number of years since diagnosis was a poor predictor both of disease severity and of the number of errors and anticipations made on the motor task. While age was also correlated with errors and anticipations, it did not relate to either disease duration or the two measures of disease severity.

Table 14 Pearson's correlation coefficients between disease duration, the measures of disease severity, errors, anticipations, and age in the PD group.

	Duration	UPDRS[a]	H and Y[b]	Errors	Anticip.[c]	Age
Duration		.24	.20	.28	.03	-.10
UDPRS			.78**	.48*	.52*	.11
H and Y				.55**	.66**	.22
Errors					.75**	.49*
Anticipations						.39

[a] Denotes the Unified Parkinson's Disease Rating Scale. [b] Denotes the Hoehn and Yahr scale. [c] Denotes anticipations.

* Indicates significant at the .05 level (2-tailed); ** Indicates significant at the .01 level (2-tailed).

Table 15 shows that both measures of disease severity, but not disease duration, strongly predicted variability (according to standard deviations) on all four dependent measures, both on the neutral cue condition and the combined cueing conditions. This suggests that as the severity of participants' symptoms worsened, their variability on the four dependent measures from trial to trial increased. Table 15 also shows this general relationship between disease severity (especially with the Hoehn and Yahr scale) and variability in the participants with PD, in this case through the coefficient of variation. Although here the pattern was slightly less clear.

Table 15 Pearson's correlation coefficients between variability (both standard deviation and the coefficient of variation) and disease duration and measures of disease severity in the PD group on the four dependent measures. Cue conditions are separated into the neutral cue condition and the combined cueing conditions.

			Disease Duration	UPDRS [a]	Hoehn and Yahr
Standard deviation	Neutral	RT	.39	.51*	.67**
		MT1	.19	.54*	.69**
		DT	.37	.72**	.53*
		MT2	.12	.68**	.76**
	Cueing	RT	.33	.61**	.74**
		MT1	.09	.65**	.69**
		DT	.36	.58**	.56**
		MT2	.11	.63**	.70**
Coefficient of variation	Neutral	RT	.39	.37	.53*
		MT1	.43	.39	.58**
		DT	.56**	.43	.29
		MT2	.29	.53*	.66*
	Cueing	RT	.22	.27	.23
		MT1	.41	.55*	.66**
		DT	.42	.37	.55**
		MT2	.42	.37	.55**

[a] Denotes the Unified Parkinson's Disease Rating Scale.

* Indicates significant at the .05 level (2-tailed). ** Indicates significant at the .01 level (2-tailed).

Moderate to strong positive Pearson's correlation coefficients were also found between the measures of disease severity and the time taken on the four dependent measures on all of

the cue conditions, in particular RT and DT (see Table 16). This relationship shows that the participants with the more severe symptoms performed the task slower than participants with less severe symptoms, irrespective of the cue condition. In contrast, disease duration and the dependent measures were related in quite a different way. While weak correlations were found with both RT and DT, moderate negative correlations were found between disease duration and both MT1 and MT2. This suggests that those participants who had been diagnosed with PD for a longer period of time were faster on MT1 and MT2 than those with a more recent diagnosis (again over all of the cue conditions).

Table 16 Pearson's correlation coefficients between disease duration and measures of disease severity in the PD group and the four dependent measures by cue condition.

		Disease Duration	UPDRS [a]	Hoehn and Yahr
RT	Valid	.18	.42	.56**
	Neutral	.19	.51*	.65**
	Part-Invalid	.13	.43*	.61**
	Full-Invalid	.16	.60**	.75**
MT1	Valid	-.42	.39	.29
	Neutral	-.43	.41	.35
	Part-Invalid	-.43	.42	.32
	Full-Invalid	-.41	.44*	.31
DT	Valid	-.08	.65**	.54*
	Neutral	-.18	.58*	.42
	Part-Invalid	-.06	.64**	.55*
	Full-Invalid	-.03	.62**	.55**
MT2	Valid	-.45*	.35	.24
	Neutral	-.47*	.37	.28
	Part-Invalid	-.45*	.38	.27
	Full-Invalid	-.45*	.36	.25

[a] Denotes the Unified Parkinson's Disease Rating Scale.

* Indicates significant at the .05 level (2-tailed); ** Indicates significant at the .01 level (2-tailed).

The correlations between disease severity and RT were found to be even stronger when the participants in the PD group performed bi-directional rather than uni-directional sequences (see Table 17). Thus, it appears that with increased response complexity, the slowing on RT was even more strongly predicted by symptom severity.

Table 17 Pearson's correlation coefficients between disease duration and measures of disease severity in the PD group and RT, by response complexity and cue condition.

		Duration [a]	UPDRS [b]	H & Y [c]
Uni-directional	Valid	.12	.31	.49*
	Neutral	.19	.42	.57**
	Part-Invalid	.10	.32	.51*
	Full-Invalid	.06	.56**	.70**
Bi-directional	Valid	.17	.48*	.60**
	Neutral	.17	.59**	.72**
	Part-Invalid	.15	.49*	.64**
	Full-Invalid	.26	.64**	.80**

[a] Denotes disease duration. [b] Denotes the Unified Parkinson's Disease Rating Scale.

[c] Denotes the Hoehn and Yahr scale.

* Indicates significant at the .05 level (2-tailed). ** Indicates significant at the .01 level (2-tailed).

Additional correlations were also calculated between disease duration and the measures of disease severity with the relative effects of cueing. There was, however, no relationship found between either disease duration or disease severity and the relative effects of cueing on any of the four dependent measures (and are not presented). While moderate positive correlations were found between the Hoehn and Yahr scale and the relative effect of cueing on DT, an examination of scatter diagrams suggested that outliers inflated these

correlations. Thus, measures of disease duration and severity did not predict how participants used (or were affected by) the cued response-related information.

4.4.5.2 The relationship between the frequency of errors and task performance

The correlations between the frequency of errors and the four dependent measures are shown in Table 18. The table shows that the frequency of errors was not related to the time taken on the four dependent measures in either the Young or Old Adult groups. While the frequency of these errors was positively correlated with RT in the PD group, in each cue condition, the examination of scatter diagrams suggest that these were inflated due to two outlying participants. In contrast, the moderate strong positive correlations with DT in the PD group were shown to be linear on scatter diagrams. This suggests that those participants who made more errors were also the slower on DT, especially across the valid, part-invalid, and full-invalid cue conditions. Furthermore, the correlation with DT on the full-invalid cue condition was found to be stronger when participants performed bi-directional sequences ($\underline{r} = 0.61$, $p < .01$) than when they performed uni-directional sequences ($\underline{r} = 0.47$, $p < .05$). This suggests that in the PD group, the number of errors predicted slowing on DT on the full invalid cue condition when performing the more complex bi-directional sequence.

Table 18 Pearson's correlation coefficients between the frequency of errors and the four dependent measures, by experimental group and cue condition.

		Young Adult	Old Adult	PD
RT	Valid	-.26	.13	.42
	Neutral	-.18	.14	.54*
	Part-Invalid	-.13	.25	.30
	Full-Invalid	-.16	.26	.45*
MT1	Valid	-.11	0	.03
	Neutral	-.02	-.01	.06
	Part-Invalid	-.09	.02	.07
	Full-Invalid	-.08	-.07	.03
DT	Valid	0	-.23	.45*
	Neutral	-.03	-.24	.34
	Part-Invalid	-.07	-.15	.49*
	Full-Invalid	-.02	-.22	.50*
MT2	Valid	-.16	-.14	.03
	Neutral	-.14	-.14	.03
	Part-Invalid	-.13	-.11	.06
	Full-Invalid	-.16	-.14	.05

* Indicates significant at the .05 level (2-tailed).

The relationship between the frequency of errors and the relative effect of cueing was also examined. The Pearson's correlation coefficients shown in Table 19 reveal some important group differences. First, there was a moderate negative correlation between the frequency of errors and the relative effect of part-invalid cueing on RT in the PD group. This shows that those participants in the PD group who made more errors were also those participants most likely to benefit from part-invalid cueing on RT. Keeping in mind the fact that benefits of part-invalid cueing were taken to reflect incomplete preparation, this correlation shows that those participants who made more errors (who were also found to be the ones with the greater symptom severity) showed the greater degree of incomplete preparation.

While there were also moderate positive correlations with DT and MT2 in the PD group, the examination of scatter diagrams suggested that these were inflated due to the influence of outlying scores.

Second, there were moderate negative correlations between the frequency of errors and the relative effect of valid cueing on both RT and MT1 in the Young Adult group. This shows that those participants in the Young Adult group with the higher number of errors were also those who benefited most from valid cueing (remembering that greater benefits are represented by more negative relative scores).

Finally, there was a moderate positive correlation between the frequency of errors and the relative effect of part-invalid cueing on DT in the Old Adult group (see Table 19). This shows that the participants in the Old Adult group who made more errors also showed the greater cost of part-invalid cueing on DT (remembering the greater the cost, the more positive the relative score).

Table 19 Pearson's correlation coefficients between the frequency of errors and the relative effect of cueing on the four dependent measures by experimental group.

		Young Adult	Old Adult	PD
RT	Valid	-.36	.02	-.20
	Part-Invalid	0	.16	-.53*
	Full-Invalid	.26	.26	-.23
MT1	Valid	-.49*	.11	-.11
	Part-Invalid	-.22	.22	.08
	Full-Invalid	-.21	-.21	-.13
DT	Valid	.30	.07	.45*
	Part-Invalid	-.24	.46*	.54*
	Full-Invalid	.20	.16	.46*
MT2	Valid	-.15	-.06	.12
	Part-Invalid	.12	.19	.38
	Full-Invalid	.02	0	.24

* Indicates significant at the .05 level (2-tailed).

4.4.5.3 The relationship between the frequency of anticipations and task performance

While there were only a small number of anticipations made in each group, the patterns between the groups varied markedly. Table 20 shows the relationship between the frequency of anticipations and the four dependent measures by cue condition. The Young Adult group showed strong negative correlations between the number of anticipations and RT on all four cue conditions (the correlations with the other dependent measures were also negative, but were smaller). An examination of the corresponding scatter diagrams confirm this relationship, suggesting that, of the participants in the Young Adult group who made anticipations (60% of the group), those who made more were also those who were faster on RT on all four cue conditions. This suggests a speed/accuracy trade-off, where the participants in the Young Adult group who were faster at initiating their response also anticipated more. The Old Adult group showed near-zero correlations between number of anticipations and the four dependent measures on all cue conditions (see Table 20). Thus, the number of anticipations was not related to the time taken on any of the four dependent measures in the Old Adult group, and is consistent with suggestions that older adults tend to choose a conservative approach on motor tasks, where speed is not chosen over accuracy (Larish & Stelmach, 1982; Rabbitt, 1979). Table 20 reveals a different pattern for the PD group. This group showed moderate to strong positive correlations between the frequency of anticipations and both RT and DT on all cue conditions. Again, scatter diagrams reveal a robust pattern, where of those participants in the PD group who made anticipations (71% of the group), those who made more were also those who were slower on these dependent measures.

Table 20 Pearson's correlation coefficients between the frequency of anticipations and the four dependent measures, by experimental group and cue condition.

		Young Adult	Old Adult	PD
RT	Valid	-.61*	.04	.42
	Neutral	-.54*	.08	.51*
	Part-Invalid	-.59*	-.01	.43*
	Full-Invalid	-.47*	.06	.60*
MT1	Valid	-.43	.02	.29
	Neutral	-.36	.04	.35
	Part-Invalid	-.39	.01	.32
	Full-Invalid	-.41	.04	.31
DT	Valid	-.31	.12	.44*
	Neutral	-.39	.15	.36
	Part-Invalid	-.40	.17	.42
	Full-Invalid	-.32	.10	.41
MT2	Valid	-.44	.01	.20
	Neutral	-.37	-.02	.22
	Part-Invalid	-.41	-.02	.21
	Full-Invalid	-.41	-.05	.23

* Indicates significant at the .05 level (2-tailed).

In addition, the correlations between the frequency of anticipations and the four dependent measures were found to vary depending on response complexity. In the Young Adult group, the correlations between anticipations and both RT and MT2 were found to be even larger when participants performed bi-directional sequences. Moderate positive correlations were also found between the frequency of anticipations and MT1 on uni-directional sequences in the PD group. These correlations are not of central importance, and so tables relating to these correlations are in Appendices D and E.

Finally, the correlations between the frequency of anticipations and the relative effect of cueing on the four dependent measures are shown in Table 21. The Young Adult group showed moderate to strong negative correlations between anticipations and the relative effect of valid cueing on RT, MT1, and MT2. This shows that those participants who

benefited most from valid cueing on these dependent measures were also those participants who made more anticipations. In contrast, moderate to strong positive correlations were found on DT in the Young Adult group. This implies that those participants who made more anticipations were also those who showed both the least benefit of valid cueing, and the greater cost of full-invalid cueing on DT. This relationship between the frequency of anticipations and the relative effects of cueing on DT in the Young Adult group is surprising. It may be that as part of this speed/accuracy trade-off, the young adult participants did not prepare the entire sequence, with subtle additional preparation undertaken in DT. In contrast, in the Old Adult and the PD groups, there was no relationship found between the frequency of anticipations and the relative benefit and cost of cueing on the four dependent measures. This suggests that the number of anticipations was not related to how participants in the Old Adult and PD groups used the cued information.

Table 21 Pearson's correlation coefficients between the frequency of anticipations and the relative effect of cueing on the four dependent measures by experimental group.

		Young Adult	Old Adult	PD
RT	Valid	-.62**	.01	-.09
	Part-Invalid	-.21	-.13	-.31
	Full-Invalid	.01	.0	-.14
MT1	Valid	-.51*	-.09	-.39
	Part-Invalid	-.19	-.16	-.24
	Full-Invalid	-.25	-.03	-.09
DT	Valid	.58*	-.17	.27
	Part-Invalid	-.11	.11	.25
	Full-Invalid	.49*	-.25	.15
MT2	Valid	-.40	.31	.05
	Part-Invalid	-.04	.10	-.02
	Full-Invalid	-.01	-.12	.20

* Indicates significant at the .05 level (2-tailed). ** Indicates significant at the .01 level (2-tailed).

4.5. Discussion

The aim of Experiment 2 was to examine motor preparation in people with PD under conditions of reduced visual information. This was done by modifying the conditions of Experiment 1. In Experiment 1, participants were shown the imperative signal while they initiated and executed the motor sequence. In Experiment 2, the imperative signal was turned off before participants initiated and executed the motor sequences.

The results from this experiment will be discussed in three sections. Section 4.5.1 discusses the time taken by the PD group, relative to the healthy Old Adult group, on the baseline neutral cue condition. This is discussed both in terms of the overall time taken on the four dependent measures, and the slowing that can be attributed directly to the reduction of relevant visual information. Section 4.5.2 discusses the effect of response complexity and the effect of cueing on the four dependent measures in the experimental groups under reduced visual information. Section 4.5.3 outlines the results of the exploratory correlation analyses.

4.5.1 Slowing of motor initiation and execution in people with PD

The PD group was significantly slower than the Old Adult group on the measures of MT1, DT, and MT2 (and narrowly failed to reach significance on RT). The 67-ms slowing on RT, coupled with the evidence of increased slowing relative to the Old Adult group in this experiment compared to Experiment 1, does suggest that the PD group experienced greater slowing in the initiation of their response with a reduction in the amount of visual information available. The slowing of the three measures of execution was expected and is consistent with previous findings (A. M. Johnson et al., 2003; Reed & Franks, 1998; Stelmach et al., 1992; P. Weiss et al., 1997). However, when calculated relative to the Old Adult group across this experiment and Experiment 1, there was no additional slowing on measures of execution that could be attributed directly to the reduction of visual information. This implies that the reduction of visual information did not exacerbate the slowing of motor execution in the PD group relative to healthy Old Adult group. This is surprising as there have been studies which found that people with PD do experience

additional difficulties in motor performance when visual information about the movement is removed (Georgiou et al., 1994; Kritikos et al., 1995). The current experiment did not completely remove the visual information available, with the target keys and the non-illuminated LEDs still visible to participants as they performed the task. It is possible that a more complete withdrawal of visual information is required before slowing in measures of execution become apparent in people with PD.

4.5.2 Motor preparation in people with PD

There are a number of findings from this experiment that suggest motor preparation is largely intact in people with PD. First, increasing response complexity had a similar effect on the dependent measures all three experimental groups. This suggests that people with PD did prepare the more complex bi-directional sequence in a similar way to the healthy adult groups. Increasing response complexity was found to lengthen RT in all groups. This reflects the additional time required to prepare the more complex sequences. In addition, the small changes in the measures of execution in all three groups with added response complexity suggests that preparation of both types of sequences was effectively complete before the initiation of the response. These findings are consistent with Experiment 1, and provide support for the idea that motor preparation is intact in people with PD.

Second, there were significant benefits of valid cueing in all three groups. This also suggests that the participants in the PD group had used the information in the cue to prepare the sequence in advance, in a similar way to healthy adults.

A third finding that suggests that motor preparation is intact in people with PD is that none of the groups reacted differently to cueing when performing the more complex bi-directional sequence. This result suggests that people with PD were able to prepare their response in advance, even when presented with more complex sequences. This was somewhat unexpected, as it has previously been found that people with PD tend to show greater impairments in their motor performance (both preparation and execution) when the task is more difficult (Harrington & Haaland, 1991; Low et al., 2002; Rand & Stelmach, 1999; Reed & Franks, 1998). It is possible that the manipulation of response complexity

needed to be greater for differences in motor preparation to become apparent. It has been suggested that increasing the number of movements in a sequence provides the most effective manipulation of response complexity (Christina & Rose, 1985; Fischman, 1984), and may be better at identifying differences between the groups in their use of cued response-related information.

Finally, it was found through the exploratory correlation analyses that, in the PD group, neither disease duration or disease severity was correlated with the relative effects of cueing. If motor preparation deteriorated with disease progression, stronger correlations with these measures would have been expected. For instance, a positive correlation with the relative effect of valid cueing would show that those with greater disease progression benefited the least from the valid cue condition. The absence of such a relationship indicates that disease progression (disease duration and disease severity) did not impact on how the cued information was used by people with PD, and suggests that motor preparation is unlikely to be directly affected by the progression of the disease.

There was no significant RT cost with full-invalid cueing relative to the neutral cue condition in any of the groups. This could be seen as either a lack of advanced preparation, or a difficulty in the storage and maintenance of the constructed motor program before its initiation (Gentilucci & Negrotti, 1999b; Gueye et al., 1998; Lewis et al., 2000; Sheridan et al., 1987). However, there are a number of reasons why this is unlikely. All three groups were found to show the same pattern, and it is unlikely that both the healthy adult groups would have experienced difficulties in the preparation, storage or maintenance of their response. In addition, the significant benefits of valid cueing on RT are inconsistent with such an interpretation. These benefits show that all three groups had adequately prepared and maintained their response until initiation was required. It is therefore more likely that much of the cost of full-invalid cueing (the modification or re-preparation of the response) was absorbed during the 250-ms presentation of the imperative signal (and was therefore not evident in RT). While 250 ms is deemed too short to complete motor preparation, this additional time available to observe the sequence before performing it would affect aspects of preparation and re-preparation.

There was, however, one finding in this experiment that does raise the possibility that people with PD experienced some difficulties in their motor preparation. Specifically, it is

possible that this group suffered incomplete preparation of the sequence. The significant interaction between Group and Cue Condition on RT shows that the three groups used the cued information differently. In this experiment, in their use of part-invalid cueing both the Young and Old Adult groups showed a similar pattern to Experiment 1, with RTs similar to the neutral cue condition. As previously suggested, this reflects a cancelling out of the valid and invalid parts of the cue. In contrast, the PD group experienced a significant benefit with part-invalid cueing relative to the neutral cue condition in this experiment but not in Experiment 1. Keeping in mind that the part-invalid cue validly cues the first movement but invalidly cues the second movement, this suggests that the valid part of the cue was more influential in the advance preparation of the response than the latter invalid part. This is likely to reflect incomplete preparation of the response.

Also perhaps reflecting this incomplete preparation, the PD group showed a negative correlation between the frequency of errors and the effect of part-invalid cueing on RT. This suggests that those participants who made more errors were also those who showed the greatest benefit of part-invalid cueing on RT. Because the frequency of errors was related to measures of disease severity in the PD group, and errors was related to the relative effect of part-invalid cueing, it was the participants with the more severe symptoms who were more likely to show a greater benefit of part-invalid cueing on RT. This suggests that as disease progresses, errors increase and preparation becomes more incomplete.

Taken together, these results indicate that people with PD did experience some difficulty in their motor preparation under conditions of reduced visual information. The importance of visual information in the motor performance of people with PD is discussed in detail in Chapter Six.

4.5.3 Exploratory correlation analyses: Predicting motor performance in people with PD

The exploratory correlation analyses pointed to a number of factors that influenced task performance in the PD group. First, the weak correlation between disease duration and disease severity is consistent with Experiment 1 and suggests that when people with PD are on anti-Parkinsonian medication, disease duration is not a useful predictor of symptom

severity. Second, both measures of disease severity (the Unified Parkinson's Disease Rating Scale and the Hoehn and Yahr scale), but not disease duration, were strongly positively correlated with the number of errors and anticipations made by participants with PD. This suggests that those participants with the more severe symptoms (but not necessarily those who had had the disease longer) made more mistakes when performing the task.

Third, disease severity and disease duration showed different patterns of correlations with the dependent measures in the PD group. Both of the measures of disease severity, but not disease duration, strongly predicted variability, measured by standard deviations, on the four dependent measures. This pattern was also present (although slightly weaker) when variability was assessed through the coefficient of variation. This indicates that as the disease progresses, in terms of symptom severity, participants show greater variability in motor initiation and execution. This is consistent with the suggestion that PD leads to increased variability and noise in the motor system (Cunnington et al., 1996Wichmann, 1996 #135; Franz & Miller, 2002; Montgomery et al., 1991; Reed & Franks, 1998; Sheridan et al., 1987; P. Weiss et al., 1997). In addition, the moderate to strong positive correlations between disease severity and RT and DT indicate that those participants with the more severe symptoms were slower on these dependent measures. It was somewhat surprising that disease severity was not also strongly correlated with the two movement time measures, since impairments of motor execution are generally regarded to be typical in people with PD.

Also surprising were the moderate negative correlations that were found between disease duration and the two movement time measures. These suggest that, while symptom severity was a poor predictor of MT1 and MT2, the length of time since diagnosis did predict the time taken on these measures – where those participants who had had PD longer were also the faster on MT1 and MT2. If a negative correlation had been found between age and disease duration, there could be several explanations for this. It could have been argued that those participants who had had the disease longer must have been diagnosed at a relatively younger age, and may still have been younger than the more recently diagnosed participants. The faster movement time measures with increased disease duration could then reflect the fact that people with PD diagnosed later in life suffer more rapid

progression of the disease (Diederich, Moore, Leurgans, Chmura, & Goetz, 2003; Jankovic & Kapadia, 2001). Another possible explanation is that older patients have been found to have a poorer outcome with anti-Parkinsonian medication than younger patients (Diamond, Markham, Hoehn, McDowell, & Muenter, 1989). If the participants with the longer disease duration were actually younger, this negative correlation could reflect the fact that the older, more recently diagnosed, participants benefited less from their anti-Parkinsonian medication. Finally, if disease duration negatively correlated with age, one could argue that general slowing due to ageing may have contributed to these correlations (Amrhein, 1996; Inui, 1997; Krampe, 2002; Light & Spirduso, 1990; Morse, 1993; Yan, Thomas, & Stelmach, 1998). However, a correlation between disease duration and age was not found, making these explanations unlikely. Furthermore, a large clinical study comprising 451 patients found that both disease duration and age were significant independent predictors of disease severity, where those who were older and had the disease longer were also those who showed greater symptom severity (as measured by Part III, the motor examination, of the UPDRS) (Levy et al., 2005). Thus, these correlations are likely to be specific to this particular group of people with PD, and may not apply to the wider PD population.

Finally, moderate to strong positive correlations were found between the frequency of anticipations and RT in the PD group. Keeping in mind the positive correlation between the frequency of anticipations and disease severity in the PD group, these strong positive correlations suggest that the participants with the more severe symptoms made more anticipations and were also those participants who were slower on RT (across all cue conditions) within non-anticipated trials. This relationship contrasts with both healthy adult groups who showed either moderate to strong negative correlations between the frequency of anticipations and RT (the Young Adult group), or very weak relationships (the Old Adult group), and highlights an important pattern of task performance in the PD group. There are two ways that these strong positive correlations between anticipations and RT in the PD group can be viewed: (a) as a compensatory strategy; or (b) as a difficulty in withholding the response until the illuminated LEDs of the imperative signal had been turned off.

First, it has been suggested that people with PD use relevant external information to compensate for their motor difficulties (Jahanshahi & Frith, 1998; Oliveira et al., 1997). The dysfunction of the basal ganglia and the underactivation of the SMA in people with PD

are thought to lead to a difficulty in the internal control of movement (Cunnington et al., 1996; Georgiou et al., 1994; Oliveira et al., 1997; Verschueren et al., 1997). However, the faulty basal ganglia circuits are less important than other neural structures in controlling the initiation and execution of externally timed movements (Schenk, Baur, Steude, & Botzel, 2003). It is argued that external information is important because it makes movements less dependent on the faulty basal ganglia (Lewis et al., 2000; Majsak et al., 1998; Oliveira et al., 1997). An alternate system – the lateral premotor system – controls and guides movement prompted by external information (Cunnington et al., 1996; Halsband et al., 1994; Hanakawa et al., 1999; Jahanshahi & Frith, 1998; Mushiake et al., 1991).

Further, different motor areas have been found to be more active in people with PD than in healthy adults while they performed motor tasks. Samuel et al. (1997) found that the lateral premotor and parietal cortices were significantly more active in people with PD than healthy adults when performing complex sequential tasks. These authors suggest that people with PD rely on alternate motor systems when performing these tasks to compensate for the basal ganglia dysfunction. Sabatini et al. (2000) also found a shift in brain activation in people with PD. While performing sequential finger movements, people with PD showed a relative increase in fMRI activation of the lateral premotor and parietal cortices and a relative decrease in the SMA and DLC. It was suggested that this overall shift in activation reflects an attempt to recover motor functioning by recruiting other motor systems to compensate for the motor deficits associated with the SMA.

Related to this is the idea that external information acts as a partial substitute for the basal ganglia that would normally be responsible for the internal triggering of the elements of a movement (Georgiou et al., 1994; Georgiou et al., 1993; Kritikos et al., 1995; McIntosh et al., 1997). A similar idea is that external cues act by drawing attention to the requirement of the task, and provide more conscious motor control that bypasses the basal ganglia (Cunnington et al., 1999a; Jahanshahi & Frith, 1998; Lewis et al., 2000; Morris et al., 1996; Oliveira et al., 1997).

In this experiment the PD group did not make significantly more anticipations than either of the healthy adult groups. However, when participants in the PD group did not anticipate, they suffered prolonged RTs. This positive correlation between the number of anticipations and RT on non-anticipated trials may reflect an increased tendency by participants in the

PD group with the more severe symptoms to anticipate in order to take advantage of the visual information of the imperative signal. Thus, the relationship between anticipations and RT in the PD group may reflect this compensatory strategy.

An alternative explanation for these correlations between anticipations and RT is that they reflect a stronger obligatory response to visual information in people with PD than in healthy adults (Praamstra & Plat, 2001). There is evidence that people with PD are more influenced by irrelevant visual information than healthy adults, showing greater RT slowing with the presence of visual distractors around a target (Praamstra et al., 1999; Praamstra et al., 1998). In addition, lateralised readiness potentials (LRPs), which indexes the starting point of motor preparation and is used to infer when a response is selected (Van der Lubbe et al., 2004), was found to be larger and earlier in the PD group in response to the visual distractors than in the healthy adult group (Praamstra et al., 1999; Praamstra et al., 1998). It was suggested that people with PD cannot help but respond more strongly to external information than healthy adults (Praamstra & Plat, 2001). It has been suggested that the dysfunction of the basal ganglia decreases the excitability of cortical inhibitory circuits in people with PD (Ridding et al., 1995), possibly making the motor cortex more susceptible to sensory input (Praamstra et al., 1998). As a result, visual information may more readily evoke movement-related activity in people with PD (Praamstra & Plat, 2001). There is also evidence from anti-saccade tasks that suggest that people with PD show increased difficulty relative to healthy adults in inhibiting the prepotent response towards the target (Briand, Strallow, Hening, Poizner, & Sereno, 1999; Crevits & De Ridder, 1997; Kitagawa, Fukushima, & Tashiro, 1994).

On this explanation then, these correlations between the frequency of anticipations and RT in the current experiment may reflect an increased difficulty in the PD group in withholding their response while the visual information of the imperative signal is presented. The participants in the PD group who suffered the greater symptom severity and prolonged RTs may also have found it harder to ignore the visual information of the imperative signal, resulting in increased tendency to respond while it was illuminated.

4.5.4 Future direction

As discussed in the previous section, it is not clear whether people with PD strategically use visual information to compensate for their difficulties in the internal control of movement, or whether visual information evokes a stronger obligatory response in people with PD. Experiment 3 aimed to decide which of these is more plausible. In Experiment 3, participants performed similar sequences to that of Experiment 1 and 2 but they were required to perform the sequence indicated by the cue and not by the imperative signal. In this experiment, participants were presented with only valid and full-invalid cue conditions. Importantly, the imperative signal provided either valid or invalid visual information about the sequence while the participant initiated and executed the sequence.

If the PD group are able to ignore such information when it is invalid and not helpful, this would indicate that the participants with PD used the visual information to compensate for their motor difficulties. In contrast, if the PD group experience difficulties in ignoring such invalid information when performing the task, this would indicate that visual information had evoked a stronger obligatory response in the participants with PD.

Chapter Five: The role of visual information in the motor control of people with PD

5.1 Introduction

5.1.1 A summary of relevant findings in Experiment 2

The pattern of anticipations in Experiment 2 suggests that external information is particularly important to people with PD. While all three groups made roughly the same number of anticipations, the relationship between anticipations and RT varied markedly between the groups. The two healthy adult groups showed a relationship that reflected a speed/accuracy trade-off (the Young Adult group) or no relationship at all (the Old Adult group). In the PD group, there was a positive correlation between anticipations and RT, so that those participants who made more anticipations also showed markedly slower RT on non-anticipated trials. Further, there was a positive correlation between anticipations and the two measures of disease severity. So the participants with PD with the more severe symptoms were both slower on RT and the more likely to make anticipations.

5.1.2 An overview of Experiment 3

As has been suggested, the relationship in Experiment 2 between anticipations and RT could be explained in two ways. People with PD may use external information to compensate for their difficulties in controlling internally driven movement. If this were the case, the PD participants may have anticipated to allow them to initiate their response while the visual information of the imperative signal was still available. Alternatively, this relationship may reflect a stronger obligatory response in people with PD. If this were the case, these participants may have found it difficult to withhold their response while the LEDs of the imperative signal were illuminated. The first aim of Experiment 3 was to decide which of these two alternatives is most likely.

In Experiment 3, participants performed a task very similar to the previous two experiments, but with one major change to the methodology. In Experiments 1 and 2,

participants performed the sequence indicated by the imperative signal. In each case, participants had previously been shown a cue sequence, which was valid, neutral, part-invalid or full-invalid, relative to the imperative signal. In Experiment 1, the LEDs of the imperative signal remained illuminated throughout the initiation and execution of the sequence. In Experiment 2, the LEDs of the imperative signal were illuminated only briefly, and were turned off before initiation. So in Experiment 2, participants performed the sequence without the guidance of the imperative signal during its initiation and execution.

In contrast to the previous experiments, participants in Experiment 3 performed the sequence defined by the previously illuminated red LEDs of the cue. The illuminated LEDs of the imperative signal provided either valid or full-invalid visual information (the valid and invalid guidance conditions), and remained illuminated while participants initiated and executed the sequence. So in Experiment 3, participants performed the sequence indicated to the cue, while either valid or invalid visual information was presented to them through the imperative signal.

If people with PD use external information strategically to compensate for their motor difficulties, it would be expected that they could ignore the invalid guidance condition to the same extent as the healthy adults. On the other hand, if visual information evokes a stronger obligatory response in people with PD, the invalid visual guidance condition would be expected to lead to both increased errors and significant slowing on the four dependent measures in the PD group.

Correlation analyses were carried out in the present experiment in order to identify patterns of task performance in the three experimental groups. It was predicted that positive correlations would be found between the measures of disease severity and task performance in the PD group (both in terms of the time taken on the four dependent measures and the number of errors made). This would indicate that the participants who suffered the more severe symptoms were also the slower and more error prone. In addition, if people with PD experience a specific difficulty in ignoring the visual information of the invalid guidance condition, this would be expected to worsen with disease progression, and be evident in strong positive correlations between disease severity and the invalid guidance condition.

Implicit in the design of this task is the assumption that participants will be able to: (a) prepare their response according to the previously illuminated cue; and (b) maintain their response until they are required to initiate it when the imperative signal is presented. In light of suggestions that people with PD either show an abnormal decay of their motor preparation (Gentilucci & Negrotti, 1999b; Gueye et al., 1998; Negrottti et al., 2005; Sheridan et al., 1987), or experience difficulties in maintaining their prepared response over time due to poor attentional control (Pollux & Robertson, 2001), a second aim of this experiment was to examine the preparation and maintenance of prepared responses in people with PD and healthy adults. To examine this, the current experiment used different foreperiods (250, 850, 2000 ms) between the cue and the imperative signal. This contrasts with both Experiments 1 and 2, which used fixed and relatively brief foreperiods (450 ms and 250 ms for Experiments 1 and 2, respectively). In the valid guidance condition, but not in the invalid guidance condition, the sequence is re-presented in the imperative signal. For this reason, the maintenance of the prepared response was examined for each guidance condition separately. The influence of foreperiod was examined initially in the valid guidance condition to assess the basic maintenance of a prepared response until response initiation (without the influence of the visual guidance in the imperative signal). The influence of foreperiod was then examined in the invalid guidance condition to assess the maintenance of the response during its initiation and execution. It was expected that if the PD group does suffer a decay in motor preparation, they would show prolonged RTs as the foreperiod lengthens in the valid guidance condition. This would indicate that they experience difficulties in maintaining their prepared response over the longer foreperiods, and consequently were required to re-prepare their response with the presentation of the imperative signal. Because the sequence is presented for a second time in the valid guidance condition, only RT is a useful dependent measure in assessing the maintenance of the prepared response. On the other hand, it was expected that difficulties in maintaining the prepared response would be evident on all four dependent measures in the invalid guidance condition, as the required response is not presented again in the imperative signal. Slowing across all four dependent measures would reflect a difficulty in maintaining the prepared response during its initiation and execution.

5.2 Method

5.2.1 Participants

Seventeen individuals with idiopathic PD participated in Experiment 3 (11:6 M:F), all of whom participated in the previous experiments. The participants in the PD group were aged between 54 and 84 years, with a mean of 69 years. Disease duration ranged between two and 18 years, with a mean of seven years. This experiment was undertaken approximately six months after Experiment 2, and was again performed under the influence of the patients' normal anti-Parkinsonian medication. There were 18 of the original healthy age-matched adults (7:11 M:F, aged between 46 and 87 years, with a mean of 68 years), and 18 of the healthy young adults (9:9 M:F, aged between 22 and 28 years, with a mean of 26 years). Again, age was not significantly different in the two older groups, t (33) = .30, p = .76. While the general ageing effect between the two healthy adult groups was included in the analysis of Experiment 3, the primary comparison of interest was that between the PD and Old Adult groups. This is consistent with the design of previous studies that have also included a group of healthy young adults but have not discussed their results in detail (Hocherman et al., 2004; Stern et al., 2005; P. Weiss et al., 1996).

5.2.2 Tests Administered

All three groups were administered the motor task, and all participants with PD were re-administered the first three sections of the Unified Parkinson's Disease Rating Scale (UPDRS) (Fahn et al., 1987) to assess symptom severity.

5.2.2.1 The Motor Task: Design and Procedure

As in the previous two experiments, participants in Experiment 3 were required to perform two-movement sequences on the response board. In all experiments, the cue sequence was illuminated, followed by the imperative signal sequence. In Experiments 1 and 2, the participants were required to perform the sequence of the imperative signal. By contrast, in

Experiment 3, the sequence that participants were required to perform was determined by the cue sequence. The sequence in the imperative signal was then either valid or invalid relative to the cue sequence.

Each trial began with the red and green LEDs above the central start key flashing on and off until that key was depressed with the participant's index finger for 2000 ms. The sequence to be performed was then presented in the cue through the illumination of two red LEDs for 750 ms. Rather than the constant foreperiod that was presented in Experiment 1 and 2 (450 ms or 250 ms, respectively), participants in Experiment 3 were presented with three different lengths of foreperiod. Of the three foreperiods presented to participants, one-third was the short duration (250 ms), one-third was the medium duration (850 ms), and one-third was the long duration (2000 ms). They were presented in a random order across trials. During the foreperiod, all LEDs were turned off. Following the foreperiod, the two green LEDs of the imperative signal were then presented (and remained illuminated until both movements had been performed). Participants were instructed to make the movements according to the cue as quickly and accurately as possible at the onset of the imperative signal. After the second movement had been performed, all LEDs were turned off for a 1500-ms inter-trial interval. Figure 5.1 depicts the time frame of a trial.

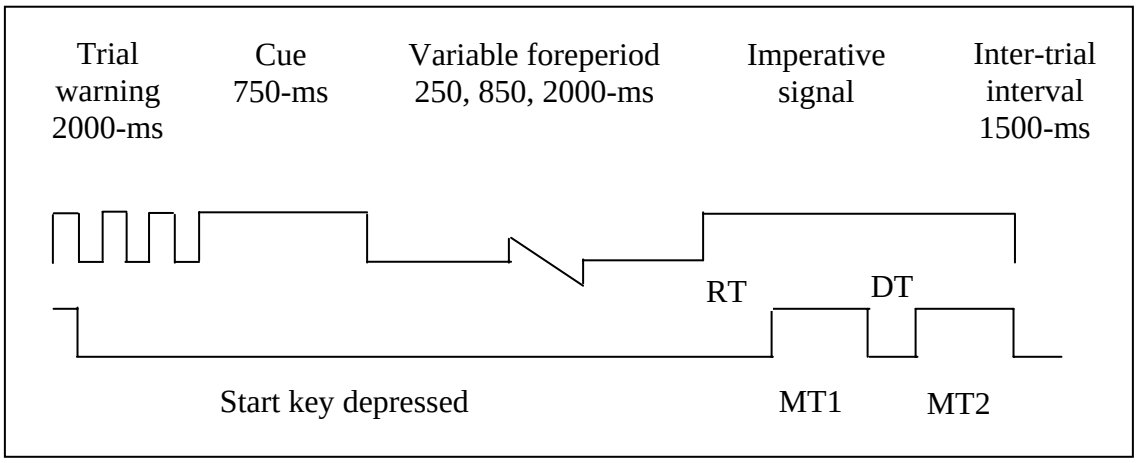

Figure 5.1 A diagrammatical representation of a typical trial in Experiment 3.
Note. It indicates the phases in which the LEDs were illuminated and turned off, and when participants were instructed to depress the start key and perform the sequence.

Trials were conduced under either a valid or invalid guidance condition: 80% of all trials were valid and 20% were invalid. On the valid guidance condition, the sequence of the illuminated imperative signal was the same as the previously presented cue. So in this case, the visual information presented to participants during the initiation and execution of the sequence was valid. On the invalid guidance condition, the sequence of the illuminated imperative signal indicated an alternate sequence to the previously presented cue. So in this case, the visual information presented to participants during the initiation and execution of the sequence was invalid.

These six conditions (two levels of guidance condition and three levels of foreperiod) were presented in 10 randomised blocks of 30 trials. In contrast to both previous experiments, the sequences in Experiment 3 comprised only uni-directional sequences. Thus, the first movement was always to one of the two target keys immediately adjacent to the central start key, and the second movement was to the outermost target key on that side of the response board. One-half of these trials contained uni-directional sequences to the left of the response board and one-half contained uni-directional sequences to the right of the response board. This followed a practice session of 15 trials, in which each condition was presented at least once. Participants performed five experimental blocks with their dominant hand and five with their non-dominant hand, alternating over the 10 blocks (the order was counter-balanced across participants).

5.2.2.2 The Unified Parkinson's Disease Rating Scale (UPDRS) and the Hoehn and Yahr scale

The first three sections of the UPDRS were again administered to the PD group to assess the severity of their symptoms. A modified global score on both the UPDRS and the Hoehn and Yahr scale were calculated for each participant.

5.3 Data Analysis

Mean median times were calculated for the two guidance conditions (valid and invalid), and the three foreperiods (short, medium, and long) for the four dependent measures. Reaction time (RT) was measured in the same way as in Experiment 1 (the time from the onset of the imperative signal to when participants lifted their finger from the start key). The three measures of execution (the first movement time, MT1; dwell time, DT; and the second movement time, MT2) were taken in the same way as both previous experiments. Because there was no baseline neutral measure in this experiment, the examination of overall group differences on the four dependent measures was taken from the valid guidance condition only. This was the more appropriate of the two guidance conditions because there are indications that invalid visual information may exert a stronger influence on people with PD than on healthy adults (Praamstra & Plat, 2001). It is possible that the valid visual information may improve the performance of the PD group, however the only disadvantage of this would be to minimise any group differences that are present.

To investigate the influence of foreperiod duration on the maintenance of motor preparation, the two guidance conditions were examined separately. Only RT was useful in the valid guidance condition because the required sequence was re-presented in the imperative signal. Thus, any difficulties in maintaining the original prepared response would not be evident following this re-presentation of the sequence. In contrast, all four dependent measures were of use in the invalid guidance condition. In this case, since the sequence was not re-presented in the imperative signal, the original prepared response needed to be maintained during its entire initiation and execution. The effect of guidance condition and any interaction that may be found between guidance condition and foreperiod in the three groups was assessed through a repeated measures analysis of variance for each of the four dependent measures. In addition, the effect of the invalid guidance condition was calculated relative to the valid guidance condition for each participant. This was done using the following formula: $((RT_{invalid} - RT_{valid})/RT_{valid}) \times 100$. This was used to examine the relative effect of the invalid guidance condition on the three groups over the four dependent measures.

Correlation analyses were also undertaken for each group to establish what factors contributed to their performance. There were two variables used. First, and specific to the PD group, Pearson's correlation coefficients were calculated between disease duration and measures of disease severity and performance on the task. Second, Pearson's correlation coefficients were calculated between the number of errors made and task performance within each group. All of these relationships were examined in terms of: (a) overall group differences on the four dependent measures between the valid and invalid guidance conditions; (b) the additional influence of foreperiod on the guidance conditions; and (c) the relative effect of the invalid guidance condition.

5.4 Results

Section 5.4.1 outlines disease severity in the PD group. Section 5.4.2 outlines the data screening of the motor task. The main results of this experiment are then outlined in the three subsequent sections. Section 5.4.3 outlines the group differences on the valid guidance condition in terms of overall time to perform the four dependent measures, and the effect of foreperiod on RT. Section 5.4.4 addresses the effect of the guidance condition on people with PD relative to healthy adults. This section is separated into: a) overall group differences on the four dependent measures between the valid and invalid guidance conditions; and b) the effect of foreperiod on the invalid guidance condition over the four dependent measures. Section 5.4.5 presents the correlation analyses.

5.4.1 Disease severity of the PD group: UPDRS and the Hoehn and Yahr scale

On this second administration of the modified UPDRS, the PD group obtained a mean global score of 43 (SEM = 3.0) out of a possible 176. The group obtained a mean stage of 2.6 (SEM = 0.1; range: 1.5 to 3.5) out of a possible 5.0 on the modified Hoehn and Yahr scale. Table 22 shows the comparison between this administration and the one in Experiment 2. Of the 21 participants with PD from Experiment 2, 17 participated in Experiment 3. There were no participants who showed a particularly large deterioration from Experiment 2.

Table 22 Mean scores of the UPDRS and the Hoehn and Yahr scale for the PD group over Experiment 2 and 3 (SEM presented in parentheses).

	Experiment 2		Experiment 3		Possible total
Global UPDRS	38	(3.0)	43	(3.0)	176
Hoehn and Yahr	2.5	(0.1)	2.6	(0.1)	5.0

5.4.2 Motor task: Data screening and preliminary analysis

5.4.2.1 The frequency of errors

Responding before the imperative signal had been presented and incorrect responses (making contact with the wrong key) were coded as errors and removed[5]. Both the Young and Old Adult groups made an average of 2% errors (SEM = 0.4 and 0.3, respectively), while the PD group made an average of 3% (SEM = 0.8). There was no significant difference between the groups.

5.4.2.2 Variability on the four dependent measures

As was done in the two previous experiments, variability within the four dependent measures was calculated for each participant (using both standard deviations and the coefficient of variation). There were significant differences in the standard deviation: of RT between the groups on both the valid and invalid guidance conditions (F (2, 52) = 8.43, p < .01, and F (2, 52) = 4.24, p < .05, respectively); of MT1 on both conditions (F (2, 52) = 8.29, p < .01 and F (2, 52) = 4.81, p < .05, respectively); of DT on both conditions (F (2, 52) = 9.81, p < .001 and F (2, 52) = 9.37, p < .001, respectively); and of MT2 on the valid guidance condition (F (2, 52) = 4.97, p < .05). The most important post hoc analyses were between the PD and Old Adult groups. While the PD group was more variable than the Old Adult group on all of these dependent measures, this only reached significance on MT2 on

[5] Due to the way the data was processed, incorrect responses and responding before the imperative signal could not be examined separately.

the valid guidance condition (t (33) = 2.35, p < .05). Using the coefficients of variation, there was only a difference on RT between the groups on the valid guidance condition (F (2, 52) = 4.27, p < .05). Post hoc analyses reveal that the Young Adult group was significantly less variable than both the Old Adult group (t (34) = 2.26, p < .05) and the PD group (t (33) = 2.60, p < .05). There were no significant differences in variability according to the coefficients of variation in the PD and Old Adult groups.

Taken together, these results are consistent with both Experiments 1 and 2 and indicate that while the PD group's performance was more variable than the healthy adult groups on the four dependent measures (as shown by the standard deviations), most of these differences disappeared when controlling for mean latency differences between the groups on the four dependent measures (through the coefficient of variation).

5.4.2.3 The effect of handedness on the performance of the motor task

As was the case in both previous experiments, the blocks performed by the left and right hand were collapsed together for the overall analysis.

5.4.2.4 The effect of practice on the performance of the motor task

There were no significant main effects of Block number or interactions on any of the four dependent measures. This indicates a similar practice effect for the three groups.

5.4.3 Group differences on the baseline valid guidance condition

The valid guidance condition was regarded as the baseline measure used to assess the three groups without the influence of invalid visual guidance (similar to the neutral cue condition of Experiment 1 and 2). It was expected that the PD group would be significantly slower across both MT1 and MT2, and possibly on RT and DT relative to the Old Adult group. In addition, if the participants with PD did suffer a difficulty in maintaining their prepared

response, greater slowing on RT relative to the Old Adult group was expected as the foreperiod lengthens.

5.4.3.1 Mean median times on the measures of response initiation and execution

Table 23 shows the differences between the groups on the valid guidance condition across the four dependent measures. There was a significant main effect of Group on all four dependent measures – RT (F (2, 50) = 13.04, $p < .001$, $\eta^2 = 0.34$); MT1 (F (2, 50) = 19.66, $p < .001$, $\eta^2 = 0.44$); DT (F (2, 50) = 14.10, $p < .001$, $\eta^2 = 0.36$); and MT2 (F (2, 50) = 14.06, $p < .001$, $\eta^2 = 0.36$). Post hoc analyses reveal that the Old Adult group was significantly slower than the Young Adult group on all four dependent measures. They took 108 ms longer on RT (t (34) = 3.78, $p < .005$), 56 ms longer on MT1 (t (34) = 4.63, $p < .001$), 22 ms longer on DT (t (34) = 2.86, $p < .01$) and 35 ms longer on MT2 (t (34) = 3.84, $p < .005$) than the Young Adult group.

In addition, the PD group was slower than the Old Adult group on all four dependent measures (see Table 23). As expected and consistent with Experiment 1, the PD group was significantly slower than the Old Adult group on both measures of movement time, where they were 102 ms slower on MT1 (t (33) = 3.34, $p < .005$), and 96 ms slower on MT2 (t (33) = 3.10, $p < .005$). In addition, while the PD group was 42 ms slower than the Old Adult group on DT (t (33) = 2.87, $p < .01$), the 40 ms slowing on RT was calculated as a moderate effect size of 0.41 through Cohen's *d* and was not significant (t (33) = 1.22, $p = .23$).

Table 23 Mean median times of the four dependent measures (in ms) by experimental group, using the valid guidance condition only (SEM presented in parentheses).

	Young Adult		Old Adult		PD		Row Means	
RT	339	(21)	447	(21)	486	(22)	424	(12)
MT1	137	(18)	193	(18)	295	(18)	208	(10)
DT	90	(9)	112	(9)	154	(9)	119	(5)
MT2	118	(18)	153	(18)	249	(18)	173	(10)
Total	683	(26)	903	(37)	1184	(79)		

5.4.3.2 The effect of foreperiod

Table 24 shows a progressive shortening of RT as the foreperiod increased in the three experimental groups (F (2, 100) = 23.14, $p < .001$, $\eta^2 = 0.32$). RT was 13 ms shorter following the 850-ms foreperiod than the 250-ms foreperiod (t (52) = 3.34, $p < .005$), and was 20 ms shorter following the 2000-ms foreperiod than the 850-ms foreperiod (t (52) = 4.76, $p < .001$). There was no interaction of Group and Foreperiod on RT, indicating that all three groups showed a similar shortening of RT with increased foreperiod. This result is important as it suggests that people with PD did not suffer a difficulty in maintaining their prepared response. If participants did suffer such a difficulty, a lengthening of RT as the foreperiod increased would have been expected, reflecting the need to re-prepare the sequence with the presentation of the imperative signal. This will be discussed in more detail in the Discussion.

Table 24 Mean median times of RT (in ms) on the valid guidance condition by experimental group and foreperiod duration (SEM presented in parentheses).

Foreperiod (ms)	Young Adult		Old Adult		PD		Row means	
250	352	(22)	465	(22)	501	(23)	439	(13)
850	340	(22)	450	(22)	488	(22)	426	(13)
2000	324	(21)	425	(21)	469	(21)	406	(12)

5.4.4 The effect of guidance condition

One of the main aims of this experiment was to determine how best to understand the influence of visual guidance on the motor performance of people with PD. If people with PD use visual information to compensate for their motor difficulties, it was expected that the PD group would be able to ignore such information when it was invalid and unhelpful. If this were the case, they would not show significantly greater slowing relative to healthy adults on the invalid guidance condition. On the other hand, if visual information evokes a stronger obligatory response in people with PD, significantly greater slowing relative to healthy adults would be expected on the invalid guidance condition.

Further, the influence of the invalid visual guidance condition may vary depending on the duration of the foreperiod. Any interactions found between guidance condition and foreperiod would be used to assess both the influence of visual guidance and the maintenance of motor preparation in people with PD.

5.4.4.1 Measures of response initiation and execution

Table 25 show the three groups' performance on the four dependent measures on the valid and invalid guidance conditions. There was a significant main effect of Guidance Condition on RT (F (1, 50) = 32.04, $p < .001$, $\eta^2 = 0.39$), with a 69-ms slowing in initiating the

sequence under the invalid guidance condition relative to the valid guidance condition, but there was no significant interaction between Group and Guidance Condition on RT (see Table 25). For MT1, while there was also a significant main effect of Guidance Condition (F (1, 50) = 5.87, $p < .05$, $\eta^2 = 0.11$), this was qualified by a significant interaction between Group and Guidance Condition on MT1 (F (2, 50) = 4.00, $p < .05$, $\eta^2 = 0.14$). Table 25 shows that while both the Young and Old Adult groups showed equivalent MT1s in the two guidance conditions, the PD group suffered an 10-ms cost on MT1 under the invalid guidance condition (t (16) = 2.12, $p < .05$).

While there was no main effect of Guidance Condition on DT (with only a 1-ms cost on invalid trials), there was a significant interaction between Group and Guidance Condition on DT (F (2, 50) = 3.85, $p < .05$, $\eta^2 = 0.13$). As shown in Table 25, both the Young and Old Adult groups produced very similar DTs with the valid and invalid guidance conditions. In contrast, the PD group again suffered a slight cost on DT (4 ms) on invalid trials (t (16) = 2.93, $p < .05$). Despite the small difference, this latter interaction may in part have reached significance because of moderate observed power (0.67) for this analysis. Finally, there was no main effect of Guidance Condition or interaction of Group and Guidance Condition on MT2 (see Table 25).

Table 25 Mean median times of the four dependent measures (in ms) by experimental group and guidance condition (SEM presented in parentheses).

		Young Adult		Old Adult		PD		Row means	
RT	Valid	339	(21)	447	(21)	486	(22)	424	(12)
	Invalid	404	(36)	500	(36)	575	(37)	493	(21)
MT1	Valid	137	(18)	193	(18)	295	(18)	208	(10)
	Invalid	138	(19)	193	(19)	306	(19)	212	(11)
DT	Valid	90	(9)	112	(9)	154	(9)	119	(5)
	Invalid	89	(9)	112	(9)	158	(9)	120	(5)
MT2	Valid	118	(18)	153	(18)	249	(18)	173	(10)
	Invalid	118	(18)	153	(18)	251	(18)	174	(10)

5.4.4.2 The relationship between guidance condition and foreperiod

There was a significant interaction between Guidance Condition and Foreperiod on RT (F (2, 100) = 25.14, $p < .001$, $\eta^2 = 0.34$). The cost of the invalid guidance condition relative to the valid guidance condition was 108 ms following the 250-ms foreperiod (t (52) = 7.26, $p < .01$), but only 63 ms following the 850-ms foreperiod (t (52) = 4.68, $p < .01$), and 37 ms following the 2000-ms foreperiod (t (52) = 3.06, $p < .01$). Figure 5.2 depicts the calculated RT change of the invalid guidance condition relative to the valid guidance condition. As in the previous two studies, a positive RT change reflects a relative cost. Thus, Figure 5.2 shows that the cost of the invalid guidance condition was the greatest on the 250-ms foreperiod, but weakened as the foreperiod lengthened. There was no significant three-way interaction between Group, Guidance Condition, and Foreperiod on RT, with all three groups displaying a similar pattern to that shown in Figure 5.2.

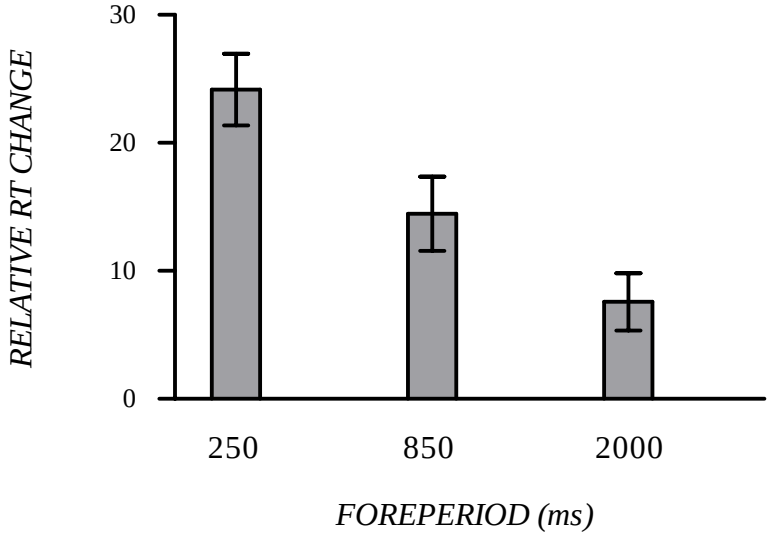

Figure 5.2 The RT change of the invalid guidance condition relative to the valid guidance condition across the three foreperiods on RT (see text for details of the relative change).

There were no significant interactions between Guidance Condition and Foreperiod Delay on any of the measures of execution. There was, however, a three-way interaction between Group, Guidance Condition, and Foreperiod Delay on MT2 (F (4, 100) = 3.74, $p < .01$, η^2 = 0.13). In the Young Adult group MT2 was identical over the three foreperiods under the valid and the invalid guidance conditions. However both the Old Adult and the PD group showed differences between the two guidance conditions over the foreperiods. Participants in the Old Adult group performed MT2 on the invalid guidance condition 3-ms faster than they did with the valid guidance condition, on the 2000-ms foreperiod (t (17) = 2.64, $p <$ .05). In contrast, participants in the PD group suffered a 7-ms cost when performing the invalid guidance condition following the 2000-ms foreperiod, although this did not reach significance (t (16) = 1.91, p = .07). Despite small group differences, this latter three-way interaction on MT2 is likely to be the result of strong observed power (0.87). Taken together, these results show that people with PD do not have a difficulty in maintaining their prepared response over time, a difficulty that would have been particularly evident in the invalid guidance condition due to the fact that the sequence is not re-presented in the imperative signal.

5.4.5 Exploratory correlation analyses

The effect of disease duration and measures of disease severity (the UPDRS and the Hoehn and Yahr scale) were examined in the PD group. Based on the results from Experiment 1 and 2, it was expected that disease duration would be a poor predictor of disease severity in the PD group; remembering that in Experiment 3 the PD participants are on their normal anti-Parkinsonian medication. It was also expected that measures of disease severity (but not disease duration) would correlate positively with participants' performance on the task. This would indicate that, as the disease progresses, those participants who suffered the greater symptom severity would also be the slower and more variable in performing the task. Further, if participants in the PD group did experience an additional difficulty in performing the task with invalid visual information, the correlations with disease severity would be expected to be even stronger on the invalid guidance condition than on the valid guidance condition. This would reflect the fact that as the disease progresses, people with PD suffer increased difficulty in performing their movements when presented with invalid

visual information. Correlations between task performance and the number of errors made are also presented for the three groups. It was expected that if the PD group did experience difficulty in performing the task with the invalid guidance condition, those participants who suffered the greatest slowing would also show the greater number of errors.

5.4.5.1 The relationship between disease duration and disease severity in the PD group and task performance

Table 26 presents the Pearson's correlation coefficients between disease duration, the two measures of disease severity, errors on the task, and the age of participants in the PD group. A very similar pattern was found to that in Experiment 2. The two measures of disease severity were strongly positively correlated with each other, but neither was related to disease duration. So when people with PD are on anti-Parkinsonian medication, the length of time since their diagnosis is a poor predictor of the severity of their symptoms. Further, while disease duration was not related to the number of errors made by participants in the PD group, both measures of disease severity were related to the number of errors. The Hoehn and Yahr scale was a particularly strong predictor of accuracy on the task in the PD group. Finally, participants' age was moderately correlated with both the Hoehn and Yahr scale and the number of errors. In contrast, age was not related to either the UPDRS or disease duration.

Table 26 Pearson's correlation coefficients between disease duration, disease severity, errors, and age in the PD group.

	Dis. Dur[a]	UPDRS	H and Y[b]	Errors	Age
Dis. Dur		-.15	-.18	.01	-.19
UPDRS			.75**	.42	.25
H and Y				.61**	.50*
Errors					.41

[a] Denotes disease duration. [b] Denotes the Hoehn and Yahr scale.

* Indicates significant at the .05 level (2-tailed). ** Indicates significant at the .01 level (2-tailed).

Table 27 shows that, as was found in Experiment 2, both measures of disease severity (but not disease duration) shared moderate to strong Pearson's correlation coefficients with variability (according to standard deviations) on the four dependent measures. This shows that as symptom severity increases, participants in the PD group show greater variability in their motor initiation and execution. In contrast, correlations with the coefficient of variation failed to indicate any significant relationship with either disease duration or measures of disease severity.

Table 27 Pearson's correlation coefficients between disease duration and disease severity in the PD group and variability (using standard deviations) on the four dependent measures, by guidance condition.

		Disease Duration	UPDRS [a]	Hoehn and Yahr
Valid	RT	-.36	.73**	.78**
	MT1	-.34	.61*	.56*
	DT	-.03	.69**	.51*
	MT2	-.47	.47	.42
Invalid	RT	-.48	.53*	.54*
	MT1	-.10	.42	.62**
	DT	-.10	.73**	.54*
	MT2	-.15	.49*	.26

[a] Denotes the Unified Parkinson's Disease Rating Scale.

* Indicates significant at the .05 level (2-tailed). ** Indicates significant at the .01 level (2-tailed).

Table 28 shows the Pearson's correlation coefficients between disease duration and measures of disease severity and the four dependent measures in the PD group. Both measures of disease severity shared strong positive correlations with RT on the two guidance conditions. This shows that those participants in the PD group with the more severe symptoms were also the slower on RT across both the valid and invalid guidance conditions. The UPDRS also shared moderate to strong positive correlations with the remaining three dependent measures, showing that the participants with the more severe symptoms were slower to perform all measures of execution across the two guidance conditions. While the Hoehn and Yahr scale predicted the time taken on the measures of execution, the relationship was somewhat weaker than that found with the UPDRS. In contrast, disease duration shared weak correlations with both RT and DT. This pattern is consistent with that found in Experiment 2, and suggests that the time since diagnosis is a poor predictor of RT and DT when participants with PD take their normal anti-Parkinsonian medication. However, disease duration did share moderate negative correlations with both MT1 and MT2. This is again consistent with Experiment 2, and suggests that those participants who had had PD longer were faster on both measures of execution. In addition, similar patterns were exhibited when the three foreperiods were examined separately. Both measures of disease severity correlated strongly with RT (with the UPDRS also strongly correlated with the three measures of execution). While disease duration was weakly correlated with RT and DT, moderate negative correlations were still found with MT1 and MT2. Finally, only weak correlations were found between disease duration and disease severity and the relative effect of the invalid guidance condition on the four dependent measures, and are therefore not presented.

Table 28 Pearson's correlation coefficients between disease duration and disease severity in the PD group and the four dependent measures, by guidance condition.

		Disease Duration	UPDRS[a]	Hoehn and Yahr
RT	Valid	.01	.78**	.65**
	Invalid	-.23	.73**	.61**
MT1	Valid	-.41	.64**	.41
	Invalid	-.44	.67**	.45
DT	Valid	-.14	.65**	.45
	Invalid	-.16	.68**	.48
MT2	Valid	-.43	.57*	.35
	Invalid	-.44	.56*	.34

[a] Denotes the Unified Parkinson's Disease Rating Scale.

* Indicates significant at the .05 level (2-tailed). ** Indicates significant at the .01 level (2-tailed).

5.4.5.2 The relationship between errors and performance on the motor task

The frequency of errors made by participants in each of the three groups was also used to examine the performance on the motor task. While the three groups were not significantly different in the number of errors made (and all produced only a small number of errors in total), correlations were still deemed to be a useful measure (see 5.4.1). Only weak to moderate correlations were found between errors and performance on the four dependent measures in the three groups (see Table 29). In the Young Adult group, errors were very weakly correlated with RT, DT, and MT2. The slightly stronger negative correlations that were found with MT1 show that those participants in the Young Adult group who made more errors were also faster on MT1, in both the valid and invalid guidance conditions (see Table 29).

Table 29 also shows that errors were weakly correlated with both MT1 and MT2 in the Old Adult and the PD groups. Although not significant, moderate positive correlations were found with RT. This relationship was stronger when participants performed the sequence under the invalid guidance condition. Thus, participants in both groups who made more errors were the slower participants on RT (especially under the invalid guidance condition). Finally, in the Old Adult group, the opposite pattern was found with DT. Again, although they did not reach significance, there were moderate negative correlations between errors and DT, showing that those participants who were more error prone were also the faster on DT. These patterns remained consistent when the correlations were made with the three foreperiods. Only weak correlations were found between the frequency of errors and the relative effect of the invalid guidance condition on the four dependent measures in all groups.

Table 29 Pearson's correlation coefficients between the frequency of errors and the four dependent measures, by experimental group and guidance condition.

		Young Adult	Old Adult	PD
RT	Valid	.05	.38	.36
	Invalid	-.05	.45	.45
MT1	Valid	-.32	.02	-.07
	Invalid	-.29	-.05	-.02
DT	Valid	.02	-.34	.10
	Invalid	.10	-.35	.12
MT2	Valid	-.17	-.03	-.06
	Invalid	-.17	-.06	-.08

5.5 Discussion

There were two main aims of Experiment 3. The first was to establish whether external people with PD use information strategically, or whether such information exerts a stronger obligatory response. The second was to determine whether people with PD suffered any difficulties in maintaining their motor preparation over time.

The first aim was examined by presenting participants with valid or invalid visual information while they initiated and executed motor sequences according to a previously illuminated cue. If participants with PD use external information strategically to compensate for their motor difficulties by making their movements less internally controlled, it was expected that they would be able to ignore such information when it is invalid and unhelpful. If this were the case, it was expected that no lengthening in their task performance, or increased errors, would be exhibited relative to healthy adults. On the other hand, if visual information evokes a stronger obligatory response in people with PD (Praamstra & Plat, 2001), then any invalid visual information would be harder to inhibit. It was expected that if this were the case, it would lead to significantly greater slowing and increased errors in the PD group.

The second aim was examined by manipulating the length of the foreperiod between the cue and the imperative signal. It was expected that if people with PD do suffer a difficulty in the maintenance of their prepared responses (either due to decay in their motor preparation or due to poor attention), they would show a greater lengthening of RTs relative to healthy adults as the foreperiod lengthened in the valid guidance condition. This would reflect the need to reprepare the response with the presentation of the imperative signal. In addition, slowing would also be expected across all four dependent measures on the invalid guidance condition as the foreperiod lengthened. Because the invalid guidance condition does not re-present the required sequence in the imperative signal, any slowing on the four dependent measures due to a lengthening of the foreperiod could be taken as evidence for difficulties in maintaining motor preparation.

The results of this experiment are discussed in the four sections below. Section 5.5.1 outlines the time taken on the four dependent measures by the PD group relative to the

healthy Old Adult group. Section 5.5.2 outlines the effect of foreperiod duration on RT on the three groups, under both the valid and invalid guidance conditions. Section 5.5.3 outlines the influence of the invalid guidance condition on people with PD and healthy adults. Section 5.5.4 addresses the correlation analyses, outlining the factors that influenced the task performance of the three groups.

5.5.1 Slowing of motor initiation and execution in people with PD

The overall group differences on the valid guidance condition were consistent with both previous experiments. The PD group was found to be significantly slower than the Old Adult group on measures of MT1, DT, and MT2. This confirms the finding that people with PD do suffer from significant slowing on measures of execution (A. M. Johnson et al., 2003; Negrottti et al., 2005; Reed & Franks, 1998; Stelmach et al., 1992; P. Weiss et al., 1997).

There is disagreement in the literature whether PD is associated with slowed RT. In this experiment, the PD group was not found to be significantly slower on RT than the Old Adult group. It has recently been suggested that significant differences are more likely to be found in task conditions where the RT of healthy adults is 300 ms or faster. In such a situation, people with PD are unable to keep up with the healthy adults (Willingham et al., 1995). In this experiment, the Old Adult group took a mean median time of 447 ms to initiate the task on the valid guidance condition. It may be that this is the reason the PD group was not found to be slower in this experiment, and that a similar task, with a more rapid RT in healthy age-matched adults, would result in a difference between the PD and Old Adult groups.

5.5.2 The maintenance of motor preparation

All three experimental groups showed a progressive benefit in their RT as the foreperiod lengthened. There was also no significant interaction between group and foreperiod on RT on the valid guidance condition. The progressive benefits to RT as the length of the

foreperiod increased can be explained in terms of increased response readiness (Bherer et al., 2003; Hauber, Giertler, & Bohn, 2001; Jurkowski, Stepp, & Hackley, 2005; Mattes & Ulrich, 1997; Van der Lubbe et al., 2004). Participants needed to be alert to the presentation of the green LEDs after only 250 ms, being the shortest foreperiod. The presentation of either of the longer foreperiods would have resulted in a progressive readiness by participants to initiate their response. The increased response readiness is due to the increased probability of the imperative signal as the foreperiod lengthened (Bherer et al., 2003; Hauber et al., 2001; Jurkowski et al., 2005; Mattes & Ulrich, 1997; Van der Lubbe et al., 2004).

If the PD group had experienced difficulties in maintaining their prepared response over the longer foreperiods (due to decay in the prepared response or due to poor attentional control), a lengthening in RT as the foreperiod increased on the valid guidance condition would have been expected. This would reflect the required re-preparation of the response with the presentation of the imperative signal. This was not found to be the case. Past research has been divided on this point. Some suggest that people with PD show an abnormal decay of their motor programs over time (Gentilucci & Negrotti, 1999b; Negrottti et al., 2005; Sheridan et al., 1987). However other past research has failed to find evidence of impaired maintenance of motor preparation in people with PD (Harrington & Haaland, 1991; Jordan et al., 1992; Stern et al., 2005; Willingham et al., 1995).

To assess the impact of foreperiod further, all dependent measures under the invalid guidance condition were examined. If participants experienced any difficulties in the initial preparation according to the cue, or in the maintenance of their motor preparation, this would be particularly evident in the invalid guidance condition. This is because in the invalid guidance condition, the sequence was not re-presented in the imperative signal. There were, however, no significant three-way interactions between group, guidance condition, and foreperiod delay for RT, MT1, or DT. This further supports the suggestion that people with PD are able to maintain their prepared response, given that RT and the early phases of motor execution were not affected by the longer foreperiods. There was a significant three-way interaction on MT2, with the PD group suffering a slightly greater cost on the invalid guidance condition with the long foreperiod than either of the healthy adult groups. While this difference was not large, it may reflect a slight difficulty in the PD

group in maintaining their prepared response during the execution of the second movement. It has been suggested that the final reach of a movement is related to on-line control (Negrottti et al., 2005). This slowing may reflect a difficulty in people with PD in controlling the final phase of the movement sequence with invalid visual information.

5.5.3 The effect of guidance condition

One aim of this experiment was to investigate whether it is more likely that people with PD use information strategically, or whether such information exerts a stronger obligatory response. This was done by comparing how people with PD and healthy adults performed the task under the valid and invalid guidance conditions. The RTs of all three groups were significantly slower in the invalid guidance condition than in the valid guidance condition. This slowing is likely to reflect the added difficulty of responding contrary to the presented visual information. This task is much like an anti-saccade task, where participants are required to inhibit the prepotent response towards the stimulus, and to produce a voluntary movement in the opposite direction to it (Briand et al., 1999; Chen, Chen, & Tsai, 1999; Cherkasova, Manoach, Intriligator, & Barton, 2002; Everling & Fischer, 1998; Kitagawa et al., 1994). Thus, the slowing in RT in all three groups of the current experiment can be taken to reflect the time needed to inhibit the visual information of the invalid guidance condition and to respond to the previously presented cue.

There was a significant interaction between guidance condition and foreperiod on RT. Participants were slower at responding in the invalid guidance condition when the foreperiod was shorter. As the foreperiod lengthened, participants were more able to ignore the invalid visual information, and move towards the correct target keys. This may be because they were provided with more time to remind themselves of the task requirements. As the foreperiod increased, the prepared response may have become more ingrained and so invalid visual information exerted less influence.

Importantly, there was no significant interaction between group and guidance condition on RT, nor was there a three-way interaction between group, guidance condition, and foreperiod on RT. This supports findings from anti-saccade tasks that also failed to find

impairment in inhibiting the salient and prepotent response in people with PD (Everling & Fischer, 1998; Fukushima, Fukushima, Miyasaka, & Yamashita, 1994; Lueck et al., 1992; Vidailhet et al., 1994). In addition, while the PD group did show an increased slowing of MT1 and DT in the invalid guidance condition, and an increased cost on MT2 following the long foreperiod delay, the greatest difference was only 10 ms and none are large enough to suggest any meaningful effect of the invalid guidance condition in the execution of the sequence.

Taken together, the pattern on RT, the similar number of errors between the groups, and the very minor slowing on the measures of execution with the invalid guidance condition suggest that the invalid information did not evoke a stronger obligatory response in people with PD. Participants in the PD group did not show evidence that the invalid visual information was more difficult to inhibit than the healthy adult groups as they initiated and executed their response. It seems then more likely that people with PD use external information strategically.

5.5.4 Exploratory correlation analyses: Predicting motor performance in people with PD

There were important patterns from the correlation analyses that also help to understand how each group performed the task. First, within the PD group, measures of disease duration and severity were not strongly correlated with each other. This is consistent with Experiment 2. Further, both measures of disease severity (the UPDRS and the Hoehn and Yahr scale) were strongly correlated with RT on both the valid and invalid guidance conditions. The UPDRS also strongly predicted the other three dependent measures. These measures of disease severity (but not disease duration) were also moderately to strongly correlated with variability on the four dependent measures (using standard deviations). Together, these show that those who suffered greater impairment from their symptoms were both slower and more variable in performing the task (Bherer et al., 2003; Kitagawa et al., 1994; Negrottti et al., 2005). Interestingly though, these correlations between disease severity and variability were not found when using the coefficient of variation. Thus, it appears that the underlying pathology of PD leads to both motor slowness and variability.

However, when allowing for the motor slowness of people with PD, this does not result in any disproportionate variability relative to healthy adults.

The correlations between RT and the measures of disease severity were very similar across the two guidance conditions. If PD led to a stronger obligatory response to visual information in people with PD (Praamstra & Plat, 2001), then stronger correlations would have been expected between disease progression and the invalid guidance condition. This would have reflected an increased difficulty for people with PD in inhibiting the invalid visual information during motor performance. The similar correlations between disease severity and the valid and invalid guidance conditions also suggest that people with PD do not have a greater obligatory response to external information than healthy adults.

Somewhat surprising were the moderate negative correlations found between disease duration and both MT1 and MT2, but not with RT or DT. These are consistent with the results of Experiment 2 and suggest that those participants who had had PD longer were also the faster on both movement time measures. However, the weak relationship that was found between disease duration and disease severity contrasts with previous research. Levy et al. (2005) found that both disease duration and age were significant independent predictors of disease severity in people with PD. Thus, these findings seem to be specific to this PD group, and may not be generalised to the wider PD population.

A final variable in examining participants' performance was the relationship between the number of errors and performance on the motor task. While errors were not related to the performance of the Young Adult group on measures of RT, DT, or MT2, weak to moderate negative correlations were found between errors and MT1 in the Young Adult group. This suggests a slight speed/accuracy trade-off, where those participants who were faster at performing MT1 across both guidance conditions were also those who made more errors. In the PD group, both measures of disease severity shared moderate positive correlations with errors. Further, while errors were not related to performance on MT1, DT or MT2 in either the PD or Old Adult groups, weak to moderate positive correlations were found with RT in both of the older groups. Thus, participants in both of these groups who made more errors were also slower on RT. Keeping in mind the relationship that was found between disease severity and both RT and errors in the PD group, this correlation between errors and RT

suggests that those participants in the PD group who suffered more severe symptoms were also those who made more errors and experienced greater slowing on RT.

5.5.5 Conclusions

In conclusion, there was little evidence to suggest that people with PD suffered significant difficulty in maintaining their prepared response over the longer foreperiods. While the lengthening on MT2 following the long foreperiod on the invalid guidance condition may reflect a slight difficulty in the final execution of the motor sequence, the PD group was no slower than the healthy adults following the longer foreperiods on RT, MT1, or DT. These findings suggest that people with PD do not suffer a difficulty in maintaining their prepared response.

The second important finding from this experiment is that the invalid guidance condition did not impact on the motor performance of people with PD more significantly than it did on that of healthy adults. The PD group did not produce significantly more errors, and their RTs were not significantly lengthened by the invalid guidance condition, than the healthy adult groups. The interactions between group and guidance condition on the measures of execution were too small to reflect any meaningful influence of the invalid guidance condition on the PD group. Finally, the correlation analyses between disease severity and RT on the two guidance conditions were very similar, indicating that as disease severity increased, individuals with PD were no more affected by the invalid guidance condition. Together, these results suggest that PD does not lead to a stronger obligatory response to external information. Instead, the results of this experiment are more consistent with the view that people with PD use external information to compensate for their motor difficulties, but are not hampered by it when it is unhelpful. External information may draw attention to the requirements of the movement, providing a more conscious motor control that in tern is less reliant on the basal ganglia. This proposition is discussed in more detail in the following chapter.

Chapter Six: General Discussion

6.1 Introduction: An overview of the thesis

This thesis first examined motor preparation in people with PD. Participants in Experiments 1 and 2 performed two-movement sequences on a response board in which the complexity of the sequence was manipulated, and in which valid, part-invalid, and full-invalid cueing was provided in advance. Both of these techniques – manipulating response complexity and cueing response-related information – are commonly used to assess motor preparation. Experiment 3 extended the investigation into motor preparation by assessing whether people with PD suffered any difficulties in maintaining their prepared response over time.

The second area of interest in this investigation was the importance of external information in the motor control of people with PD. This was first examined in Experiments 1 and 2 by varying the amount of available relevant visual information. Experiment 1 assessed the motor performance of people with PD under conditions where visual information about the movement remained present during its initiation and execution. Experiment 2 reduced the amount of visual information by showing the visual information only before the initiation and execution of the sequence. This manipulation was used to investigate whether or not, with a reduction of relevant visual information, there was a greater deterioration in the motor preparation and execution of people with PD relative to healthy adults. Experiment 3 further investigated the role of visual information. Specifically, it sought to decide whether it is more likely that external information is used strategically by people with PD to compensate for their motor impairments, or whether such information evokes a stronger obligatory response on the preparation and execution of movement in people with PD. This was investigated by presenting either valid or invalid visual information to participants as they initiated and executed their response. It was expected that if people with PD use external information strategically, they would be able to ignore invalid information, but that if invalid visual information evoked a stronger obligatory response, they would suffer deterioration in their motor performance.

Section 6.2 discusses the examination of motor preparation in people with PD. This section also discusses the results in relation to the various explanations of how PD affects motor

preparation. Section 6.3 outlines the influence of external information on the motor control of people with PD. Section 6.4 outlines a secondary, but important, finding that suggests that anti-Parkinsonian medication affects the relationship between cognitive and motor performance in people with PD. Section 6.5 addresses the methodological limitations of the investigation and their implications. Section 6.6 concludes the investigation.

6.2 Motor preparation in people with PD

There are a number of findings from this investigation that support the suggestion that motor preparation is largely preserved in people with PD. First, in both Experiment 1 and 2, the manipulation of response complexity had a similar effect on RT and measures of execution in people with PD and healthy adults. The RT of participants with PD did lengthen when performing the more complex bi-directional sequences. However this lengthening was similar to that shown by the healthy adult groups. This is consistent with some of the previous research into this issue (Bekkering et al., 2001; Reed & Franks, 1998; Stelmach & Worringham, 1988; P. Weiss et al., 1996; P. Weiss et al., 1997). In Experiment 1, this result was found in both the PD ON and the PD OFF groups.

Bekkering et al. (2001) found progressive lengthening of RT from the single movement to a two-movement uni-directional sequence, and from the uni-directional to a bi-directional sequence in both people with PD and healthy adults. This suggests that the preparation of goal-directed movement is not impaired in people with PD. Reed and Franks (1998) also found a similar lengthening of RT in people with PD and healthy age-matched adults with increased response complexity. Participants in this task were required to make a single extension movement towards a target or an extension/flexion movement to the target and back to where they started. The increased complexity of making a second movement with a change of direction increased RT in both groups by a similar extent. Again, this shows evidence of normal preparation in people with PD as the complexity of the response increased.

The manipulation of response complexity in the current investigation also had a similar effect on people with PD and healthy adults, as measured by the three measures of

execution. This further supports the idea that motor preparation is intact in people with PD. Any lengthening in these measures would suggest that additional preparation of the sequence was required during the execution of the sequence (Jennings, 1995; Stelmach et al., 1989; P. H. Weiss et al., 1999). So the manipulation of response complexity had a similar effect on RT and the measures of execution in the PD and healthy adult groups. This suggests that people with PD are able to prepare the more complex sequence before its initiation.

Second, the PD groups showed significant RT benefits of valid cueing in both Experiments 1 and 2. These results are consistent with previous findings (Hocherman et al., 2004; Jahanshahi et al., 1992a; A. M. Johnson et al., 2003; Pollux & Robertson, 2001; Praamstra et al., 1996; Willingham et al., 1995). Willingham et al. (1995) had participants make aimed movements towards a target key with either their right or left index finger. A valid cue was presented before the imperative signal indicating the required target key. Participants with PD and healthy age-matched adults showed similar benefits of being cued this information, suggesting that they were able to prepare their response in advance. Johnson et al. (2003) also found similar RT benefits with valid cueing about an upcoming movement in people with PD (both on and off their medication, which is similar to Experiment 1) and healthy adults. In this task, participants were required to move from a central start key to one of two peripheral target keys. These authors concluded that people with PD were able to use the information in the valid cue to prepare the response in advance (A. M. Johnson et al., 2003). The RT benefit of valid cueing demonstrated in Experiments 1 and 2 suggests that people with PD are able to use the response-related information in the cue to prepare the sequence in advance. In Experiment 1, this result was again found in both the PD ON and the PD OFF groups.

Third, in Experiment 1, both people with PD (on and off their anti-Parkinsonian medication) and healthy adults showed RT costs on the full-invalid cueing relative to the neutral cue condition. This reflects an initial preparation according to the cue, and the need to re-prepare the sequence following the presentation of the imperative signal (Hocherman et al., 2004; Jennings, 1995; P. H. Weiss et al., 1999). In Experiment 2 no such cost was found. However, this does not necessary count against the suggestion that motor preparation is intact in people with PD. In Experiment 2, the two healthy adult groups also

did not show a significant cost to their RT with full-invalid cueing. It may be that participants in all groups in Experiment 2 were able to absorb the cost of the invalid cue within the 250-ms presentation of the imperative signal before they were required to initiate their response. So, the lengthening of RT in Experiment 1, despite no lengthening in Experiment 2, provides further support for advance preparation of the response by people with PD.

Fourth, in Experiment 1, there were very similar RTs in the part-invalid cue condition relative to the neutral cue condition in both PD groups, and in the healthy adult group. While Jennings (1995) interpreted a reduced cost of part-invalid cueing in people with PD as reflecting incomplete preparation, an alternative explanation is that similar RTs in the part-invalid and neutral cue conditions reflect advanced preparation of the motor sequence where the benefits and costs of the valid and the invalid parts of the cue cancelled each other out.

Fifth, none of the cue conditions had a significant impact on measures of execution in any of the experimental groups. It seems then that preparation was not continuing during the execution of the sequence. This can also be taken as evidence of preserved motor preparation in people with PD.

Sixth, correlation analyses from Experiment 2 showed that while measures of disease severity predicted overall RT slowing in the PD group, there were only very weak correlations between these measures and the benefits and costs of cueing. If PD directly affected motor preparation, one would have expected stronger correlations between disease severity and the use of cueing. This would have reflected the direct relationship between disease progression and difficulties in motor preparation. The absence of any strong correlation suggests that motor preparation is not directly affected by the progression of the disease.

Seventh, Experiment 3 suggests that the PD group were able to maintain their prepared response following the longer foreperiods. This is supported by previous research that has also failed to find evidence of impaired maintenance of motor preparation in people with PD (Harrington & Haaland, 1991; Jordan et al., 1992; Willingham et al., 1995).

Taken together, the above findings suggest that motor preparation is largely preserved in people with PD, both on and off their anti-Parkinsonian medication. Certainly in relation to individuals on their anti-Parkinsonian medication, this is consistent with previous research (Bekkering et al., 2001; Gauntlett-Gilbert & Brown, 1998; Jahanshahi et al., 1992a; A. M. Johnson et al., 2003; Reed & Franks, 1998; Stelmach et al., 1986; J. Wang et al., 1998; Willingham et al., 1995).

6.2.1 Are there subtle difficulties in the motor preparation of people with PD?

While most of the findings from these three experiments provide evidence for intact motor preparation, there were three main findings that suggest that people with PD may suffer some subtle difficulties in motor preparation. First, there was a significantly reduced benefit of valid cueing in the PD OFF group relative to both the Old Adult and the PD ON groups in Experiment 1. Second, there was no significant cost of the full-invalid cue condition in the PD ON group in Experiment 1. Third, in Experiment 2, there was a significant benefit of part-invalid cueing relative to the neutral cue condition in the PD group, but in neither of the two healthy adult groups. All three results will be discussed in terms of the underlying pathology of PD and how these subtle difficulties can best be explained in light of such strong evidence that motor preparation is primarily intact in people with PD.

There are four main explanations of how PD affects motor preparation. First, it has been suggested that PD leads to a direct deficit in the selection and construction of motor programs (Bloxham et al., 1984; Harrington & Haaland, 1991; Stelmach et al., 1989). On this account, an underactivation of the direct pathway and over-activation of the indirect pathway leads to a reduction in thalamic output (Contreras-Vidal, 1999; Graybiel, 2000; Groves, 1983; Kandel et al., 2000; Wichmann & DeLong, 1996). Given the importance of the complex and motor circuits of the basal ganglia for motor preparation (Catalan et al., 1998; Cunnington et al., 1996; Jahanshahi & Frith, 1998; H.-C. Wang et al., 1999), a disruption of these circuits in people with PD (Mandir & Vaughan, 2000; Sabatini et al., 2000) would specifically affect motor preparation.

It could be suggested that these subtle differences are due to a deficit in selecting and constructing motor programs. Deficits in the selection and construction of motor programs would be expected to lead to an overall reduction in the effect of all cueing. However, results from the current investigation are not consistent with this. The fact that the PD groups did show significant benefits and costs of cueing in Experiments 1 and 2 suggests that they were able to select and construct motor programs according to the presentation of cues. Further, that the group differences in Experiments 1 and 2 were only subtle and did not produce a consistent pattern across experiments, also suggests that they are less likely to reflect a direct difficulty in the selection and construction of motor programs.

Second, it has been suggested that PD interferes with the maintenance of motor programs (Gentilucci & Negrotti, 1999b; Gueye et al., 1998; Sheridan et al., 1987; J. R. Wickens, 1993). It could be argued that the subtle differences mentioned above reflect a loss of the prepared response over time. However, if this were the case, one would again have expected a reduction in the effect of cueing across all cue conditions in both experiments. This was not found. Instead there was some evidence of increased, rather than decreased, costs of full-invalid cueing in the PD OFF group in Experiment 1. Further, the results from Experiment 3 strongly suggest that people with PD do not suffer a difficulty in the storage and maintenance of motor preparation. In this experiment the PD group did not show any difficulty maintaining their prepared response with the lengthening of the foreperiod. Also, a direct difficulty in the maintenance of motor preparation would be more likely to show in pronounced and consistent group differences. However, the group differences in Experiments 1 and 2 were only subtle and did not produce a consistent pattern. This also suggests that the differences that do exist are less likely to reflect a direct difficulty in the maintenance of their motor preparation.

Third, it has been suggested that PD leads to an abnormal slowness in motor preparation and execution. If this were the case, people with PD would require more time between a cue and an imperative signal to fully use advanced information, and more time to complete changes to incorrectly prepared movements (Jahanshahi et al., 1992a; A. M. Johnson et al., 2004; Scarpa & Castiello, 1994; P. H. Weiss et al., 1999). It could be argued that the subtle difficulties described above are due to reduced information processing and a subsequent slowness in organising the response. The use of variable foreperiods may have been useful

in Experiment 1 and 2 to examine this possibility further. However, if people with PD were abnormally slow in using the cues, a reduced effect of cueing would have been found across all cueing conditions in these two experiments. This was not found to be the case. Further, that the group differences in Experiments 1 and 2 were only subtle and did not produce a consistent pattern across experiments, also suggests that they are less likely to reflect an abnormal slowness in organising the response. Thus, the results from the current investigation are also not consistent with this explanation.

Finally, it has been suggested that PD leads to an increased noise in the motor system, resulting in a decreased efficiency and greater variability in both motor preparation and execution (Cunnington et al., 1996Wichmann, 1996 #135; Franz & Miller, 2002; Montgomery et al., 1991; Reed & Franks, 1998; Sheridan et al., 1987; P. Weiss et al., 1997). Normally, the two pathways of the basal ganglia influence frontal brain regions through varied thalamic output that results in focused amplification and suppression of cortical activation (Mandir & Vaughan, 2000; Reed & Franks, 1998; J. R. Wickens, 1993). One of the roles of pallidal neurons in the indirect pathway of the basal ganglia is to terminate pre-movement activity in frontal brain regions (such as the SMA), allowing the release of relevant motor programs (Cunnington et al., 1996; Gentilucci & Negrotti, 1999a; Lang et al., 1990; Lewis et al., 2000; P. Weiss et al., 1997; Willingham et al., 1995). It has also been suggested that the basal ganglia normally increase the signal-to-noise ratio in the selection of different motor programs and sub-programs, thus assisting the release of selected motor programs and suppressing the release of others (Reed & Franks, 1998; Stern et al., 2005; J. Wickens et al., 1994; J. R. Wickens, 1993).

As mentioned, the patterns of group differences across experiments were subtle and inconsistent. This is most consistent with the view that PD decreases the efficiency and introduces noise and variability to the motor system. The larger standard deviations on the four dependent measures in the PD group relative to the healthy adult groups also suggest greater variability in the motor performance of the participants with PD. In addition, measures of disease severity shared moderate to strong positive correlations with variability on the four dependent measures in the PD group in both Experiments 2 and 3. This shows that as symptom severity increased, the variability of motor initiation and execution also increased in people with PD. Taken together, these results are consistent with the view that

PD decreases the efficiency of, and introduces added noise and variability to, the motor system.

It was also found that group differences in variability were either reduced or absent when using the coefficient of variation. This suggests that, while the dysfunction of the basal ganglia leads to variability in motor performance, it was not significantly greater than the variability that was found in the healthy adult groups relative to their mean latencies on the four dependent measures. Thus, it seems that the underlying pathology of PD leads to both slowed motor performance and increased variability, but that the latter is no greater than would be expected according to their slowed motor performance.

The findings from this investigation suggest that the most plausible explanation for how PD affects motor preparation is that it results in decreased efficiency and added noise in the motor system. The increased variability in the PD groups, and the subtle and inconsistent group differences of cueing in Experiments 1 and 2 both support this idea. The other explanations seem less likely given the findings discussed.

6.3 The importance of external information on people with PD

There are a number of findings from this investigation that highlight the importance of external information in the motor preparation and execution of people with PD. The presence of incomplete preparation in Experiment 2, but not in Experiment 1, suggests that the PD group had greater difficulty preparing a response when initiated and executed under reduced visual information. This is consistent with suggestions that people with PD do experience greater difficulty in both internally controlled motor preparation (Gueye et al., 1998) and motor execution with a reduction of relevant visual information (Cooke et al., 1978; Georgiou et al., 1994; Georgiou et al., 1993; Jones et al., 1992; Kritikos et al., 1995). This may again reflect the decreased efficiency and added noise in the connection between the basal ganglia and the SMA in people with PD, a connection that is critical in the preparation and control of internally-guided movements (Cunnington et al., 1996; Cunnington et al., 1999a; Gueye et al., 1998; Hanakawa et al., 1999; Jenkins et al., 2000; Mandir & Vaughan, 2000; Mushiake & Strick, 1995; Taniwaki et al., 2003).

Correlation analyses from Experiment 2 also highlight the importance of external information in people with PD. In contrast to both healthy adult groups, the PD group showed moderate to strong positive correlations between anticipations (responses wrongly initiated while the imperative signal was still illuminated) and RT, showing that those in the PD group who made more anticipations were also the slower on RTs across all cue conditions. As anticipations were also positively correlated with disease severity in the PD group, it appears that those who suffered more severe symptoms were both slower on RT and more likely to make anticipations. There seemed to be two possible explanations for this pattern.

First, external information may be used to reduce the reliance on the faulty basal ganglia circuit, and instead rely more on the lateral premotor system, which is driven more by external information to control and guide movement (Cunnington et al., 1996; Halsband et al., 1994; Hanakawa et al., 1999; Mushiake et al., 1991). Oliveira et al. (1997) argue that the underactive SMA in PD (which should guide movements through internal control mechanisms) can be compensated for by the use of external information. It has also been suggested that people with PD use external information strategically to assist their movements (Georgiou et al., 1994; Georgiou et al., 1993; Kritikos et al., 1995; Majsak et al., 1998; McIntosh et al., 1997; Romero et al., 2003; Sheppard et al., 1996). It is thought that external information triggers upcoming elements of a movement, partially acting as a substitute for the basal ganglia that would normally be responsible for this internal triggering mechanism (Georgiou et al., 1994; Georgiou et al., 1993; Kritikos et al., 1995; McIntosh et al., 1997). A related idea is that external cues may act by drawing attention to the requirements of the task (Cunnington et al., 1999a; Jahanshahi & Frith, 1998; Oliveira et al., 1997). By doing so, the motor circuit of the basal ganglia, which is linked more strongly to automatic internal control mechanisms, may be partially by-passed (Cunnington et al., 1999a; Morris et al., 1996; Oliveira et al., 1997).

In Experiment 1, the illuminated LEDs of the imperative signal acted as an external trigger for response initiation. In Experiment 2, the illuminated LEDs of the imperative signal were turned off before the initiation of the response. With the reduction of visual information in Experiment 2, greater demand was made on internal control mechanisms both to withhold the response while the imperative signal was illuminated, and to initiate the response when

the imperative signal was turned off. The participants in the PD group were found either to make more anticipations or, on those trials in which they did not anticipate, they had longer RTs. It may then be that these participants either strategically anticipated, to use the visual information of the imperative signal, or were left with prolonged RTs when forced to rely on their internal control mechanisms.

On the other hand, the relationship between anticipations and RT may reflect an increased difficulty by people with PD to withhold their response until the visual information of the imperative signal was removed (Praamstra et al., 1999; Praamstra & Plat, 2001; Praamstra et al., 1998). There are suggestions that the dysfunction of the basal ganglia leads to external information evoking a stronger obligatory response, where people with PD cannot help but to respond to early visual information more than healthy adults (Praamstra & Plat, 2001). The correlation in Experiment 2 between anticipations and RT in the PD group may reflect this. The illuminated LEDs of the imperative signal may have evoked a stronger response in the participants in the PD group, prompting them to respond more than healthy adults while the imperative signal was still illuminated.

Experiment 3 was designed in an attempt to decide which of these explanations is the most plausible. Experiment 3 presented valid and invalid visual information to people with PD and healthy adults during the initiation and execution of motor sequences. It was expected that if people with PD use external information strategically to compensate for their motor difficulties, they should be able to ignore such information when it is invalid and unhelpful. On the other hand, if the dysfunction of the basal ganglia results in external information evoking a stronger obligatory response in people with PD, then invalid visual information should lead to deterioration in task performance in the PD group, where these participants would experience difficulties in ignoring the invalid visual guidance condition while they initiate and executed their response.

The results of Experiment 3 suggest that visual information does not evoke a stronger obligatory response on people with PD. First, the lengthening in RT under the invalid guidance condition relative to the valid guidance condition was similar in the PD group and the healthy adult groups. All groups were slower at initiating their response with invalid visual information, and the PD group was no more affected by invalid information than healthy adults. Second, the participants in the PD group did not make significantly more

errors than healthy adults. Third, the minor slowing on measures of execution on the invalid guidance condition in the PD group, while statistically significant, was not large enough to reflect any meaningful differences to the healthy adults in response to the invalid information.

The correlations in Experiment 3 also provide support for this. The correlations between measures of disease severity and RT were the same across the two guidance conditions. This indicates an equivalent relationship between disease progression and slowing on RT on the two guidance conditions. If external information were to evoke a stronger obligatory response in people with PD, then stronger correlations would have been expected between measures of disease severity and the invalid guidance condition, reflecting the increased difficulty to inhibit the invalid visual information as the disease progresses for people with PD.

Taken together, the findings from Experiment 3 suggest that visual information does not evoke a stronger obligatory response on people with PD. It thus appears more plausible that people with PD use external information strategically to assist their movements.

6.4 The influence of cognitive functioning on the motor performance of people with PD

An additional finding from this investigation is worth highlighting. Exploratory correlation analyses suggest that anti-Parkinsonian medication influenced the effect of cognitive functioning on the motor control of people with PD. In Experiment 1 moderate to strong negative correlations were found between cognitive functioning (CAMCOG scores) and RT on all four cue condition in both the PD ON and the Old Adult groups. Furthermore, participants in both of these groups who showed higher cognitive functioning were also those who made fewer errors on the task. These correlations show that those participants in these groups who scored higher on the tests of cognitive functioning were also those who were both faster at initiating their response and who made fewer errors on the motor task. This is likely to reflect the fact that those who show higher functioning on one domain will

generally show higher functioning on the other (Krampe, 2002; Salthouse & Somberg, 1982).

In contrast to both the Old Adult and PD ON group, moderate to strong *positive* correlations were found between cognitive functioning (specifically with attention and executive functions) and RT in the PD OFF group. Consistent with the two other experimental groups, these measures of cognitive functioning were negatively correlated with errors in the PD OFF group. Together, these correlations indicate that the participants in the PD OFF group who scored higher on the tests of attention and executive functions slowed their RT to improve the accuracy and control of their response. This relationship is likely to reflect the importance of executive functions and attention on motor preparation. Executive functions and attentional control are responsible for several relevant processes. They allocate attention and maintain goal-relevant information in mind (Bunge et al., 2002; De Pisapia & Goddard, 2003; MacDonald et al., 2000), allow irrelevant and inappropriate information to be inhibited (Bunge et al., 2002; Luks et al., 2002; Matsumoto et al., 2003) and guide any switching between different response options (Rushworth et al., 2004). Thus, it seems that those participants in the PD OFF group who scored higher on tests of attention and executive functions were better able to control their response and reduce their errors than those who scored lower on these tests.

So the relationship between RT, attention and executive functions, and errors was found in the PD OFF group but not in the PD ON group. This was despite very similar (and preserved) performances in both PD groups on the Attention and Executive Functions scales of the CAMCOG. These group differences highlight the role of anti-Parkinsonian medication on this relationship between motor preparation and attention and executive functions. It has been found that anti-Parkinsonian medication affects different cognitive processes in different ways. The withdrawal of anti-Parkinsonian medication has a detrimental effect, and its administration has a beneficial effect, on processes such as task-set switching, attention, and executive function in people with PD (Cools et al., 2001; Pillon et al., 2003). The positive correlations between RT and attention and executive functions in the PD OFF group may be because the reduction of anti-Parkinsonian medication unmasks the underlying capabilities of the participants, and thus better differentiates these processes within the PD OFF group. So these positive correlations

between RT and attention and executive functions in the PD OFF group suggest that these cognitive processes affect motor control differently in people with PD, depending on whether they are on or off their anti-Parkinsonian medication.

6.5 Methodological limitations

There were some aspects of the methodology of the current investigation that could be improved to clarify further our understanding of motor preparation and the importance of external information in people with PD. First, clear difficulties of motor preparation in people with PD may not have been found in the current investigation for two methodological reasons. The overall symptom severity ratings in the participants with PD were relatively mild. Thus, it is possible that more clear deficits in motor preparation may only become apparent in more severely affected people with PD. It is also possible that the motor tasks in the current investigation were not difficult enough to reveal any clear difficulties in motor preparation that may be present in people with PD. These two possibilities should be examined in future research before any strong conclusions should be drawn.

Second, reducing the amount of relevant visual information in Experiment 2 produced smaller differences between people with PD and healthy adults than has been found in previous research (Georgiou et al., 1994; Georgiou et al., 1993; Jones et al., 1992; Kritikos et al., 1995). In Experiment 2, the PD group was slower on the measures of execution than the healthy adult group. However, the slowing of the PD group relative to the healthy old adult group was no greater in Experiment 2 than in Experiment 1. The reduction of visual information, in itself, then does not seem to have contributed to the slowing of measures of execution in the PD group relative to healthy adults. This is possibly due to the fact that both the un-illuminated LEDs and the corresponding target keys remained visible to participants as they initiated and executed the sequences. To further address the importance of visual information in the preparation and execution of movement in people with PD, a more complete removal of visual information would be recommended.

Third, in Experiment 3, while the valid guidance condition was presented directly into the participant's central field of view, the invalid guidance condition was not. This is because participants tended to direct their gaze towards the illuminated LEDs of the cue in preparing their response. Modifying this task so that the valid and invalid guidance conditions were both presented within the same central field of view would be useful to further investigate the influence of invalid visual information in people with PD relative to healthy adults. Fourth, future research assessing the influence of visual information could include a neutral guidance condition (providing neither valid nor invalid visual information about the sequence). This would be useful to allow a direct comparison both with any benefits of valid visual information and any difficulties with invalid visual information.

Finally, there was some important clinical information of the participants with PD was not able to be collected for this investigation. This included information such as: (a) the presence of dyskinesia; (b) the dosages of medication in each participant over the duration of the investigation; and (c) the classification of patients into the tremor-dominant versus akinesia/bradykinesia types of presentation. Such information would have allowed an examination of the effects of these characteristics on the different aspects of motor preparation and execution. Unfortunately, because this clinical information was unavailable, these important issues could not be examined more thoroughly.

6.6 Summary

This investigation sought first to extend our understanding of motor preparation in people with PD. The experiments that made up this investigation assessed a number of aspects of motor preparation. The first two experiments assessed the ability of people with PD: (a) to prepare motor sequences of different complexity (sequences with and without a change of direction); (b) to use cued information about the sequence to prepare their response in advance; and (c) to prepare motor sequences in conditions of reduced visual information. The third experiment further addressed motor preparation by assessing the ability of people with PD to maintain their prepared response over time.

The results suggest that people with PD were affected by manipulating response complexity and cued information in a very similar way to healthy adults. In addition, there was no evidence that people with PD suffered any difficulty in maintaining their prepared response over longer foreperiods. Taken together, these results suggest that motor preparation is largely preserved in people with PD. There were, however, some group differences in the benefits and costs of cueing across the experiments. On all three experiments there was also evidence of increased variability in the participants with PD across the four dependent measures, and in Experiments 2 and 3 strong positive correlations were found between variability and measures of disease severity. These results suggests that the most likely explanation for the way PD interferes with the motor system is that it leads to decreased efficiency and added noise and variability in the motor system.

The second area of interest in this investigation was the importance of external information in the motor control of people with PD. This was assessed initially in Experiment 2 by providing less relevant visual information during the initiation and execution of the sequences than was done in Experiment 1. It was investigated in more detail in Experiment 3 by providing valid and invalid visual information during the initiation and execution of motor sequences. The results of Experiment 2 indicate that the reduction of relevant visual information resulted in incomplete motor preparation in the PD group in contrast to healthy adults. However there was no evidence from Experiment 3 that external information exerted a stronger obligatory response in people with PD. Rather, external information is more likely to be used strategically by people with PD to draw attention to the requirement of the movement, and thus provide more conscious motor control that partially bypasses the basal ganglia.

6.6.1 Conclusions

As discussed in Chapter One, it has been suggested that dopamine acts to facilitate task relevant input and reduce task irrelevant input (noise) through the frontostriatal circuits (Stern et al., 2005). The motor preparation of people with PD appears to be strongly related to dopamine in the frontostriatal circuits. It would seem then that the dopaminergic depletion in PD leads to increased noise in the frontostriatal system, resulting in greater

variability in motor preparation and execution. Anti-Parkinsonian medication is thought to be effective in that it increases the efficiency of activation (by raising the signal-to-noise ratio) within the prefrontal cortex (Cools et al., 2002; Remy & Samson, 2003).

Also discussed previously, cognitive processes such as attention and executive functions are also controlled by dopamine within these frontostriatal circuits, and are known to influence motor preparation (Bunge et al., 2002; Luks et al., 2002; Matsumoto et al., 2003; Rushworth et al., 2004). In Experiment 1 it was found that the relationship between these cognitive processes and RT differed in people with PD depending on whether they were on or off their anti-Parkinsonian medication. These results imply that the influence of these cognitive processes on the motor preparation of people with PD is dependent on the administration of anti-Parkinsonian medication.

Finally, the importance of external information in people with PD can also be understood in terms of the depletion of dopamine in the frontostriatal circuits. An activity involving minimal relevant visual information is likely to place greater demands on the internal control mechanisms of the frontostriatal circuits than one where more relevant visual information is available. The reduction of relevant visual information, from Experiment 1 to Experiment 2, influenced the participants with PD more than the healthy adults. Furthermore, the results of Experiment 3 suggest that people with PD use external information strategically to assist in their movements. This may be because external information draws attention to the requirement of the movement, providing a more conscious control that allows the faulty basal ganglia to be partially bypassed.

In summary, the dopaminergic depletion of PD disrupts normal frontostriatal functions, leading to difficulties in motor control. Any reduction of anti-Parkinsonian medication in people with PD also appears to influence the normal relationship between aspects of motor control and cognitive processes linked to the frontostriatal circuits. When demands on these circuits are high, such as with a reduction of relevant visual information, subtle difficulties in motor preparation become apparent in people with PD. These difficulties in motor control may, however, be partially compensated for by the strategic use of relevant visual information to reduce the demands on the impaired internal control mechanisms of the frontostriatal circuits.

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Appendix A

The effects of age on the preparation of a two-movement sequence

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Abstract

Motor preparation is commonly inferred from the effects of cues that give advance information about the movement to be performed in a choice reaction time task. The benefits and costs in reaction time (RT) of valid and invalid cues relative to a neutral cue condition are taken to reflect advanced preparation. When a two-movement sequence is required, a part-invalid cue which validly cues the first movement and invalidly cues the second can be used to examine the preparation of each movement separately. In the current study, younger and older participants performed cued two-movement sequences to target keys. The required sequence of key presses was signalled by illuminated light-emitting diodes above the target keys. A cue, which appeared before the imperative signal, was either valid (both movements of the required sequence were validly cued), full-invalid (both movements were invalidly cued), part-invalid (the first movement was validly cued and the second element invalidly cued), or neutral (no response-specific information was given). The older group showed similar RT costs in the part-invalid and full-invalid cue conditions, suggesting in both the re-preparation of both movements in the sequence following the imperative signal. The younger group also showed similar RT costs in the part-invalid and full-invalid cue conditions early in the test session, again suggesting re-preparation of both movements. With practice however, an RT benefit in the part-invalid cue condition emerged in this group, suggesting the development of a more efficient approach in which re-preparation occurred only for the invalidly cued second movement.

Keywords: Motor preparation; Aging; Reaction time

PsycINFO classification: 2330; 2340; 2860

1. Introduction

Reaction time (RT) has traditionally been used as the principal measure of motor preparation, with longer RTs taken to reflect a greater amount of preparation occurring before the execution of a movement (Rosenbaum, 1980). A method commonly used to investigate motor preparation is to cue relevant information about the movement in advance. A cue that carries valid information of the required response in a choice reaction time task facilitates RT, reflecting preparation of the movement before the imperative signal (Goggin & Stelmach, 1990; Gueye, Viallet, Legallet, & Trouche, 1998; Larish & Frekany, 1985; Larish & Stelmach, 1982; Müller-Gethmann, Rinkenauer, Stahl, & Ulrich, 2000; Rosenbaum, 1980; Weiss, Stelmach, Chaiken, & Adler, 1999; Zelaznik & Hahn, 1985). Advance invalid information lengthens RT, reflecting the time required to re-prepare the movement in response to an imperative signal requiring a different movement to that which had been prepared (Goggin, Stelmach, & Amrhein, 1989; Larish & Stelmach, 1982; Stelmach, Goggin, & Amrhein, 1988). A two-movement sequence allows each to be cued separately in advance by, for example, validly cuing the first movement and invalidly cuing the second. The partial validity of such cues allows preparation of the movements to be examined separately (Jennings, 1995).

Although it is well documented that movement becomes slower and more variable with aging (Amrhein, 1996; Inui, 1997; Krampe, 2002; Light & Spirduso, 1990; Morse, 1993; Yan, Thomas, & Stelmach, 1998), there remains disagreement whether motor preparation remains intact. The similar RT benefits of spatial cuing shown by younger, middle-aged, and older groups has been taken to reflect preserved preparation (Adam et al., 1998; Larish & Stelmach, 1982). In contrast, there is evidence which suggests that motor preparation deteriorates with aging. The slower and more variable RTs shown by middle-aged and older individuals are more pronounced within complex movements (e.g., by increasing the number of movements to be performed or requiring both hands to perform the task; Inui, 1997; Yan et al., 1998), a finding taken to reflect progressive age-related deterioration of motor preparation (Light & Spirduso, 1990; Yan et al., 1998; Yan, 2000). In support, smaller RT benefits of cuing in middle-aged and older than in younger individuals have been found as movement complexity increases,, again suggesting age-related deterioration in preparation (Adam et al., 1998).

A reduction in RT costs of invalid cuing with age has also been found when the task requires a change in the direction of an invalidly cued movement, suggesting that little or no preparation of movement direction had occurred in older adults (Goggin et al., 1989). This reduced cost appeared to occur only when the foreperiod between the cue and the imperative signal was 1000 ms or longer (with equivalent costs to a younger group at shorter foreperiods), suggesting that a decay of preparation over time in older adults, rather a lack of preparation, was responsible (Amrhein, Stelmach, & Goggin, 1991; Amrhein, Von Dras, & Anderson, 1993).

Finally, movement execution time has been reported to be longer, more variable, and to include hesitations in middle-aged and older than in younger individuals, a finding thought to reflect an age-related deterioration in motor preparation and a greater reliance on on-line control (Yan et al., 1998; Yan, 2000). In conclusion, while there remains some disagreement, there is evidence that motor preparation deteriorates with age. The current study used valid and invalid (both part-invalid and full-invalid) cuing of two-movement sequences in young and middle-aged participants to examine preparation and re-reparation of each of the movements in the two age groups.

2. Method

2.1. Participants

Twenty-three healthy individuals aged between 23 and 61 years were recruited through The University of Western Australia and Sir Charles Gairdner Hospital. All were self-reported right handers. Two age groups were created, a younger group with 12 participants (4:8 Male:Female; aged between 23 and 27 years with a median of 25 years), and an older group with 11 participants (5:6 Male:Female; aged between 38 and 61 years with a median of 57 years). All participants gave informed consent to the study, which was approved by the Human Research Ethics Committee of Sir Charles Gairdner Hospital.

2.2. Design and Procedure

Participants were required to perform different two-movement sequences in response to the illumination of two of five light-emitting diodes (LEDs) positioned above corresponding target keys on a response board. The five circular target keys (30-mm diameter) were arranged horizontally, and equally spaced 60 mm apart (from centre to centre). Two LEDs, one green and one red, were positioned vertically above each target key (see Figure 1). Illumination of a red LED indicated the target key of the first movement, and was always above one of the target keys immediately adjacent to the central start key. Illumination of a green LED indicated the target key of the second movement in the sequence, and was either above one of the outermost target keys (for a uni-directional sequence) or above the start key (for a bi-directional sequence). An example is shown in Figure 1.

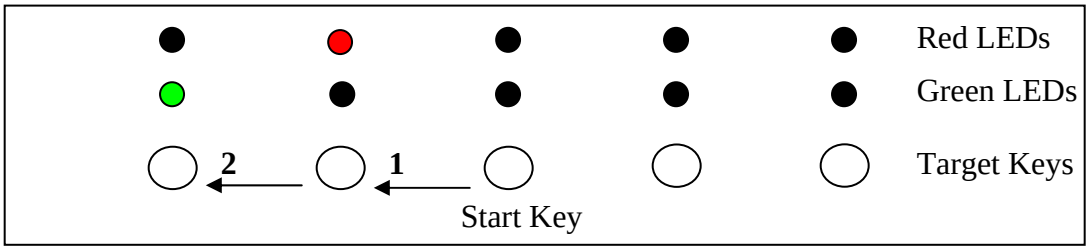

Figure 1 A schematic representation of the response board showing the upper two rows of light-emitting diodes (LEDs) and the lower row of target keys. The LEDs shown depict a uni-directional sequence.

Each trial began with the red and green LEDs above the central start key flashing on and off until that key was depressed with the participant's right index finger for 2000 ms. The impending sequence was then cued by the simultaneous illumination of a red and a green LED for 750 ms. Following a 450-ms foreperiod during which all LEDs were off, the imperative signal (the illumination of a red and a green LED, indicating the sequence to be performed) was presented. Participants were instructed to make the movements to the target keys indicated by the imperative signal as quickly and accurately as possible. The imperative signal remained on until both movements had been executed. All LEDs were then turned off for a 2000–ms inter-trial interval.

There were four cue conditions. On valid trials, the cue gave valid information about the required response (the illuminated red and green LEDs in the cue and imperative signal were identical, indicating the same target keys). On invalid trials, the cue indicated a different sequence to that required by the imperative signal. On half of these trials (full-invalid trials), the imperative signal differed from the cue in the position of both the red and the green LEDs, and hence required a sequence in which both movements differed from those that were cued. On the remaining half (part-invalid trials), the imperative signal differed from the cue only in the position of the green LED, and hence required a movement sequence in which the second movement of the sequence differed from that which was cued. On neutral trials, the cue consisted of the illumination of all five red LEDs, giving no information about the response to be made on that trial. On catch trials, a cue was presented but was not followed by an imperative stimulus. These four conditions were presented in eight randomised blocks of 44 trials, in which 24 trials (55%) were valid, 8 (18%) were neutral, 8 (18%) were invalid (half part-invalid and half full-invalid), and 4 (9%) were catch trials. This followed a practice session of 14 trials, in which each condition was presented at least once.

2.3. Data analysis

RT was measured as the time (in ms) taken to lift the finger from the start key with the onset of the imperative stimulus. Three other dependent measures, the first movement time (MT1, the time taken to reach the first target), dwell time (DT, the time spent on the first target key), and the second movement time (MT2, the time taken to move from the first to the second target key) were also taken. Median times (in ms) for each measure were taken for each participant in each cue condition, and the mean of these median times was calculated for each age group. All conditions except for the full-invalid cue condition comprised both uni-directional and bi-directional sequences; full-invalid trials were made up only of uni-directional sequences. The relative benefits and costs of cue condition were calculated for each participant by dividing the difference between the median RT in the relevant cue condition and that in the neutral condition by the median RT in the neutral condition and multiplying the result by 100. For example: $((RT_{valid} - RT_{neutral})/RT_{neutral}) \times$

100. Thus negative values represent RT benefits and positive values represent RT costs relative to the neutral cue condition.

Trials that contained an anticipatory error (responding before the imperative signal) and those with an incorrect response (making contact with the wrong key) were removed from analysis. An average of 8% of trials were removed for each participant. There was little difference between the two age groups, with an average of 7% errors in the younger group (Mean = 7.1; SEM = 0.4) and 8% in the older group (Mean = 7.8; SEM = 0.4).

3. Results and discussion

The relative RT benefits and costs of the different cue conditions are shown for each age group in Figure 2. There was a significant main effect of Cue Condition on RT (F (3, 63) =67.48, $p < .001$, $\eta^2 = 1.0$). Both the younger and older age groups showed a benefit of valid cuing (t (11) = 8.61, $p < .001$ and t (10) = 6.00, $p < .001$, respectively) and a cost of full-invalid cuing (t (11) = 2.68, $p < .05$ and t (10) = 2.57, $p < .05$, respectively), showing that cues in these conditions had been used by both groups to prepare the sequence in advance of the imperative signal. The similar RT cost in the two age groups to re-prepare the movement sequence in the full-invalid cue condition is consistent with previous findings of equivalent re-preparation costs in different age groups with brief foreperiods (Amrhein et al., 1991; Amrhein et al., 1993). The main effect of cue condition was qualified by a significant interaction of Age and Cue Condition (F (3, 63) = 3.70, $p < .05$, $\eta^2 = .78$), with the older group, but not the younger group, showing a cost of part-invalid cuing (t (10) = 4.01, $p < .005$ and t (11) = .09, $p = .93$ respectively).

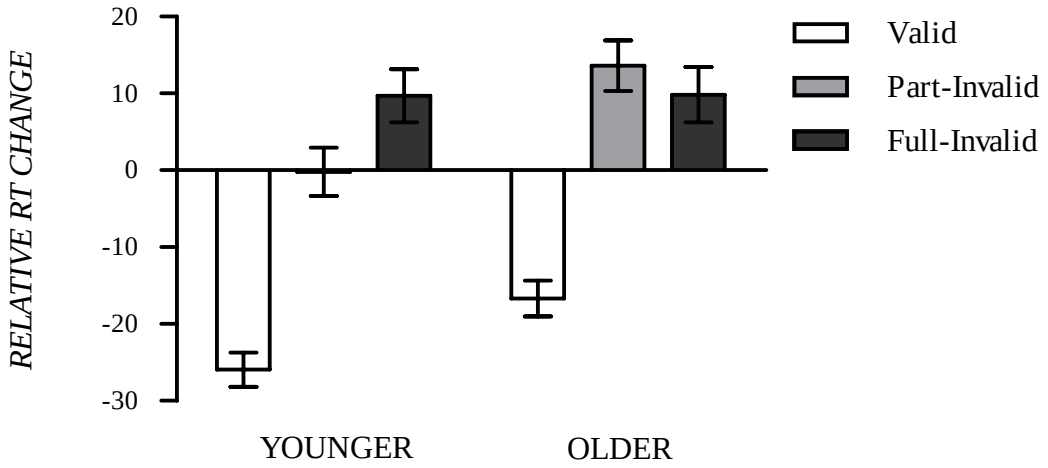

Figure 2 The effect of cue condition on reaction time in the two age groups (error bars represent ± 1 SEM). Negative values indicate an RT benefit, whereas positive values indicate an RT cost relative to the neutral cue condition.

Further analysis showed that while the RT costs and benefits of full-invalid and valid cues were stable throughout the testing session for both age groups, differences emerged in the part-invalid cue condition with practice (see Figure 3). The three-way interaction between Block, Cue Condition, and Age was significant ($\underline{F}$ (9, 189) = 1.95, $\underline{p} < .05$, $\underline{\eta}^2 = .83$). These results point to an age-related difference in the re-preparation of the response following part-invalid cuing. As can be seen is Figure 3, the older group showed an RT cost in the part-invalid cue condition which matched that shown in the full-invalid cue condition throughout the testing session, indicating that both the first and second movement of the sequence were re-prepared following an imperative signal which required a movement sequence different to that specified by the cue.

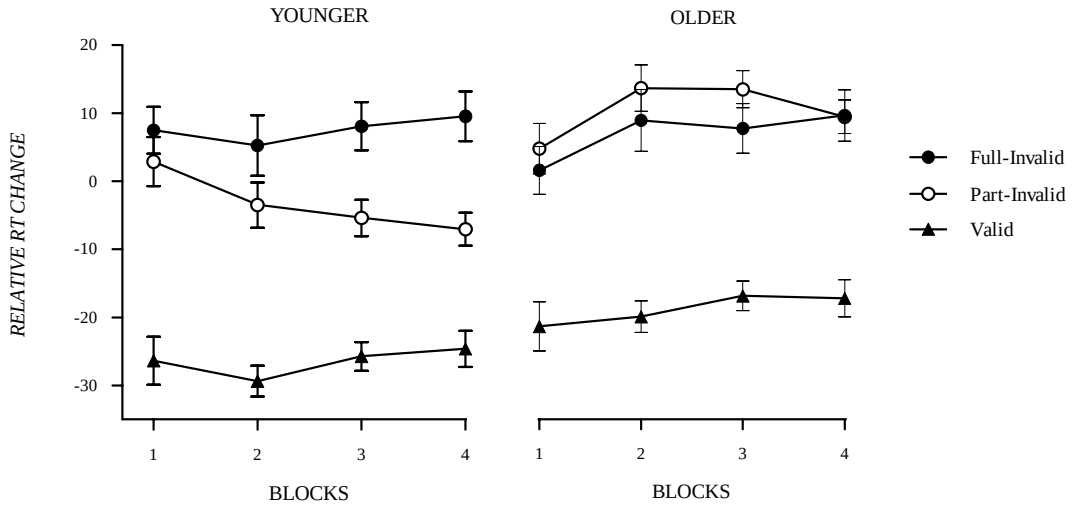

Figure 3 The effect of cue condition on reaction time in the two age groups over blocks of 88 trials (errors bars represent ± 1 SEM). Negative values indicate an RT benefit, whereas positive values indicate an RT cost relative to the neutral cue condition.

The similar RT cost of part-invalid and full-invalid cue condition in the younger group early in the test session also indicates that both movements of the sequence were re-prepared by this group (see Figure 3). However, the emergence of an RT benefit in the younger group in the part-invalid cue condition with practice suggests that this group was able to re-prepare a movement more efficiently by altering the invalidly cued second movement while maintaining the preparation of the validly cued first movement. The smaller RT benefit of the part-invalid cue condition than the valid cue condition late in training for the younger group reflects the additional time required to modify the preparation of the second movement following the imperative signal.

Had the younger group prepared only the first movement of the sequence in advance, the RT benefit would have been similar in the part-invalid and valid cue conditions because the first movement in both conditions was always validly cued. Furthermore, the younger group would have shown slowing in measures of execution (MT1, DT, or MT2) with part-

invalid cuing, reflecting the preparation of the second movement. However, this was not the case. Within all three measures of execution, the part-invalid cue condition in the younger group was not reliably and incrementally more costly than the neutral cue condition over the testing session. The average cost of the part-invalid cue condition relative to the neutral cue condition over the trial blocks presented in Fig. 3 was 2 ms in MT1, 0 ms in DT, and 1 ms in MT2. Greater costs would be expected if preparation of the second movement was occurring during execution of the sequence. These results, coupled with the smaller RT benefit in the part invalid cue condition than the valid cue condition, argue against on-line preparation of the second movement in the younger group and age-related differences in the extent of preparation in a multi-movement sequence.

Instead, the current results point to strategic differences between the age groups in the re-preparation of invalidly-cued responses, with the younger group re-preparing only the invalidly cued second movement following the part-invalid cue condition, which is less costly than re-preparation of both movements of the sequence (Quinn & Sherwood, 1983; Larish & Frekany, 1985). The relationship between age and the relative effect of the part-invalid cue condition on RT in the last four blocks is shown in Fig. 4. The strong positive correlation (r = .71, 95% confidence interval = .43 to .88) illustrates this age-related change in strategy following task practice, whereby younger participants were more likely to show an RT benefit on the part-invalid cue condition whereas older participants were more likely to show an RT cost.

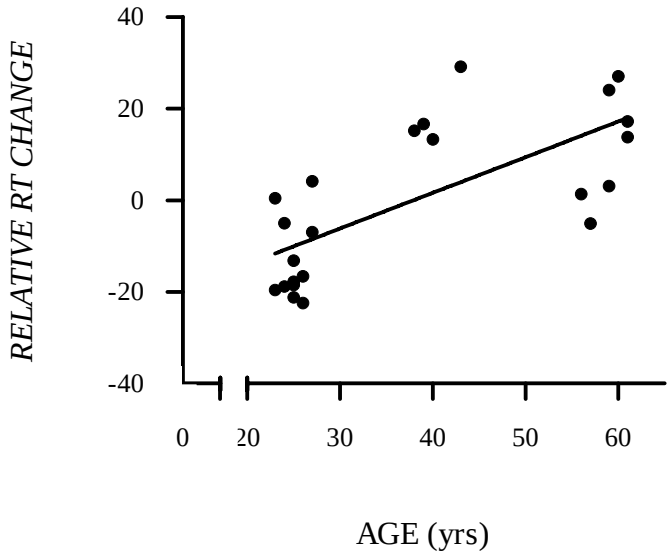

Figure 4 The relationship between age and part-invalid cue condition for each individual over the final four blocks. Points below zero indicate a benefit, while points above zero indicate a cost relative to neutral.

Bennett & Castiello (1995) reported that an older group took longer to adjust their movement in response to a change in the size of a target after movement initiation. In addition, the reaching and grasping phases of the movement were less strongly coupled in the younger than the older group when the target size was changed, showing that both movement phases could be re-prepared separately. These results have been taken to reflect an emerging inflexibility in the re-preparation of different components of a movement with age (Bennett & Castiello, 1995). The group differences in re-preparation following the part-invalid cue condition in the current study may also reflect such changes. Rather than developing a more efficient approach where only the invalidly cued second movement is re-prepared following the imperative signal, as shown in the younger group, the older group maintained their initial strategy of re-preparing both movements in the sequence throughout the testing session.

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Appendix B

Information and Consent forms

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Participant Information

PROJECT: The preparation of complex sequential movements in individuals with Parkinson's disease

INVESTIGATORS: A.P. Geoff Hammond/ A.P. Mike Anderson/ Keira Thomson

PURPOSE OF STUDY: Parkinson's disease is a degenerative disease that significantly affects movement and motor control in individuals with this disease. There is disagreement as to whether Parkinson's disease affects the preparation of movement, the execution of movement, or both. The current study aims to assess the nature of motor preparation in Parkinson's disease patients to determine if deficits are present in the preparatory stages of movement.

All procedures are non-invasive

PROCEDURE: You will initially be required to complete two tests to measure a range of cognitive functions that will take roughly 30 minutes. The third task will require you to complete various simple one- and two-movement sequences using your index finger. Illumination of lights above response buttons will indicate the location and the order of the movements to be performed. You will see a red light above one of the response buttons and a green light above another response button. The red light will indicate the first button to press, while the green will indicate the second button to press (when only one movement is required, only a red light will be presented). On each trial, the lights will be presented twice. On the first, you will be required to observe the sequence indicated by the lights without performing the corresponding movements (keeping your index finger on the start key). On the second, you will be required to tap out the sequence according to the lights as quickly and accurately as possible.

CONFIDENTIALITY: Any information about you that is obtained in connection with this study will remain confidential and will be disclosed only with your written permission. However, the results of the study may be published or disclosed to other people in a way that will not identify you. The results of this study will be stored in a locked cabinet for 5 years.

CONSENT: The study will be carried out in a manner conforming to the principles set out by the National Health and Medical Research Council. You are free to withdraw your consent and discontinue with your participation at any time. Your participation in this study does not prejudice any right to compensation, which you may have under statute or common law.

FURTHER INFORMATION: If you have any questions regarding this study you can contact Keira Thomson on 9380 1418. You will be given a copy of this information sheet and consent form to read and keep prior to indicating your consent to participate by signing the consent form.

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Consent Form

PROJECT: The preparation of complex sequential movements in individuals with Parkinson's disease

INVESTIGATORS: A.P. Geoff Hammond/ A.P. Mike Anderson/ Keira Thomson

I have been given clear information (verbal and written) about this study and have been given time to consider whether I want to take part.

I have been told about the possible advantages and risks of taking part in the study and I understand what I am being asked to do.

I have been able to ask questions and all questions have been answered satisfactorily.

I know that I do not have to take part in the study and that I can withdraw at any time during the study without affecting my future medical care. My participation in the study does not affect any right to compensation that I may have under statute or common law.

I agree to take part in this research study and for the data obtained to be published provided my name or other identifying information is not used.

……	……	……
Name of Participant	Signature of Participant	Date
…….	…….	……
Name of Investigator	Signature of Investigator	Date

The Human Research Ethics Committee at the University of Western Australia requires that all participants are informed that, if they have any complaint regarding the manner in which a research projected is conducted, it may be given to the researcher, or alternatively, to the Secretary, Committee of Human Rights, Registrar's Office, University of Western Australia, Nedlands, Western Australia 6907 (telephone number 9380-3703). All study participants will be provided with a copy of the Information Sheet and Consent Form for their personal records.

All study participants will be provided with a copy of the Information Sheet and Consent Form for their personal records.

Appendix C

Participant	Age	Sex	Hand	Disease duration (yrs)	Medication
PD1	70	M	R	17	Sinemet,
PD2	75	M	R	3	Madopar
PD3	74	M	R	1	Sinemet
PD4	64	F	R	7	Madopar
PD5	70	M	R	2	Madopar
PD6	60	F	R	4	Sinemet, Cabaser
PD7	70	M	R	6	Madopar, Cabaser, Eldepryl
PD8	83	F	R	2.5	Sinemet
PD9	80	M	R	4	Madopar, Symmetrel
PD10	70	M	R	12	Madopar
PD11	73	M	R	12	Sinemet, Selegiline, Cabasar
PD12	72	M	R	8	Madopar
PD13	64	F	L	1	Madopar
PD14	60	M	R	11	Madopar, Cabaser, Comtan
PD15	58	M	R	6	Sinemet, Cabergoline, Selegiline
PD16	64	F	R	10	Madopar, Cabaser
PD17	72	M	R	7	Madopar, Cabaser
PD18	75	F	R	9	Sinemet, Comtan, Cabergoline
PD19	77	M	R	4	Madopar
PD20	53	F	R	12	Madopar, Cabaser
PD21	53	M	R	1	Sinemet, Cabergoline
PD 22	54	M	R	12	Madopar, Selegiline, Symmetrel
PD 23	61	M	R	1	Cabaser[6]
PD 24	69	F	R	1	De Novo

[6] This participant was de novo until Study Three

Appendix D

Pearson's correlation coefficients between the frequency of anticipations and RT and MT1 by experimental group and response complexity.

			Young Adult	Old Adult	PD
RT	Uni-directional	Valid	-.53*	-.08	.51*
		Neutral	-.48*	.14	.60*
		Part-Invalid	-.54*	-.10	.46*
		Full-Invalid	-.42	.11	.64*
	Bi-directional	Valid	-.65**	.14	.49*
		Neutral	-.55*	0	.66**
		Part-Invalid	-.60**	.08	.55*
		Full-Invalid	-.50*	.04	.62**
MT1	Uni-directional	Valid	-.42	.02	.36
		Neutral	-.34	.25	.47*
		Part-Invalid	-.39	.14	.45*
		Full-Invalid	-.40	.13	.46*
	Bi-directional	Valid	-.43	-.03	.19
		Neutral	-.38	-.05	.31
		Part-Invalid	-.39	-.06	.26
		Full-Invalid	-.38	.04	.24

* Indicates significant at the .05 level (2-tailed). ** Indicates significant at the .01 level (2-tailed).

Appendix E

Pearson's correlation coefficients between the frequency of anticipations and DT and MT2 by experimental group and response complexity.

			Young Adult	Old Adult	PD
DT	Uni-directional	Valid	-.30	.10	.46*
		Neutral	-.43	.07	.39
		Part-Invalid	-.39	.16	.47*
		Full-Invalid	-.29	.09	.44*
	Bi-directional	Valid	-.32	.17	.43
		Neutral	-.36	.16	.34
		Part-Invalid	-.43	.26	.37
		Full-Invalid	-.32	.16	.44*
MT2	Uni-directional	Valid	-.37	.04	.20
		Neutral	-.27	0	.20
		Part-Invalid	-.31	-.03	.18
		Full-Invalid	-.34	-.04	.20
	Bi-directional	Valid	-.45*	.02	.23
		Neutral	-.46*	-.02	.23
		Part-Invalid	-.43	.01	.29
		Full-Invalid	-.49*	-.02	.27

* Indicates significant at the .05 level (2-tailed). ** Indicates significant at the .01 level (2-tailed).