The Speech Movement Disorder in Parkinson's Disease and its Rehabilitation Using Augmented Visual Feedback

by

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Abstract

This dissertation comprises three studies that address the goals of better understanding the effects of Parkinson's disease (PD) on speech movements and the development of a novel rehabilitation approach using augmented visual feedback (AVF) for individuals with an articulatory disorder due to PD. The first study examined jaw and tongue movements during sentence production in PD with respect to speech intelligibility and across different speaking styles, which are often used as intervention approaches (e.g., loud, clear speech). The results revealed consistently smaller jaw movements in individuals with PD relative to a control group. The results further showed that smaller tongue movement size was associated with lower ratings of speech intelligibility. The verbal cues to increase loudness, improve clarity, and reduce speaking rate generally resulted in changes in movement size and speed for both speakers with PD and healthy controls but the extent of change was smaller for the patient as compared to the control group. Using Cochrane-based methods, the second study systematically reviewed the PD literature that pertained to the use of AVF in motor rehabilitation. The findings showed that AVF is an effective tool for motor rehabilitation in PD. Treatment success can be further enhanced by providing large amounts and a high intensity of treatment, gamifying feedback, and providing knowledge of performance feedback in real-time and on 100% of practice trials. Taken together, the results of the first two studies guided the development of a novel therapy aimed at increasing tongue movement size using AVF, which provided visual feedback regarding movement performance, in addition to verbal cues. The final study investigated the effects of this novel therapy on tongue movement size and speech intelligibility in five patients with PD. The results indicated that AVF (+ verbal cue) may be beneficial in training participants to use large speech movements, compared to a verbal cue alone. The treatment effect on intelligibility was, however, not beneficial in 4/5 patients. The optimal extent of articulatory expansion needed to elicit benefits in speech intelligibility requires further investigation. Overall, this body of work furthered our understanding of the speech movement disorder in PD, and laid the groundwork for expanding evidence-based treatment options for this population in the future.

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Chapter 1
Introduction and Literature Review

1 Introduction

Parkinson's disease (PD) is the second most common neurodegenerative disease that affects adults over the age of 60 (Bertram & Tanzi, 2005). PD results from a loss of dopaminergic neurons in the substantia nigra of the basal ganglia and associated Lewy pathology (Bertram & Tanzi, 2005; Fearnley & Lees, 1991). As a result of neurodegeneration, individuals with PD experience motor deficits that include, but are not limited to, the cardinal symptoms of bradykinesia, tremor, rigidity, and postural instability (Jankovic, 2008). These motor deficits can lead to functional impairments during motor tasks, such as walking, writing, swallowing, and speech (Jankovic, 2008).

Almost 90% of individuals diagnosed with PD develop a motor speech disorder as the disease progresses (Logemann, Fisher, Boshes, & Blonsky, 1978). The most common speech disorder associated with the disease is known as hypokinetic dysarthria (HKD), which can occur at any stage of the disease, and typically worsens with disease progression (Klawans, 1986). HKD is characterized by deficits in the phonatory, prosodic, and articulatory subsystems (Duffy, 2013) leading to reduced speech intelligibility (Tjaden, Sussman, & Wilding, 2014; Weismer, Jeng, Laures, Kent, & Kent, 2001). As a result of HKD, patients with PD may experience reduced communicative autonomy, social isolation, and an overall reduced quality of life (Miller, Noble, Jones, & Burn, 2006; Pinto et al., 2004).

Much of the focus on speech therapy for patients with PD in the last few decades has been on targeting the phonatory and prosodic aspects of speech, yet 45% of patients experience difficulties in articulation (Logemann et al., 1978). The articulatory abnormalities in PD are not well understood, and there is a need to develop therapies that directly address the underlying articulatory movement disorder in PD.

Thus, the overarching aim of my dissertation work is, based on an improved understanding of sentence-level articulatory kinematics and their association with intelligibility, to evaluate the initial efficacy of a novel movement-based speech therapy in PD. This dissertation begins with an introduction focused on a review of the relevant literature (Chapter 1), followed by three studies conducted to address the overall aim (Chapters 2–4). The final chapter discusses the major contributions of the dissertation work to the field and considers implications for future research.

The reader is advised that Chapters 2–4 are verbatim manuscripts that have been submitted to journals, and as a result, some information may be redundant across chapters.

1.1 Epidemiology of Parkinson's Disease

PD is named after James Parkinson, who first described key motor features of the disorder in *An Essay on the Shaking Palsy* in 1817 (Parkinson, 2002). Today, more than 7 million people are affected by PD worldwide and reported incidence rates are estimated between 8-18 per 100,000 persons (de Lau & Breteler, 2006). Characterized as a disease of aging, the prevalence of PD in individuals aged over 60 is approximately 1.0% (de Lau & Breteler, 2006; Wirdefeldt, Adami, Cole, Trichopoulos, & Mandel, 2011) and rises to 2.6% for those aged 85 to 90 (de Rijk et al., 2000). As the number of people aged 60 and above increases, the incidence of PD is also expected to rise exponentially (Dorsey et al., 2007).

While the exact cause of PD is unknown, risk factors include a positive family history of PD (Gorell, Peterson, Rybicki, & Johnson, 2004), exposure to toxic materials (Priyadarshi, Khuder, Schaub, & Priyadarshi, 2001), and sex, with a higher incidence and relative risk (1.5:1) reported for males compared to females (Wooten, Currie, Bovbjerg, Lee, & Patrie, 2004). Life expectancy post-diagnosis is on average 15 years (Rajput & Birdi, 1997) and significantly increases for those who are diagnosed with 'early-onset' PD before the age of 50 (Ishihara, Cheesbrough, Brayne, & Schrag, 2007).

1.2 Neuropathology of Parkinson's Disease

Clinical diagnosis of PD is based on presenting symptoms and response to treatment. The diagnosis can, however, only be confirmed by autopsy post-mortem (Braak et al., 2003; Rizzo et al., 2016) with evidence of dopaminergic neuronal loss in the substantia nigra of the basal ganglia in association with Lewy pathology (Dickson et al., 2009; Gelb, Oliver, & Gilman, 1999). Since the early 2000s, PD has been recognized as a multisystem disorder, with both motor and non-motor symptoms (Braak, Ghebremedhin, Rüb, Bratzke, & Del Tredici, 2004; Klingelhoefer & Reichmann, 2017). The motor symptoms of PD result primarily from the degeneration of dopaminergic cells in the substantia nigra pars compacta (SNpc) (Fearnley & Lees, 1991), while the non-motor symptoms are related to more widespread involvement (Dickson et al., 2009).

Braak and colleagues proposed a pathological staging scheme for the progression of PD, which can be broadly subdivided into pre-symptomatic (Stages I-III) and symptomatic (Stages IV-VI) stages (Braak et al., 2003; Braak et al., 2004). According to this scheme, specific sets of neurons with long and thin unmyelinated axons are predisposed to developing pathological protein aggregations, known as Lewy bodies and Lewy neurites (Braak et al., 2004). Each stage is marked by the continual development of Lewy pathology in predictable regions, ultimately resulting in apoptosis (cell death). Specifically, the scheme suggests that the neural degeneration begins in lower brainstem nuclei and progresses rostrally to the SNpc as well as to higher cortical regions (Braak et al., 2004).

The systematic progression of the disease begins in the olfactory bulb, the dorsal glossopharyngeal and vagus nuclei in the medulla oblongata, and in the pontine tegmentum (Stage 1-2) (Braak et al., 2004). While these stages are considered pre-symptomatic, many individuals with PD retrospectively recall changes in their olfaction (Haehner et al., 2009), autonomic function (e.g., bowel movements; Abbott et al., 2001), sleep (Postuma, Lang, Massicotte-Marquez, & Montplaisir, 2006), and mood (Schuurman et al., 2002) in the years prior to motor symptom onset. In Stages 3 and 4, the pathology moves upwards and targets the dopaminergic cells in the SNpc and other nuclear gray areas of the midbrain and basal forebrain, resulting in the classic motor symptoms of the disease (Braak et al., 2004). In the final stages, Stage 5 and 6, Lewy pathology spreads to the cerebral cortex, and the multisystem nature of the disease is observed, manifested as autonomic, limbic and motor symptoms (Braak et al., 2004).

Dopaminergic neurons in the SNpc predominantly project to the striatum, and, therefore, dopamine cell-loss results in the depletion of striatal dopamine (Moore, 2003). Striatal dopamine typically modulates the excitability of the neurons (Schultz, 2007) by activating the direct pathway and suppressing the indirect pathway, leading to a net increase of information flow through the basal ganglia (Alexander & Crutcher, 1990). Reduced nigrostriatal input in PD leads to increased inhibitory output from the globus pallidus interna, and subsequently, to the cortex. As a result, initiation of movement is suppressed, and the motor characteristics (e.g., hypokinesia, bradykinesia) of PD present (Rodriguez-Oroz et al., 2009). By the time motor symptoms present clinically, 60% of SNpc cells are lost, and 80% of the associated striatal dopamine is depleted (Dauer & Przedborski, 2003).

1.3 Clinical Symptoms in Parkinson's Disease

The cardinal motor symptoms of PD are bradykinesia, rigidity, tremor, and postural instability (Jankovic, 2008), and are usually characterized by a unilateral or asymmetric presentation at onset. Additional motor impairments include gait disturbances, micrographia, dysphagia, and dysarthria (Boonstra, Van Der Kooij, Munneke, & Bloem, 2008; Kalf, de Swart, Bloem, & Munneke, 2012; Shukla et al., 2012; Tjaden, 2008).

1.3.1 Bradykinesia, Hypokinesia, Akinesia

Bradykinesia, hypokinesia, and akinesia collectively refer to a group of functional impairments in voluntary movements (Berardelli, Rothwell, Thompson, & Hallett, 2001) and are present in approximately 80% of patients at symptom onset (Pagano, Ferrara, Brooks, & Pavese, 2016). These movement impairments describe different, although related, aspects of movement, and are suggested to arise from basal ganglia dysfunction secondary to low levels of striatal dopamine in the putamen (Dickson, 2008; Rabey & Burns, 2008). They are likely, however, to vary in their specific pathophysiological mechanisms (Rodriguez-Oroz et al., 2009). Bradykinesia is characterized by reduced speed of movements, hypokinesia describes reduced amplitude or frequency of movement, and akinesia refers to a delay or absence in movement (Jankovic, 2008). This group of impairments is of particular interest as they may affect movements of the speech musculature (Sapir, 2014).

1.3.2 Rigidity

Rigidity in PD is characterized by increased muscle tone and resistance to passive movement and occurs in 75-90% of patients with PD (Hoehn & Yahr, 1967; Hughes, Daniel, Blankson, & Lees, 1993; Pagano et al., 2016). It can affect both limb and axial muscles and is more noticeable when a joint is examined slowly (Rodriguez-Oroz et al., 2009). Rigidity has also been reported in the ribcage (Huber, Stathopoulos, Ramig, & Lancaster, 2003; Solomon & Hixon, 1993) and orofacial musculature (Caligiuri, 1987; Hunker, Abbs, & Barlow, 1982). The presence of rigidity has been shown to be associated with reduced ribcage excursion (Solomon & Hixon, 1993) and reduced movement amplitudes of the lips (Chu, Barlow, & Lee, 2015).

1.3.3 Tremor

Tremor at rest is one of the most common and recognizable symptoms of PD (Jankovic, 2008) and is the presenting symptom for approximately 70-80% of patients (Hoehn & Yahr, 1967; Pagano et al., 2016). Parkinsonian tremor is a low-frequency (4-6Hz) oscillatory movement, and usually occurs distally in the limbs but can also affect the jaw and lips (Rodriguez-Oroz et al., 2009). The tremor is typically inhibited during movement and sleep (Jankovic, 2008).

1.3.4 Postural Instability

Postural instability refers to the tendency to be unstable when standing upright and usually occurs after the onset of the other cardinal features (Jankovic, 2008). Postural instability compromises an individual's ability to maintain balance during tasks such as walking, turning, and standing from sitting (Morris, Iansek, Smithson, & Huxham, 2000), and significantly increases the risk of falls in PD (Landers et al., 2008).

1.4 Medical Treatment in Parkinson's Disease

The medical approaches to the treatment of PD can be categorized as pharmacological or surgical. Pharmacological interventions are typically initiated in the early stages of PD, while surgical interventions are performed in advanced PD (Guttman, Kish, & Furukawa, 2003).

Pharmacological treatments include both neuroprotective and symptomatic treatments. Neuroprotective drugs aim to slow the development and progression of the disease by targeting pathogenic pathways associated with neurodegeneration (Schapira, Olanow, Greenamyre, & Bezard, 2014). While advances have been made in identifying potential neuroprotective agents for PD, further investigations are required. The majority of available pharmacological treatments, therefore, aim to address the motor and non-motor symptoms in PD. Motor symptoms are primarily treated with levodopa, in isolation or combined with dopamine agonists, monoamine oxidase-B inhibitors, anticholinergic agents, amantadine, and/or catechol-O-methyl transferase inhibitors (Connolly & Lang, 2014). The treatment of non-motor symptoms depends on their presentation (e.g., sleep disorders, depression, constipation; Rao, Hofmann, & Shakil, 2006).

Levodopa is the most effective drug for the treatment of motor symptoms in PD (Connolly & Lang, 2014; Ferreira et al., 2013). As a metabolic precursor to dopamine, levodopa aims to reduce motor symptoms by artificially replacing dopamine-depleted cells. Levodopa was first discovered in the 1960s, but patients often experienced side effects, such as nausea and vomiting, until it was later combined with carbidopa (Rao et al., 2006). Approximately 50% of patients, however, develop levodopa-induced complications within several (5-10) years of starting levodopa treatment (Obeso et al., 1999). These include motor fluctuations and involuntary movements, known as dyskinesias (Aquino & Fox, 2015; Calabresi, Di Filippo, Ghiglieri, Tambasco, & Picconi, 2010). At this stage, patients may become candidates for surgical intervention.

Deep brain stimulation (DBS) is the most frequently performed surgical procedure for the treatment of advanced PD (Fasano, Daniele, & Albanese, 2012). High-frequency electrical stimulation is used to modulate neuronal activity in the globus pallidus interna (GPi), subthalamic nucleus (STN), pedunculopontine nucleus (PPN), or the ventralis intermedius nucleus (VIM) (Fasano et al., 2012). The benefit and long-term impact of DBS have been shown in a number of high-quality studies, particularly for the treatment of bradykinesia, rigidity and tremor (Fasano et al., 2012; Hamani, Richter, Schwalb, & Lozano, 2005; Hariz et al., 2008; Volkmann et al., 2004).

The medical management of PD, however, has limited and inconsistent effects on the remediation of motor speech difficulties in PD (Pinto et al., 2005; Pinto et al., 2004; Plowman-Prine et al., 2009; Schulz & Grant, 2000). When examined "on" levodopa medication, patients with PD have shown improved, deteriorated, or unchanged speech symptoms, relative to the "off" stage (de Letter, Santens, de Bodt, Boon, & van Borsel, 2006; Goberman, Coelho, & Robb, 2005; Ho, Bradshaw, & Iansek, 2008; Sanabria et al., 2001; Skodda, Grönheit, & Schlegel, 2011). Even when improvements have been reported, the magnitude of change has been small and often not considered to be clinically meaningful (Theodoros, 2011). Further, DBS has frequently been associated with exacerbation of motor speech impairment (Kluger, Foote, Jacobson, & Okun, 2011; Pinto et al., 2005; Rodriguez-Oroz et al., 2005). The variation in treatment responses between the limb and speech motor systems is likely explained by significant differences in the respective neuroanatomy and neurophysiology of limb and speech motor control (Kent, 2004). Ultimately, the limited effects of medical treatment on the speech impairment in PD underlie the need for effective behavioural management approaches to speech therapy in this population.

1.5 Dysarthria in Parkinson's Disease

Dysarthria is defined as "a collective name for a group of speech disorders resulting from disturbances in muscular control over the speech mechanism due to damage of the central or peripheral nervous system" and includes issues "due to paralysis, weakness or incoordination of the speech musculature" (p. 246, Darley, Aronson, & Brown, 1969b). Dysarthria can be subdivided into a number of types that are distinguished perceptually and are associated with specific lesion sites (Darley, Aronson, & Brown, 1975).

In PD, up to 90% of patients develop dysarthria, the most prevalent being HKD (Hartelius & Svensson, 1994; Ho, Iansek, Marigliani, Bradshaw, & Gates, 1998; Logemann et al., 1978). HKD is characterized by a cluster of perceptual symptoms related to phonation, prosody, and articulation (Darley, Aronson, & Brown, 1969a; Darley et al., 1969b). Phonatory impairments include reduced vocal loudness, low pitch, and a breathy voice quality; prosodic impairments relate to monoloudness, monopitch, and reduced stress; and articulation in PD is characterized by imprecise consonants, short rushes of speech, and variable speaking rate (Darley et al., 1969a, 1969b). Individuals with PD may experience various combinations of these symptoms (Duffy, 2013). However, the early stages of HKD are typically associated with phonatory/prosodic impairments, while articulation disorder develops as the disease progresses (Logemann et al., 1978). As a result, patients experience an overall reduction in their speech intelligibility (Miller, Noble, Jones, Allcock, & Burn, 2008; Tjaden et al., 2014; Weismer et al., 2001) that affects their ability to communicate with family and friends, and as members of society (Miller et al., 2006). Subsequent feelings of inadequacy, frustration, and a loss of independence related to their communication ability can lead to withdrawal and social isolation; ultimately resulting in a reduced quality of life (Miller et al., 2008; Miller et al., 2006).

A number of factors have been proposed to explain the motor speech disorder in PD. Traditionally, these factors included some of the primary features of the disease – namely, bradykinesia, hypokinesia, akinesia, and rigidity (see review; Sapir, 2014). More recently, additional explanatory factors have been considered. Among them is a deficit in the internal but not the external cueing of movements (Weir-Mayta et al., 2017). As a result, patients show difficulties in the internal regulation of movements (e.g., speech, walking), but can often demonstrate improvements when externally cued to speak louder or more clearly, or to walk with auditory or visual cues (Goberman & Elmer, 2005; Rochester et al., 2005; Suteerawattananon, Morris, Etnyre, Jankovic, & Protas, 2004; Tjaden et al., 2014). Further, as the basal ganglia play a central role in the processing of sensory information (Boecker et al., 1999), evidence of sensory deficits has been reported in the phonatory system (Hammer & Barlow, 2010), in oral articulators (Schneider, Diamond, & Markham, 1986), as well as in the perception of auditory stimuli in individuals with PD (Ho, Bradshaw, & Iansek, 2000). Additionally, deficits in sensorimotor integration, i.e., the use of sensory information in the guiding of movement (Clark, Adams, Dykstra, Moodie, & Jog, 2014), may also affect the speech mechanism in patients with PD (Mollaei, Shiller, & Gracco, 2013). Difficulties in temporal processing and dysrhythmia (Harrington et al., 2011; Jones, Malone, Dirnberger, Edwards, & Jahanshahi, 2008) may also impact the temporal control of speech – manifesting as changes in speaking rate (Skodda & Schlegel, 2008) and timing of speech movements (Ackermann, Konczak, & Hertrich, 1997; Caligiuri, 1987). In sum, multiple physiological factors may underlie the signs and symptoms of HKD in individuals with PD. Given the impact of these factors on the quality of movement, studying articulatory movements may offer important insights into the underlying mechanisms of HKD in patients with PD.

1.6 Articulatory Movement Disorder in Parkinson's Disease

As previously described, articulation in PD is perceptually characterized by imprecise consonants, short rushes of speech, and variable speaking rate (Darley et al., 1969a, 1969b). Perceptual descriptors are limited, however, in their ability to delineate the underlying nature of the articulatory movement disorder in PD, and should be supplemented with quantitative instrumental assessment (Kent, 1996). Specifically, some information regarding movements of the jaw, lips, and tongue can be inferred from the analysis of acoustic recordings of speech or more completely and directly using kinematic methods.

1.6.1 Acoustic Studies

Acoustic studies historically provided substantial insight into the spatial and timing functions of oral articulators in HKD. Acoustic measures of formant frequencies reflect vocal tract configuration during speech production (Walsh & Smith, 2012). For example, tongue height and protrusion/retraction are reflected in the first (F1) and second (F2) formants, respectively, and formant transitions indicate the overall rate of change in the shape of the vocal tract during speech production (Kent, 1993). Existing acoustic studies in PD are suggestive of smaller, slower articulatory movements (hypokinesia, bradykinesia) and impaired articulatory timing and durations, inferred from measures of vowel space area (VSA), formant transitions, voice onset time (VOT), and segment/sentence durations.

Disease-related changes in formant frequencies have been documented in a number of studies reporting VSA compression (Skodda, Visser, & Schlegel, 2011; Tjaden, Lam, & Wilding, 2013; Tjaden & Wilding, 2004; Whitfield & Goberman, 2014), reduced formant transitions during diphthongs (Tjaden, Richards, Kuo, Wilding, & Sussman, 2013; Tjaden & Wilding, 2004; Walsh & Smith, 2012; Weismer et al., 2001), and smaller F2 ranges in connected speech (Yunusova, Weismer, Kent, & Rusche, 2005). Smaller VSA ranges of F2 point towards smaller overall articulatory movements (Yunusova et al., 2005), and reduced formant transitions indicate changes in movement speed (Walsh & Smith, 2012). Taken together, these findings suggest the presence of hypokinesia and bradykinesia in the oral musculature during speech production.

Acoustic reports of articulatory timing and durations are also suggestive of the articulatory abnormalities in PD, although the findings have been inconsistent. A number of studies reported increased, decreased, or comparable to normal mean VOT, an essential characteristic of clearly articulated stop consonants (Bunton & Weismer, 2002; Fischer & Goberman, 2010; Flint, Black, Campbell-Taylor, Gailey, & Levinton, 1992; Forrest, Weismer, & Turner, 1989; Weismer, 1984). Increased VOT for word-initial stop consonants indicates delayed initiation of phonation and reduced integrity of coordination between phonatory and articulatory gestures (Weismer, 2006). In contrast, decreased VOT may result from stiffness of the phonatory musculature in PD. Reports of durations, both at the segmental (individual sound) and sentence level, have varied within and across studies (Flint et al., 1992; McAuliffe, Ward, & Murdoch, 2006; Weismer, 1984; Weismer et al., 2001).

1.6.2 Kinematic Studies

Although acoustic studies offer insight into the articulatory deficit in PD, kinematic studies are necessary to provide a direct assessment of the effect of the disease on the motor performance of the jaw, lips, and tongue. To the best of our knowledge, a total of 19 speech kinematic studies have been published to date in PD. The majority of them conducted analysis at the segmental level of speech production, examining movement characteristics of opening and closing gestures (i.e., movements away from and towards a consonant constriction). Only two studies to date have examined measures taken across recordings of connected speech at the sentence or passage levels (Walsh & Smith, 2012; Weismer, Yunusova, & Bunton, 2012).

Early kinematic studies in PD primarily examined movements of the easily accessible jaw and lips (Ackermann, Gröne, Hoch, & Schönle, 1993; Ackermann, Hertrich, Daum, Scharf, & Spieker, 1997; Ackermann, Konczak, et al., 1997; Bandini et al., 2016; Caligiuri, 1987; Connor, Abbs, Cole, & Gracco, 1989; Forrest & Weismer, 1995; Forrest et al., 1989; Hirose, Kiritani, Ushijima, Yoshioka, & Sawashima, 1981; Walsh & Smith, 2012; Yunusova, Weismer, Westbury, & Lindstrom, 2008). More recently, improvements in technology have facilitated the study of the tongue, which is hidden from view during speech production (Goozée, Shun, & Murdoch, 2011; Wong, Murdoch, & Whelan, 2010; Wong, Murdoch, & Whelan, 2011; Wong, Murdoch, & Whelan, 2012; Yunusova et al., 2008).

1.6.2.1 Jaw and Lips

Movements of the jaw and lower lip in individuals with PD have been characterized by a reduction in movement size and speed at the segmental level (Ackermann, Konczak, et al., 1997; Caligiuri, 1987; Connor et al., 1989; Forrest & Weismer, 1995; Forrest et al., 1989; Hirose et al., 1981). Further, when both articulators have been examined, movements of the jaw have shown a greater effect of the disease than the lower lip (Connor et al., 1989; Forrest et al., 1989). Findings regarding upper lip movement during speech production in individuals with PD have shown smaller or comparable to normal movement amplitudes and no changes in movement speed (Connor et al., 1989; Forrest et al., 1989).

Only one study to date has examined movements of the jaw and lower lip in a single sentence produced by patients with PD (Walsh & Smith, 2012). Walsh and Smith (2012) employed measures to capture range of movement amplitude and velocity based on 80% of points in the displacement and velocity trajectories, respectively, in order to identify the primary operating range of motion during sentence production. Their findings showed that at the sentence level, jaw and lip movements were significantly smaller and slower in individuals with PD as compared to healthy controls.

1.6.2.2 Tongue

Fewer reports and inconsistent findings exist for movements of the tongue during speech production in individuals with PD. Yet, the tongue is considered to be the primary articulator for speech production, as its position and shape have a large effect on the overall shape of the vocal tract and resulting acoustic signal (Smith, 1992). Instances of both increased and decreased tongue movement size have been reported at the segmental level in speakers with PD, compared to healthy controls (Wong et al., 2010; Wong et al., 2011; Wong et al., 2012; Yunusova et al., 2008).

A single study reported passage-level data for individuals with PD, where measures of jaw, lips, and tongue (blade, body, and dorsum) movements were taken across a whole passage read at a normal comfortable speaking rate and loudness (Weismer et al., 2012). The results from Weismer et al.'s study suggested a tendency for speakers with PD to use smaller and slower movements across all articulators, including the tongue.

In addition to having only limited knowledge of the tongue effects in PD, particularly at the sentence level, the majority of movement studies have included only participants with very mild or "just noticeable" symptoms of dysarthria, and the findings may not be representative of speakers who show greater involvement of the articulatory subsystem (Weismer et al., 2012; Wong et al., 2010; Wong et al., 2011; Wong et al., 2012). In our work, we address these limitations by analyzing tongue and jaw movements in sentences produced by a relatively large number of participants with PD, with varying degrees of dysarthria severity, compared to their age-matched healthy controls.

1.7 Association between Articulatory Movements and Speech Intelligibility

Understanding the relationship between articulatory movements and speech intelligibility is crucial to the development of movement-based therapies, as improving speech intelligibility is a central goal in dysarthria therapy (Yorkston, Strand, & Kennedy, 1996). In the past, acoustic studies have shown an association between acoustic measures, such as vowel space area and formant transitions, and speech intelligibility decline (McRae, Tjaden, & Schoonings, 2002; Weismer et al., 2001).

Only two studies have directly examined associations between speech kinematics and intelligibility in PD, however. Forrest et al. (1989) conducted a study comparing lower lip amplitude and velocity between three speakers with mild speech intelligibility deficit and three with relatively more severe speech intelligibility deficit. The results showed a tendency for the more severely impaired speakers to have smaller and slower lower lip movements, as compared to their less impaired peers, during a closing gesture of a consonant-vowel-consonant (CVC) syllable.

In a more recent study, the movement-intelligibility relationship was assessed in a sample size of 22 patients with PD, and scaled intelligibility showed a significant positive correlation with average speed of a marker attached to the tongue body during passage reading (Weismer et al., 2012). Similar associations were examined, but not found, for the measures of jaw, lip, and tongue blade movements in this study (Weismer et al., 2012), suggesting that the tongue body movements may be particularly important when considering the impact that the disease has on speech intelligibility (Weismer et al., 2012).

While analyzing movements at the segmental level sheds light on the control of articulators during individual gestures, patients with PD experience greater reduction in intelligibility during connected speech, for example, when saying sentences or reading passage-length material (Kempler & Van Lancker, 2002; Weismer et al., 2001). As a result, connected speech is typically targeted in therapy to maximize intelligibility gains (Yorkston, Hakel, Beukelman, & Fager, 2007). Establishing a relationship between changes in articulatory movements and speech intelligibility would provide means for identification of specific targets for a movement-based therapy aiming to improve speech intelligibility.

1.8 Articulatory Movements and Speaking Styles

Varying speaking style, such as increasing vocal loudness, increasing clarity, or manipulating speaking rate, are among common approaches to the treatment of dysarthria in PD (Hustad & Weismer, 2007; Tjaden, Lam, et al., 2013; Tjaden et al., 2014). The underlying premise of these approaches is that a speaker applies the selected strategy across utterances, instead of focusing on the production of individual sounds. By doing so, they target multiple physiological subsystems, including prosody, phonation, and articulation, at the same time (Dromey & Ramig, 1998). With the exception of loud speech (see below), these treatment approaches have not been evaluated empirically in this population, however, and the kinematic studies of these speaking conditions, outside of a structured treatment, are also limited.

Loud and clear speech have been characterized by larger movement size and faster movement speed of the jaw and lower lip when examined in opening and closing gestures of CVC syllables (Darling & Huber, 2011; Dromey, 2000). Clear speech, but not loud speech, has also been associated with an increase in lower lip spatiotemporal variability when examined across multiple repetitions of a sentence in PD (Dromey, 2000). To date, tongue movements have only been examined in loud speech relative to normal production, and reports have been inconsistent. One study showed that speaking louder was associated with increased tongue movement speed during opening and closing gestures of a VCV syllable (Goozée et al., 2011). A further study examining tongue movements of two speakers revealed that speakers can employ different strategies to achieve loud speech; one increased tongue movement size and speed, while the second speaker reduced maximum acceleration (Wong, Kuruvilla-Dugdale, & Ng, 2016). Finally, a slower rate of speech was associated with increased lower lip movement variability for individuals with PD, but measures of movement size or speed have not yet been examined (Kleinow, Smith, & Ramig, 2001).

No kinematic study to date has examined the effect of multiple speaking styles on multiple articulators for the same group of speakers with PD. A more comprehensive understanding of the effects of varying speaking styles is needed in order to establish a physiological basis for these speaking strategies as potential treatments in PD.

1.9 Behavioural Treatment of Dysarthria in Parkinson's Disease

Since the 1980s, a number of different approaches to speech therapy in PD have been reported in the literature (see reviews, Atkinson-Clement, Sadat, & Pinto, 2015; Herd et al., 2012; Yorkston, Hakel, et al., 2007). These include therapies addressing respiratory control (Smith, Ramig, Dromey, Perez, & Samandari, 1995), phonation (de Swart, Willemse, Maassen, & Horstink, 2003; Ramig, Countryman, Thompson, & Horii, 1995; Ramig et al., 2001; Richardson, Sussman, Stathopoulos, & Huber, 2014), and prosody (Johnson & Pring, 1990; Le Dorze, Dionne, Ryalls, Julien, & Ouellet, 1992; Martens et al., 2015).

One approach in particular, the Lee Silverman Voice Treatment (LSVT® LOUD) program, has been widely practiced in the field (Ramig et al., 1995; Ramig et al., 2001). LSVT is a speech treatment aimed at increasing vocal loudness. The effectiveness of LSVT has been reported with respect to the outcome measures of phonatory performance (e.g., dB SPL, fundamental frequency variation; Ramig et al., 1995; Ramig et al., 2001) and speech intelligibility (Cannito et al., 2012). Randomized Control Trials (RCTs) of LSVT reported a greater magnitude of improvement in measures of phonatory performance compared to interventions targeting respiratory support alone (Ramig et al., 1995) or articulation (Halpern et al., 2007); however, the patients recruited into these studies have been characterized as having relatively mild symptoms of dysarthria. Further, not all individuals with PD present with reduced vocal loudness/monopitch (Adams & Dykstra, 2009), and those that present with significant articulatory disorders seem to respond poorly to the program (Fox, Ebersbach, Ramig, & Sapir, 2012). The high effort required for maintaining loud speech is an additional concern in this intervention (Schneider, 2007).

Other approaches have used auditory feedback, via small assistive devices, to elicit changes in rate, vocal loudness and/or pitch. These approaches are based on the Lombard effect (Lombard, 1911), where speakers are expected to reflexively adjust their speech in the presence of noise. They can involve presenting delayed auditory (DAF) or frequency-altered feedback (FAF) of the speaker’s own speech, or multi-talker babble noise (e.g., Brendel, Lowit, & Howell, 2004; Richardson et al., 2014; Stathopoulos et al., 2014; van Nuffelen, de Bodt, Vanderwegen, Van De Heyning, & Wuyts, 2010; Wang, Metman, & Bernard, 2008). Reports of these approaches to date have primarily focused on their effect in single recording sessions, rather than in the context of treatment efficacy/effectiveness. One study reported pre-post treatment data for a group of patients who heard multi-talker babble noise via the SpeechVive device in an 8-week treatment program. Improvements following treatment were seen in measures of phonation (e.g., dB SPL), interarticulator timing (i.e., voice onset time, percent voicing), and intelligibility in 6/10 participants (Richardson et al., 2014); however, treatment efficacy or effectiveness has not yet been established in an RCT (or comparable design) study.

Overall, the existing speech interventions target phonatory and prosodic deficits but do not directly address the underlying speech movement disorder in PD. As a result, the 45% of individuals with PD who experience articulatory impairments have limited treatment options.

This highlights the need to develop treatments with specific candidacy outlined, rather than focusing on a single treatment approach for all patients with PD (Yunusova et al., 2017). Heterogeneity in presentation is a challenge observed across the PD phenotype (Foltynie, Brayne, & Barker, 2002) and, as such, a range of therapy options are required to meet the varying needs of this population.

1.10 Challenges of Motor Rehabilitation in Parkinson's Disease

Motor rehabilitation plays an important role in the management of motor symptoms in PD, and the support for rehabilitation therapies, including physio-, occupational and speech therapy, is growing (Gage & Storey, 2004; Nijkrake et al., 2007). An ongoing challenge of the rehabilitation therapies is the development of effective treatments for patients with PD, given the complex nature of the disease (Abbruzzese, Marchese, Avanzino, & Pelosin, 2016). In particular, individuals with PD experience impairments in their motor learning abilities due to the significant role that the basal ganglia play in motor learning (Doyon et al., 2009; Wu, Chan, & Hallett, 2010). Studies have shown that individuals with PD can successfully acquire or re-acquire motor skills, however, they do so at a slower rate than their neuro-typical peers and, therefore, require a greater amount of practice (Hayes, Hunsaker, & Dibble, 2015; Siegert, Taylor, Weatherall, & Abernethy, 2006). Further, implicit motor learning mechanisms, which depend on motor practice instead of declarative memory, are particularly affected in PD (Nieuwboer, Rochester, Muncks, & Swinnen, 2009). Consequently, individuals with PD appear to benefit from explicit forms of motor learning, especially at the later stages of motor learning when skill transfer occurs (Abbruzzese et al., 2016).

One of the most challenging aspects of rehabilitation therapy is to motivate clients to perform a sufficient number of trials during training to produce lasting change in their control of movement. Motivation can be significantly reduced in PD, as the dopamine-dependent circuits for motivation are affected in the brain (Drui et al., 2014). Effective therapies need to be highly motivating in order to engage patients in the learning process of rehabilitation.

Finally, patients with PD demonstrate a deficit in the ability to use internal cues to monitor and adjust their motor performance (Brown & Marsden, 1988; Georgiou et al., 1993; Stolwyk, Triggs, Charlton, Iansek, & Bradshaw, 2005). They tend to rely more on external stimuli to perform motor movements and learn motor patterns (Adamovich, Berkinblit, Hening, Sage, &

Poizner, 2001; Lewis, Byblow, & Walt, 2000; Schettino et al., 2006; Weir-Mayta et al., 2017). The addition of visual information seems to capitalize on a relative strength in PD, and help to compensate for proprioceptive deficits often observed during motor tasks (Jobst, Melnick, Byl, Dowling, & Aminoff; Klockgether, Borutta, Rapp, Spieker, & Dichgans, 1995; Rickards & Cody, 1997).

1.11 Augmented Visual Feedback in Motor Rehabilitation

Augmented feedback is defined as “extrinsic feedback provided to a learner” that “supplements the information that is naturally available” (p. 39, Swinnen, 1996). AVF provides a visual depiction of movement and can supplement an individual’s intrinsic (auditory, somatosensory) feedback (Schmidt & Wrisberg, 2008). AVF has been shown to enhance motor learning in both healthy and disordered populations (e.g., stroke; Molier, Van Asseldonk, Hermens, & Jannink, 2010). It may be particularly suited to the underlying nature of the motor disorder in PD as a treatment modality as it engages visual sensory channels and can make the learning process more explicit by providing visual information regarding the treatment goal and movement characteristics (Lee, Swinnen, & Serrien, 1994). Further, when incorporated into engaging games, AVF may provide a means of developing highly motivating therapies (Barry, Galna, & Rochester, 2014). In PD, there has recently been an increase in the number of studies reporting novel therapies employing AVF, particularly in the area of physiotherapy (Barry et al., 2014). However, there is a lack of a systematic evaluation of the effect of AVF-based interventions on the recovery of motor functions in PD.

1.12 Augmented Visual Feedback in Speech Rehabilitation

AVF has a long history in speech therapy, where traditionally a mirror was used to highlight key components of articulatory movements and to encourage self-monitoring during speech practice (e.g., Rosenbek, Lemme, Ahern, Harris, & Wertz, 1973). More recently, technologies such as ultrasound, electropalatography, and electromagnetic articulography have facilitated the visualization of speech movements or contact patterns of the tongue, and studies have revealed positive results of visual feedback-based treatments in both pediatric and adult client groups (e.g., Gibbon et al., 2001; Mauszycki, Wright, Dingus, & Wambaugh, 2016; McNeil et al., 2010). In adults with acquired apraxia of speech, for example, studies have shown that patients are able to use visual feedback regarding tongue position to improve their speech production

(Mauszycki et al., 2016; McNeil et al., 2010). To the best of our knowledge, only two studies to date examined the effect of acoustic-based AVF when delivered as part of speech therapy programs in PD (Johnson & Pring, 1990; Scott & Caird, 1984). Johnson and Pring provided AVF regarding pitch and intonation contours of phrases. Other elements of their treatment, however, did not incorporate visual feedback, such as respiratory control tasks and articulation exercises. Scott and Caird provided AFV regarding vocal loudness and showed similar results for the experimental group and a control group who received comparable treatment without visual feedback. To date, the effect of AVF regarding articulatory movements has not been assessed in PD.

1.13 Treatment Design Factors

In addition to the method at the center of the therapeutic program (e.g., AVF), rehabilitation therapies can vary in a number of treatment design factors, and specific factors have been associated with enhanced motor learning and improved treatment outcomes. These factors include (1) treatment amount (Lohse, Lang, & Boyd, 2014); (2) treatment intensity (Kwakkel, Wagenaar, Koelman, Lankhorst, & Koetsier, 1997); (3) gamification of feedback (Barry et al., 2014); (4) nature of feedback, i.e., information about the outcome of movement (knowledge of results, KR) vs. the quality of moment (knowledge of performance, KP) (Young & Schmidt, 1992); (5) timing of feedback (e.g., real-time/concurrent vs. delayed) (Schmidt & Wulf, 1997); and (6) frequency of feedback (e.g., every trial vs. summary of 5 trials) (Winstein & Schmidt, 1990). Some of these factors have been studied directly in rehabilitation programs or motor learning paradigms in patients with PD. For instance, in a group of patients with PD with gait abnormalities, treadmill training programs showed better outcomes following low-to-medium intensity (2-3 times/week) training than high-intensity training (5 times/week) (Pelosin et al., 2016). Additionally, a reduced feedback schedule enhanced the retention of motor skills in a hand-positioning task relative to a spatial target (Chiviacowsky, Campos, & Domingues, 2010) and a speech-timing task (Adams, Page, & Jog, 2002). While often not experimentally manipulated within studies, these treatment design factors are implicitly incorporated into the design of rehabilitation programs. We do not yet have clear recommendations to guide the development of a novel treatment employing AVF in PD. It is important to first examine more closely how these factors have been varied across studies and their subsequent effect on study outcomes.

1.14 Current Studies

There is a significant need in the field to develop and evaluate the efficacy of novel speech therapy methods for patients with PD. In this dissertation, we explored the possibility of developing a treatment method that directly addresses the underlying articulatory movement abnormalities in the disease. Prior to the evaluation of this method, we studied speech movements in PD and identified potential speech movement targets for therapy. We also determined key components of enhanced outcomes for motor treatment in PD, based on a review of the existing rehabilitation literature, which informed the design of treatment.

A series of three studies was conducted. The first study (Chapter 2) aimed to further our understanding of the speech movement disorder in PD and the physiological mechanisms underlying existing approaches to dysarthria treatment. These aims were addressed by (1) examining the association between speech movements and speech intelligibility in PD, and (2) comparing the effect of varying speaking styles on speech movements in PD.

The objective of the second study (Chapter 3) was to systematically review the use of augmented visual feedback-based treatments (AVFT) for motor rehabilitation in the PD literature. Using Cochrane-based methodology, this study (1) evaluated the effectiveness of AVFT for motor rehabilitation and (2) compared the effect of different treatment design factors associated with enhanced outcomes of AVFT.

The final study (Chapter 4) built on the findings of the previous studies – a novel speech therapy program using a verbal cue and AVF was developed, incorporating a movement target identified in the first study and optimal design factors determined in the second study. This study sought to establish the preliminary effects of this novel therapy approach when implemented in a 10-session program. Specifically, this study assessed the effects of the therapy on speech movements and speech intelligibility.

Chapter 2
Sentence-Level Movements in Parkinson's Disease: Loud, Clear, and Slow Speech

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2 Sentence-Level Movements in Parkinson's Disease: Loud, Clear, and Slow Speech

Abstract

Purpose: To further understand the effect of Parkinson's disease (PD) on articulatory movements in speech and to expand our knowledge of therapeutic treatment strategies, this study examined movements of the jaw, tongue blade, and dorsum during sentence production with respect to speech intelligibility, and compared the effect of varying speaking styles on these articulatory movements.

Method: Twenty-one speakers with PD and 20 healthy controls produced three sentences under normal, loud, clear, and slow speaking conditions. Speech intelligibility was rated for each speaker. A 3D electromagnetic articulograph tracked movements of the articulators. Measures included articulatory working spaces, ranges along the first principal component, average speeds, and sentence durations.

Results: Speakers with PD demonstrated a significant reduction in jaw movements as well as shorter than normal sentence durations. Between-speaker variation in movement size of the jaw, tongue blade, and tongue dorsum was associated with speech intelligibility. Analysis of speaking conditions revealed similar patterns of change in movement measures across groups and articulators; larger than normal movement sizes and faster speeds for loud speech; increased movement sizes for clear speech; and larger than normal movement sizes and slower speeds for slow speech.

Conclusions: Sentence-level measures of articulatory movement are sensitive to both disease-related changes in PD and speaking style manipulations.

Keywords: Parkinson's disease, electromagnetic articulography, articulatory working space, movement speed.

2.1 Introduction

Parkinson's disease (PD) is a progressive neurodegenerative disease affecting voluntary movements, including those of the jaw, face, lips, and tongue, during speech and non-speech tasks (Schulz & Grant, 2000). Up to 90% of patients develop a speech disorder, most commonly hypokinetic dysarthria, as the disease progresses (Ho et al., 1998). In addition to the abnormalities in the phonatory and prosodic domains, 45% of patients show difficulties with speech articulation including imprecise consonants and short rushes of speech (Logemann et al., 1978). As a consequence, speech intelligibility becomes reduced, and patients experience loss of communication abilities and social isolation (Pinto et al., 2004).

Kinematic studies provide a direct insight into the articulatory changes in PD. Early studies of jaw and lip movement showed a reduction in movement size and speed as well as impaired duration at the segmental (opening/closing gestures) level (Ackermann et al., 1993; Ackermann, Konczak, et al., 1997; Connor et al., 1989; Forrest & Weismer, 1995; Forrest et al., 1989; Yunusova et al., 2008). Impaired articulation is, however, more likely to occur in connected speech in PD than at the word or syllable level (Kempler & Van Lancker, 2002; Weismer et al., 2001) and, therefore, the examination of articulation at the sentence level is required. Movements of jaw and lips at the sentence level have been reported, to the best of our knowledge, in a single study of patients with PD and showed a reduction in the ranges of jaw/lip motion and velocity (Walsh & Smith, 2012). Considerably less is known about tongue movements in this population, and existing studies have reported inconsistent findings. Increased tongue movement amplitude and speed were found in studies of opening/closing gestures (Wong et al., 2010; Wong et al., 2011), while a study of the tongue tip and dorsum during a passage reading task showed an overall reduction in tongue movement size and speed (Weismer et al., 2012). Further, reports of sentence durations have varied within and across studies, with observations of shorter and comparable to normal durations for speakers with PD (Flint et al., 1992; McAuliffe et al., 2006; Weismer et al., 2001).

Measures of articulatory kinematics have rarely been examined in relation to speech intelligibility, yet acoustic studies suggest, albeit indirectly, that speech intelligibility may be related to the extent of articulatory movement impairment in PD (Kim, Kent, & Weismer, 2011; McRae et al., 2002). Two studies — one reporting speech kinematics at the segmental level and one at the passage level — have reported associations between articulatory movement measurements and intelligibility in PD. Specifically, Forrest et al. (1989) examined changes in lower lip amplitude and velocity as a function of intelligibility between more and less affected individuals and found smaller movement and reduced velocity in more affected speakers. The findings were based only on three speakers with mild and three speakers with severe intelligibility deficits and, thus, might be limited in their generalizability. More recently, a positive correlation between scaled intelligibility and average speed of the tongue, but not the jaw or lips, during a passage reading task was reported for speakers with PD (Weismer et al., 2012). Assessing the relationship between speech intelligibility and articulatory movement is important in order to identify key movement parameters that contribute to impaired communication in hypokinetic dysarthria.

Most kinematic studies to date report findings related to a single stimulus, which limits the interpretation of findings as well as the generalizability of results. Further, the effect of PD on articulatory kinematics may vary based on the stimulus examined. Stimulus effects have been observed at the acoustic level (Kent et al., 1992; Kim, Weismer, Kent, & Duffy, 2009); for kinematic parameters (Yunusova et al., 2008); and in terms of sentence durations (Flint et al., 1992; Weismer et al., 2001). For example, words with larger F2 slopes (Kim et al., 2009) and movement extents (Yunusova et al., 2008) appeared to be more sensitive to dysarthria that those with smaller slopes and extents. Certain sentences also appeared to be more sensitive to durational changes in dysarthria than other sentences (Flint et al., 1992; Weismer et al., 2001). In the current study, we examined three different sentences that were designed to elicit large articulatory movements.

Adjusting speaking style, such as increasing loudness or clarity, is a frequently used approach in the treatment of dysarthria (Hustad & Weismer, 2007). These adjustments are applied across utterances and aim to address impairments across multiple physiological subsystems, including respiration, phonation, articulation, and resonance simultaneously (Dromey & Ramig, 1998). The resulting changes, particularly those that occur in the articulatory subsystem, are currently not well understood. Although a number of studies evaluated the effect of loud, clear, or slow speaking styles on jaw and lip movements at the segmental level in PD (Darling & Huber, 2011; Dromey, 2000; Kleinow et al., 2001), limited and inconsistent results are available for the tongue (Goozée et al., 2011; Wong et al., 2016). Both loud and clear speech in PD were characterized by an increase in movement size and velocity (Darling & Huber, 2011; Dromey, 2000); however, clear speech has also been shown to increase spatiotemporal variability when examined across sentence repetitions (Dromey, 2000). An increase in lip movement variability was also reported for individuals with PD during slow speech, but measures of movement size or speed have not been examined (Kleinow et al., 2001). When compared to control speakers, individuals with PD seem to use different control strategies to vary their speaking style (Darling & Huber, 2011; Goozée et al., 2011). For example, in a study of tongue movements during opening/closing gestures, speakers with PD depended on increasing their velocity during loud speech, in contrast to control speakers who increased their velocity, acceleration, as well as, distance traveled (Goozée et al., 2011). Among limitations of the published research are the emphasis on opening/closing gestures at the segmental level, the focus on relatively mild speakers or those without dysarthria, limited speech material, and limited conditions analyzed for the same group of speakers.

The overall goal of the current study was to examine the effect of speech intelligibility and speaking conditions on articulatory movements of the jaw and tongue during sentences produced by speakers with PD and healthy controls. Participants within the PD group were recruited to represent a broad range of speech intelligibility. The following research questions were addressed:

How do sentence-level jaw and tongue movements differ between speakers with PD and healthy controls in the normal speaking condition, and is the articulatory movement variation across speakers with PD associated with variation in their speech intelligibility?

What are the effects of loudness, clarity, and rate manipulations on articulatory movements, and are there differences in how the two speaker groups perform in different speaking conditions?

Based on previous literature, we hypothesized that group differences would be observed in jaw and tongue movements during sentences and that movement measures would vary systematically with speech intelligibility. Furthermore, we expected that speaking conditions would elicit changes in articulatory movements for both groups; however, the degree of change in measures of movement size and speed may vary by group.

2.2 Methods

2.2.1 Participants

Twenty-one adults diagnosed with PD (M/F = 16/5) and a control group of 20 healthy adults (M = F) were recruited for the study. Participant demographic and clinical characteristics are presented in Table 2-1. All speakers completed the Montreal Cognitive Assessment (MoCA) (Nasreddine et al., 2005), passed a vision screening, and had pure tone thresholds of 40dB or better in at least one ear at 1000, 2000, and 4000Hz (Ventry & Weinstein, 1983). The control participants reported a negative history of neurological impairments, speech and/or language disorders, and medications affecting speech. The patients with PD reported being optimally medicated during the recording session. Speech intelligibility was determined in two ways: (1) using the Sentence Intelligibility Test (SIT) (Yorkston, Beukelman, Hakel, & Dorsey, 2007); and (2) using a measure of scaled intelligibility obtained by direct magnitude estimation (DME) with a modulus (Weismer & Laures, 2002; Yunusova et al., 2005). Both procedures are described below. Speakers with PD represented a wide range of speech intelligibility, ranging from 61.0% to 99.1% on the SIT and an average of 52.1 to 339.4 on the DME task. Ten speakers with PD performed more than 1.5 *SD* below the control mean on the DME task.

Table 2-1. Summary of participant demographic and clinical characteristics.

Group	***n*** **(M/F)**	**Age (years)**	**MoCA (/30)**	**SIT (%)**	**DME**
Control	10/10	70.74 (9.34)	27.6 (1.35)		223.85 (29.99)
PD	16/5	68.86 (3.44)	26.06 (3.17)	92.73 (8.69)	177.73 (47.32)

Note. Values in parentheses are standard deviations. MoCA = Montreal Cognitive Assessment; SIT = Sentence Intelligibility Test; DME = Direct Magnitude Estimation Scaled Intelligibility; PD = Parkinson's disease.

2.2.2 Speaking Tasks

Participants read three sentences: *'Sally sells seven spices,' 'Take the tasty tea on the terrace,'* and *'Clever Kim called the cat clinic.'* The sentences were loaded with consonants targeting the front ('s', 't') and back ('k') of the tongue, while a combination of high and low vowels was included to elicit large articulatory movements. Each sentence was repeated four times, and the order of sentences was randomized across participants. The sentences were first read at a normal comfortable speaking rate and loudness, followed by loud, clear, or slow speaking conditions presented in a random order. Speaking condition instructions were adapted from previous studies (Perkell, Zandipour, Matthies, & Lane, 2002; Tjaden et al., 2014; Tjaden & Wilding, 2005). For example, ‘please speak twice as loud as your normal voice’ was used to elicit loud speech. In addition to the instruction to speak ‘twice as slow’ for the slow rate condition, participants were asked to prolong their speech sounds, instead of inserting pauses between the words. For the clear condition, participants were asked to read in a ‘clear style of speech, as if making yourself understood in a noisy environment.’ Sentences produced with errors, or not following the instructions, were not accepted and were re-recorded. The stimulus materials and their manner of presentation were pilot-tested to ensure usability and accessibility for the participants (Hamidi, Baljko, Economopoulos, Livingston, & Spalteholz, 2015). The total number of sentences recorded was 1968 (3 sentences x 4 repetitions x 4 conditions x 41 speakers).

2.2.3 Instrumentation and Signal Processing

Articulatory movements were captured using a 3D electromagnetic tracking system, the Wave Speech Research System (WAVE; Northern Digital Inc., Canada), which records articulatory positions of small sensors attached to the articulators with sub-millimeter accuracy when in close proximity to the field generator (Berry, 2011). Kinematic data were recorded at a maximum allowed sampling rate of 400Hz. Simultaneously, a synchronized acoustic signal was recorded directly onto the hard drive of a computer at 22 kHz, and 16 bit resolution, using a lapel microphone (Countryman B3P4FF05B) positioned approximately 15cm from the speaker’s mouth.

One six degree-of-freedom (DOF) reference sensor attached to a headband was placed on the forehead during recording. Two five-DOF sensors were attached to the mandibular gum line, between the canine and incisor teeth on both sides of the jaw using stoma adhesive (Stomahesive, Convatec). Two other five-DOF sensors were placed on the midline of the tongue using PeriAcryl®90 Oral Tissue Adhesive, non-toxic dental glue (Glustitch). One sensor was placed at the tongue blade (TB), and a second sensor was placed at the tongue dorsum (TD), 10mm (mean = 10.45mm, *SD* = 1.32mm) and 30mm (mean = 28.47mm, *SD* = 2.86mm) from the tongue tip, respectively. Jaw and tongue sensor positions were collected relative to the head, following the built-in WAVE positional-transformation routine. Tongue movements were not decoupled from the jaw movements.

Occasionally during data collection sensors became loose on the tongue and were removed, or their position was not trackable due to a suboptimal head position within the electromagnetic field, leading to missing data and/or distinct artifacts in the data. As a result, tongue blade data were not analyzed for one control speaker, and tongue dorsum data were omitted for seven speakers (PD, $n = 2$; control, $n = 5$).

The kinematic data were post-processed using MatLab 2014a software (MathWorks, 2014). The post-processing steps included: (1) interpolating and resampling the data uniformly at 400Hz; and (2) low pass filtering the data using a 5th-order Butterworth filter at 15Hz to remove high-frequency noise. The acoustic recordings were post-processed using Goldwave Version 6 software (Goldwave Inc., 2015) to remove non-speech high-frequency noise, attributed to the WAVE, from the signal using a high-pass filter at 9.8kHz.

2.2.4 Intelligibility Ratings and Procedures

Speech intelligibility was determined using the SIT (Yorkston, Beukelman, et al., 2007) to allow comparison to patient demographics in other studies, and using the DME with modulus approach to obtain scaled intelligibility scores for use in statistical analysis.

2.2.4.1 Sentence Intelligibility Test

During the SIT, participants with PD were asked to read a list of 10 sentences varying in length from 5 to 15 words that were randomly generated by the test software. The recordings were transcribed by one naïve listener who was unfamiliar with the test materials and the speech patterns of the participants. The listener heard the stimuli through external noise-cancelling headphones (BOSE QuietComfort 15) in a quiet room and could listen to the recordings up to a maximum of two times. SIT scores were calculated by the software as the percent of words correctly transcribed out of the total number of words.

2.2.4.2 Direct Magnitude Estimation Task

For the DME task, the three experimental sentences recorded in the normal speaking condition by all speakers were rated by a group of naïve listeners. Prior to rating, the recordings were equated for root-mean-square amplitude to minimize intelligibility effects due to audibility (Tjaden et al., 2014), and the stimuli were then mixed with speech-shaped noise at a signal-to-noise-ratio (SNR) of -5dB (van Engen, Phelps, Smiljanic, & Chandrasekaran, 2014); both processing steps were completed using Goldwave Version 6 software (Goldwave Inc., 2015).

Forty listeners were recruited (M/F = 9/31, mean age = 24.68±4.14), and all had pure tone thresholds of 20dB or better for frequencies ranging from 250 to 8000Hz bilaterally. The listeners were native speakers of English, had at least a high school diploma, and reported no history of speech or language disorders. The recordings were presented once through headphones (BOSE QuietComfort 15) in a sound-treated booth (Industrial Acoustics Company, Inc.) using E-prime Software 2.0 (Psychology Software Tools, Inc.). The listeners scaled intelligibility of each sentence based on ‘the ease with which the sentence was understood” with reference to a modulus, which was assigned a score of 100 and repeated every 10 sentences. The stimuli (all repetitions of the experimental sentences in the normal speaking condition, $N = 492$) were divided into eight subsets; each subset contained recordings from five to six speakers ($n = 60$ and $n = 72$, respectively), with at least two speakers from each group (PD, controls). The subsets were each judged by five randomly assigned listeners.

Intra-rater reliability was calculated based on 10% of repeated stimuli in each subset, and a minimum coefficient of $r = .60$ was required to include a listener's data in the analysis. Thirty-seven of the 40 listeners achieved this criterion. Pearson product-moment correlations across the remaining 37 listeners ranged from .60 to .90 (mean = .75, $SD = .08$), representing a moderate-strong agreement within listeners. To examine interjudge reliability, an intraclass correlation coefficient (ICC) was calculated for all subsets of listener data (Neel, 2009; Tjaden et al., 2014) and the average ICC values ranged from .53-.86 (mean = .76, $SD = .12$). All intra- and interjudge correlations were statistically significant ($p<.001$). The geometric mean of ratings across listeners in a subset was used to calculate the scaled intelligibility score for each recording, and then averaged across the three sentences for each speaker.

2.2.5 Measurements

Sentence onsets and offsets were determined using acoustic landmarks in a combined waveform and wideband spectrographic display (TF32) (Milenkovic, 2005). Sentence duration, in milliseconds (ms), was measured from the acoustic onset and offset for each sentence. Acoustic boundaries were chosen because of the differences in the kinematic landmarks between sentences. The acoustic landmarks were also used for parsing kinematic data into individual sentences.

Sound Pressure Level (SPL) and articulatory rate were calculated for each sentence to assess whether speakers adjusted speaking rate and loudness following verbal instructions. Mean SPL was calculated for each recording and expressed relative to the normal condition. The mean root-mean-square amplitude was determined for vowel intensities using a MatLab function *rms*, and voltages were converted to decibels (dB SPL) with reference to each speaker's recordings in the normal condition (Darling & Huber, 2011; Tjaden et al., 2014). Articulatory rate was measured as the number of syllables per second (SPS) for each sentence. As the sentences were relatively short and did not contain pauses greater than 200ms, pause durations did not have to be removed prior to the calculation of articulatory rate.

Kinematic measures were chosen based on prior studies of dysarthria in PD demonstrating changes in size and speed of speech movements (e.g., Walsh & Smith, 2012), and were calculated for the jaw, tongue blade, and dorsum. Example measurements for a single sentence ('Sally sells seven spices') produced by a control speaker (C28) in the normal speaking style are shown in Figure 2-1. The measures are shown in two dimensions for simplification; however, the measurements were conducted in three-dimensional space.

(1) Articulatory working space (AWS) was used to capture the overall movement size of an articulator during each sentence (Bunton & Leddy, 2011; Weismer et al., 2012). AWS was calculated as the volume of a convex hull encompassing the movement trajectory of the sentence (mm^3), using a MatLab function *convhull*.

(2) Movement range along the first principal component (PC1 range; mm) was measured to examine the movement size along the dimension accounting for greatest variance (Adams, Weismer, & Kent, 1993; Mefferd & Green, 2010; Yunusova et al., 2010). Principal component analysis was conducted for each sentence trajectory; the principal components were identified and the trajectory data were re-expressed in the coordinate system defined by the principal components. In Matlab, the range of movement along the first principal component axis was measured as the distance between extrema in the new axes defined by the principal components using the *princomp* function.

(3) Average speed (mm/s) during each sentence was computed in order to represent the overall tendency across a sentence, instead of peak values associated with specific sounds or gestures. In Matlab, average speed was calculated for each articulator as the mean absolute value of the first derivative of 3D Euclidean distance from the onset to the offset of the sentence (Yunusova et al., 2010).

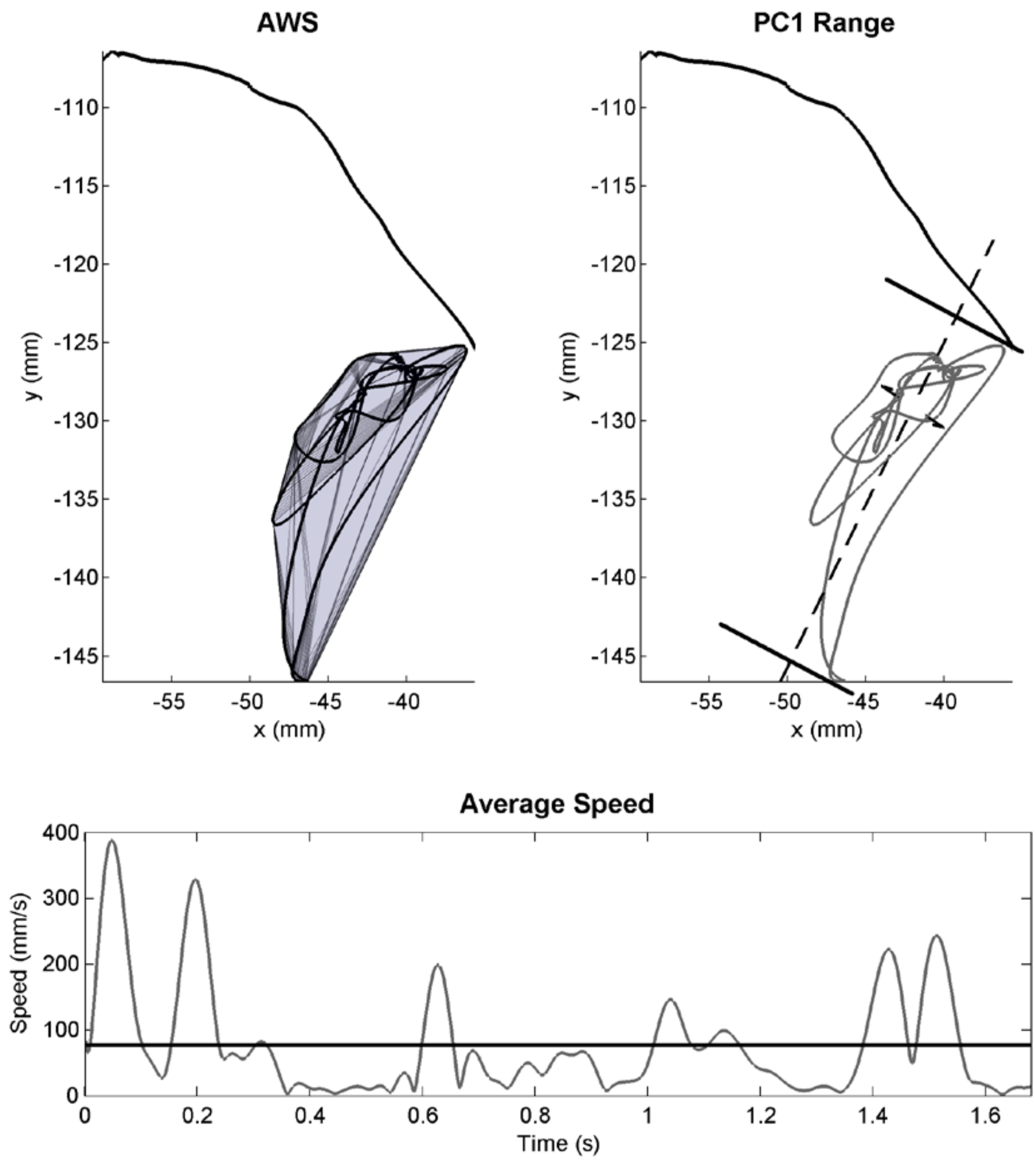

Figure 2-1. Articulatory working space (AWS), range along the first principal component (PC1 Range), and average speed of the tongue blade during the sentence 'Sally sells seven spices' for a single speaker (C28, male, aged 75 years) in the normal speaking condition.

2.2.6 Statistical Analysis

Data were first visually examined for outliers and variable distributions. Outliers, defined as data points greater than 3 *SD* above the group mean for each articulator and condition were removed; 166 (1.78%) data points (based on individual sentence repetitions) were removed for the control group, and 58 (0.74%) for the PD group. Outliers were randomly distributed across articulators and conditions. All analyses were conducted in R version 3.2.3 (R Core Team, 2015). The packages lme4 (v1.1-10) (Bates, Maechler, Bolker, & Walker, 2015) and lmerTest (v.2.0-30) (Kuznetsova, Brockhoff, & Christensen, 2016) were used for linear mixed-effect (LME) models. Denominator degrees of freedom were calculated based on the Satterthwaite approximation to account for differing variances. An alpha level of .05 was used for all main effects.

The effect of instruction (i.e., responding to cues for loud, clear, and slow speech) was evaluated by measuring dB SPL and percent change in articulatory rate, both relative to the normal condition, and employing two-way analyses of variance (ANOVAs) with the main effects of condition and group and a condition-by-group interaction. Post-hoc pairwise comparisons were conducted using t-tests with Bonferroni-correction for multiple tests to control for family-wise error rate.

LME models were used for all remaining analyses to account for inter-subject variability and multiple repetitions per speaker. Separate models were run for each articulator (jaw, TB, TD) and measure (AWS, PC1 range, average speed, sentence duration). Standard diagnostic plots suggested non-constant error variance in these models and the data were log-transformed for the analyses. Interaction terms were included in the final model when inclusion of the interaction term led to a better model fit, as determined by smaller absolute Akaike Information Criterion (AIC) values.

First, to evaluate the effect of PD on sentence-level speech kinematics, group differences (PD versus controls) were examined for the normal speaking condition. In the LME models, group and sentence were specified as fixed factors and subject was included as a random intercept. Sentence was included as a fixed factor due to inherent differences in movement sizes and durations between sentences. To assess if specific sentences were more sensitive to group differences, the interaction between group and sentence was examined. Paired comparisons were conducted by fitting additional LME models, and p-values were Bonferroni-corrected.

Further, the effect of speech intelligibility on articulatory kinematics was assessed in the normal speaking condition for the speakers with PD. LME models predicted articulatory kinematics from scaled (DME) intelligibility scores. Separate models were specified per sentence, and subject was included as a random intercept.

Finally, the effect of speaking condition (normal, loud, clear, and slow) on articulatory kinematics was evaluated using LME models, where speaking condition and group were specified as fixed factors, sentence was added as a covariate, and the intercept term was allowed to vary by subject. To examine if both groups responded in a similar way to varying speaking conditions, the two-way interaction between condition and group was evaluated. Post-hoc comparisons were performed by fitting additional LME models for significant effects and were adjusted using Bonferroni correction.

2.3 Results

2.3.1 Effect of Instruction on Measures of Loudness and Articulatory Rate

Figure 2-2 shows changes in dB SPL and articulatory rate in loud, clear, and slow conditions, relative to the normal condition. Larger change values correspond to louder dB SPL and slower articulatory rate, respectively. Analysis of change in dB SPL revealed a significant effect of condition ($F(2, 116) = 28.34$, $p < .001$), but not group ($F(1, 116) = .36$, $p = .552$). The condition-by-group interaction was not significant ($F(2, 116) = 1.03$, $p = .359$). Pairwise comparison between conditions showed that the magnitude of increase in SPL was greater for loud as compared to clear ($p < .001$) and slow conditions ($p < .001$). dB SPL results between clear and slow conditions were not significantly different.

Change in articulatory rate differed significantly between groups ($F(1, 115) = 8.19$, $p = .005$), as well as conditions ($F(2, 115) = 36.22$, $p < .001$) but there was no interaction between condition and group ($F(2, 116) = 1.30$, $p = .276$). Articulatory rate was slower in loud, clear and slow conditions, as compared to the normal condition. Across conditions, speakers with PD slowed their articulatory rate to a lesser extent than control speakers. For both groups, articulatory rate decreased to the greatest extent in slow as compared to both loud ($p < .001$) and clear ($p < .001$) conditions. Greater slowing of articulatory rate was observed in clear relative to the loud condition ($p < .001$).

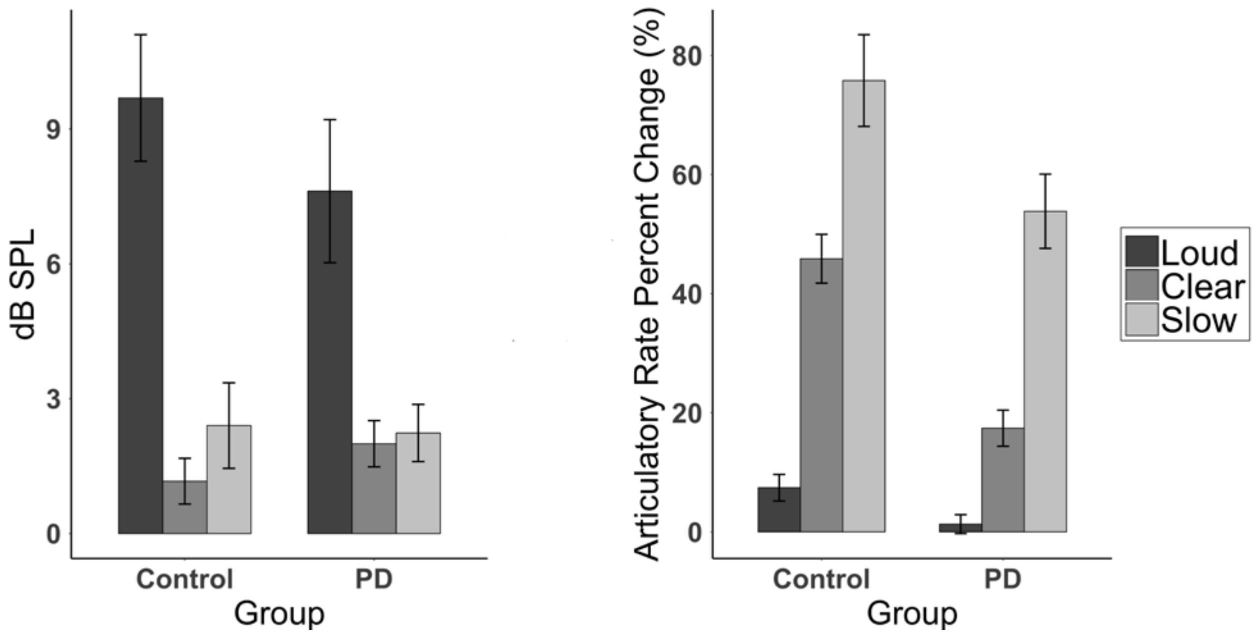

Figure 2-2. Mean and standard errors of change in dB SPL and articulatory rate (%) across speaking conditions relative to the normal condition.

2.3.2 Group Differences in the Normal Speaking Condition

Table 2-2 summarizes the data by measure, articulator, condition, and group. For all of the group analyses, inclusion of the group-by-sentence interaction term did not result in a better model fit and the interaction term was not included in the final models. A significant group difference was detected for AWS of the jaw (F(1, 39.14)= 7.17, p = .011); smaller movements of the jaw were observed for speakers with PD as compared to controls. Analysis of sentence durations also revealed a significant group effect (F(1, 39.28) =4.16, p = .048), with speakers with PD showing shorter sentence durations than the control group. PC1 range (Jaw, (F(1, 39.26)= 0.67, p = .419); TB, F(1, 38.06) =0.51, p = .478); TD, F(1, 27.53) =.31, p = .584) and average speeds (Jaw, F(1, 39.08) =1.80, p = .187; TB, F(1, 37.07) =3.62, p = .065; TD, F(1, 28.81) =2.56, p = .120) for all articulators were not significantly different between groups. Further, no differences were detected between groups for AWS of the tongue blade (F(1, 37.62) =0.06, p = .810) or tongue dorsum (F(1, 27.60) =0.01, p = .975

Table 2-2. Means and standard deviations (*SD*) of the kinematic measures and sentence durations by articulator, speaking condition and group.

Articulator	Measure	Normal		Loud		Clear		Slow	
		Control	PD	Control	PD	Control	PD	Control	PD
Jaw	AWS (mm^3)	29.53 (23.82)	16.60 (17.69)	68.90 (65.49)	35.37 (34.92)	66.07 (61.51)	25.68 (24.51)	59.36 (52.19)	23.90 (29.67)
	PC1 Range (mm)	9.95 (4.36)	9.41 (2.98)	14.07 (5.22)	11.97 (3.97)	13.16 (4.99)	11.07 (3.71)	12.14 (4.47)	10.66 (4.16)
	Average Speed (mm/s)	25.69 (11.70)	28.42 (8.26)	32.94 (14.68)	35.98 (10.46)	25.95 (12.44)	29.11 (8.24)	22.02 (11.61)	23.70 (6.83)
TB	AWS (mm^3)	206.81 (148.04)	236.43 (191.79)	372.80 (292.79)	336.57 (275.72)	336.97 (245.00)	302.67 (240.23)	331.67 (265.97)	291.12 (218.17)
	PC1 Range (mm)	16.05 (3.97)	16.90 (4.78)	19.67 (5.19)	18.97 (5.32)	18.95 (5.24)	18.68 (5.31)	18.10 (4.67)	18.51 (5.32)
	Average Speed (mm/s)	42.55 (16.28)	54.59 (15.51)	50.37 (20.68)	62.13 (17.24)	39.84 (16.42)	53.26 (14.09)	35.20 (15.05)	45.05 (14.63)
TD	AWS (mm^3)	246.64 (169.38)	247.05 (217.92)	391.71 (290.96)	341.50 (286.24)	375.18 (291.94)	312.75 (249.13)	377.80 (291.06)	311.55 (252.15)
	PC1 Range (mm)	18.94 (3.65)	18.18 (4.57)	21.47 (4.41)	20.45 (5.37)	21.41 (4.62)	20.54 (5.38)	21.82 (3.96)	20.48 (5.11)
	Average Speed (mm/s)	43.55 (19.82)	51.03 (16.76)	51.07 (21.04)	57.96 (17.90)	39.64 (19.79)	50.32 (15.54)	35.24 (16.72)	41.56 (14.43)
	Sentence Duration (ms)	2847.31 (573.93)	2596.35 (631.83)	3038.18 (730.23)	2631.00 (633.88)	4048.73 (1081.78)	3057.48 (831.13)	5006.95 (1942.47)	4069.50 (1745.94)

Note. PD = Parkinson's disease; TB = Tongue Blade; TD = Tongue Dorsum; AWS = Articulatory Working Space; PC1 Range = Range along the first principal component.

Kinematic measures showed substantial variability among speakers in the PD group, who differed greatly in the severity of their intelligibility impairment. Using scaled intelligibility as a predictor of articulatory kinematics, a positive association was found between scaled intelligibility and kinematic measures of the jaw, tongue blade, and tongue dorsum. Across all sentences, a positive association was found between PC1 range of the tongue blade and intelligibility (s, $F(1, 16.98) = 10.56$, $p = .005$; t, $F(1, 17.80) = 8.87$, $p = .008$; k, $F(1, 17.97) = 6.55$, $p = .020$). For the tongue dorsum, AWS of the 't' sentence was positively associated with intelligibility ($F(1, 14.54) = 5.67$, $p = .031$). Further, positive associations between tongue dorsum PC1 range and intelligibility of the 's' and 't' sentences neared significance (s, $F(1, 12.90) = 4.65$, $p = .051$; t, $F(1, 14.59) = 4.55$, $p = .050$). For the jaw, PC1 range of the 'k' sentence was positively associated with intelligibility ($F(1, 17.89) = 5.78$, $p = .027$). For these significant associations, higher ratings of scaled intelligibility were associated with larger articulatory movement size. Scaled intelligibility was not associated with the measures of average speed or sentence durations.

2.3.3 Articulatory Kinematics across Speaking Conditions

Figure 2-3 shows means and standard errors for all kinematic measures across speaking conditions. Table 2-3 reports findings for significant pairwise comparisons for the main effect of condition when controlling for group and sentence.

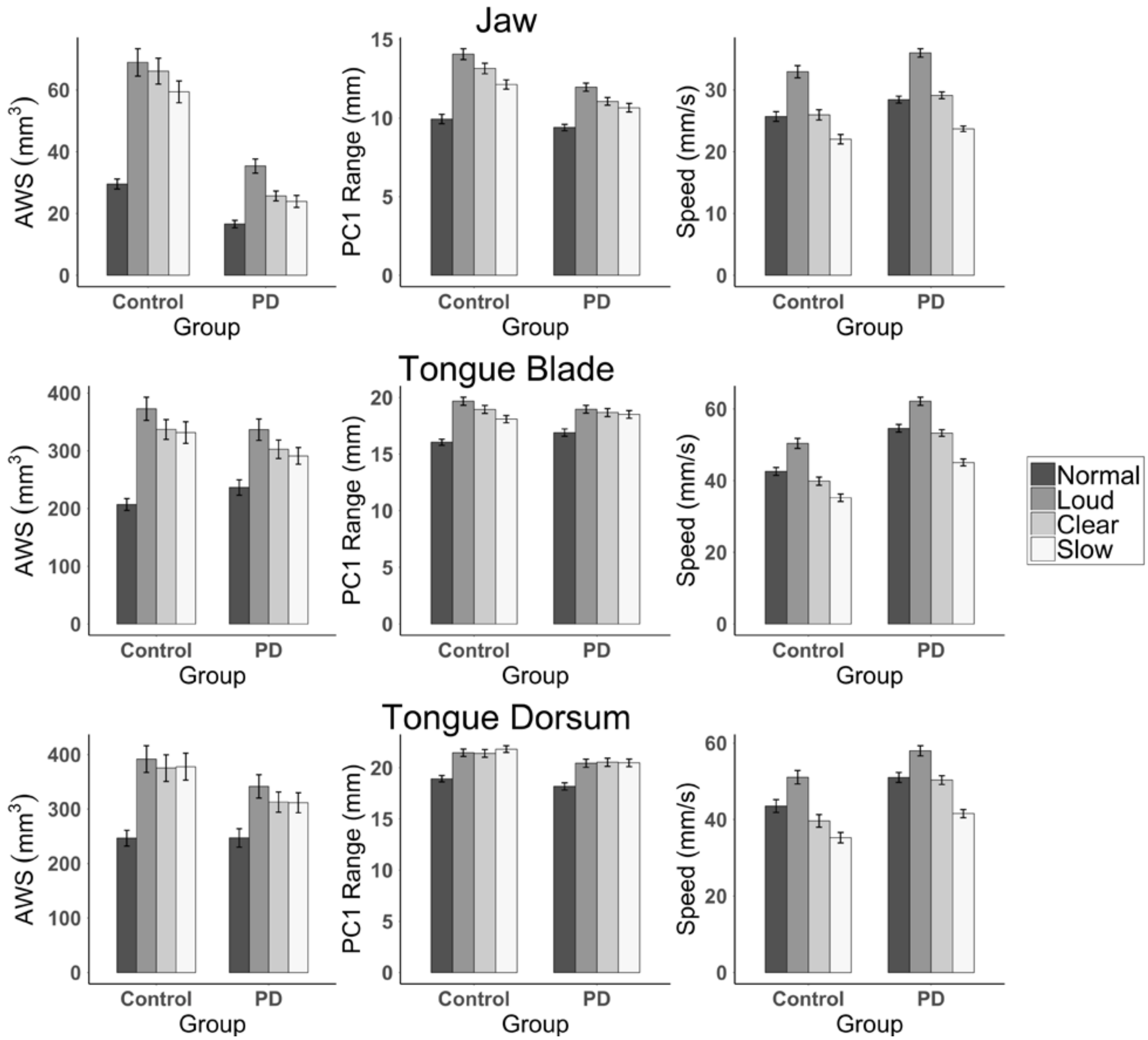

Figure 2-3. Mean and standard error of articulatory working space (AWS), range along the first principal component (PC1 Range), and average speed across speaking conditions.

Table 2-3. Summary of significant pairwise comparisons for analysis of speaking conditions.

Articulator	Measure	Comparison	*B*	*P*
Jaw	AWS (mm^3)	Normal < Loud	-0.69	< .001
		Normal < Clear	-0.58	< .001
		Normal < Slow	-0.47	< .001
		Loud > Clear	0.11	.037
		Loud > Slow	0.22	< .001
		Clear > Slow	0.11	.025
	PC1 Range (mm)	Normal < Loud	-0.58	< .001
		Normal < Clear	-0.36	< .001
		Normal < Slow	-0.26	< .001
		Loud > Clear	0.22	< .001
		Loud > Slow	0.32	< .001
		Clear > Slow	0.10	.002
	Average Speed (mm/s)	Normal < Loud	-0.22	< .001
		Normal > Slow	0.19	< .001
		Loud > Clear	0.21	< .001
		Loud > Slow	0.41	< .001
		Clear > Slow	0.20	< .001
TB	AWS (mm^3)	Normal < Loud	-0.37	< .001
		Normal < Clear	-0.35	< .001
		Normal < Slow	-0.32	< .001
	PC1 Range (mm)	Normal < Loud	-0.34	< .001
		Normal < Clear	-0.24	< .001
		Normal < Slow	-0.23	< .001
		Loud > Clear	0.10	< .001
		Loud > Slow	0.11	< .001
	Average Speed (mm/s)	Normal < Loud	-0.12	< .001
		Normal > Clear	0.05	< .001
		Normal > Slow	0.23	< .001
		Loud > Clear	0.17	< .001
		Loud > Slow	0.35	< .001
		Clear > Slow	0.18	< .001
TD	AWS (mm^3)	Normal < Loud	-0.33	< .001
		Normal < Clear	-0.35	< .001
		Normal < Slow	-0.31	< .001
	PC1 Range (mm)	Normal < Loud	-0.22	< .001
		Normal < Clear	-0.21	< .001
		Normal < Slow	-0.26	< .001
	Average Speed (mm/s)	Normal < Loud	-0.10	< .001
		Normal > Clear	0.05	< .001
		Normal > Slow	0.23	< .001
		Loud > Clear	0.15	< .001
		Loud > Slow	0.33	< .001
		Clear > Slow	0.18	< .001

Note. TB = Tongue Blade; TD = Tongue Dorsum; AWS = Articulatory Working Space; PC1 Range = Range along first principal component.

2.3.3.1 Jaw

Analysis of jaw AWS revealed a significant difference by group ($F(1, 39) = 9.59$, $p = .004$) and condition ($F(3, 1774.40) = 117.98$, $p < .001$). The interaction between condition and group was also significant ($F(3, 1774.40) = 8.60$, $p < .001$). Across conditions, smaller jaw AWS was observed for speakers with PD than controls. Further analysis revealed that both groups increased their AWS in loud, clear, and slow speaking conditions, compared to the normal condition. For the speakers with PD however, loud, clear, and slow jaw AWS differed significantly (loud > clear > slow > normal). For controls, the increase in jaw movement size was similar across conditions (loud = clear = slow).

PC1 range of the jaw differed across conditions as well, as indicated by a significant main effect of condition ($F(3, 1771.35) = 113.80$, $p < .001$). The main group effect ($F(1, 39.07) = 2.18$, $p = .148$) was not significant, and the condition-by-group interaction term was not included in the final model. Post hoc analysis revealed that all contrasts between conditions were significant, with the largest PC1 range observed during loud, followed by clear, slow, and normal conditions for both groups (loud > clear > slow > normal).

A significant effect of condition was found for average speed of jaw movements ($F(3, 1770.10) = 382.12$, $p < .001$), without a group effect ($F(1, 39.00) = 2.09$, $p = .157$). The condition-by-group interaction was not assessed in the final model. For both groups, faster average speeds were observed in the loud condition as compared to all other conditions; and slower average speeds were observed in the slow condition as compared to all other conditions.

2.3.3.2 Tongue blade

Statistical analysis of TB AWS showed a significant main effect of condition ($F(3, 1676.70) = 78.73$, $p < .001$) and a significant interaction between condition and group ($F(3, 1676.70) = 6.86$, $p < .001$). The main effect of group was not significant ($F(1, 38.70) = 0.47$, $p = .495$). Post-hoc analysis by group revealed that the pattern of change in AWS across conditions was the same for both healthy controls and speakers with PD. For both groups, AWS was statistically larger in loud, clear, and slow speaking conditions, compared to the normal speaking condition. Further, AWS was similar between loud, clear, and slow conditions. Although the pattern of change was the same for both groups, there was a difference in magnitude of change between the two groups with control speakers increasing their AWS to a greater extent as compared to speakers with PD (Figure 2-3).

There was a significant effect of condition on PC1 range of the TB ($F(3, 1726.68) = 68.21$, $p < .001$), without a main effect of group ($F(1, 38.23) = 0.15$, $p = .702$). The final model did not include the condition-by-group interaction term. Pairwise comparisons revealed that speakers in both groups increased their PC1 range in loud, clear, and slow conditions, relative to the normal condition, and loud PC1 range was greater than the slow condition.

Examination of average speeds indicated a significant main effect of condition ($F(3, 1725.22) = 400.99$, $p < .001$), but not a main effect of group ($F(1, 37.92) = 2.90$, $p = .097$). The condition-by-group interaction term was not included in the final model. All contrasts between conditions were significant. For both groups, loud condition elicited the fastest speeds, followed by normal, clear, and slow conditions.

2.3.3.3 Tongue dorsum

TD AWS varied significantly across conditions ($F(3, 1250.10) = 48.04$, $p < .001$) without a main effect of group ($F(1, 28.74) = 0.21$, $p = .650$). The condition-by-group interaction was not assessed in the final model. Post-hoc pairwise comparisons showed that TD AWS was statistically larger in loud, clear, and slow speaking conditions, compared to the normal speaking condition for both groups. The increase in TD AWS was similar across conditions (loud = clear = slow).

Analysis of PC1 range showed a significant main effect of condition ($F(3, 1264.14) = 46.39$, $p < .001$) and again, similar results for both groups (group effect, $F(1, 28.65) = 0.30$, $p < .587$. The condition-by-group interaction term was not included in the final model. Post-hoc analysis revealed that PC1 range increased during loud, clear, and slow conditions, as compared to the normal speaking condition. Further, PC1 range was similar between loud, clear, and slow conditions.

There was a significant main effect of condition for TD average speed (F(3, 1275.00) = 269.79, p < .001), but not a main effect of group ($F(1, 28.93) = 3.52$, $p = .071$). The final model did not assess the condition-by-group interaction. Pairwise comparisons showed that all conditions differed from normal in average speed; fastest speeds were observed in the loud condition, followed by normal, clear, and slow conditions for both groups.

2.4 Discussion

2.4.1 Summary of Findings

The current study examined the effect of speech intelligibility and varying speaking conditions on sentence-level articulatory kinematics in speakers with PD and control speakers. We found that speakers with PD had smaller than normal jaw movements as well as shorter sentence durations, as compared to control speakers. The measures of the tongue and, to a lesser degree, jaw movement size varied with speech intelligibility, with more affected participants showing greater movement reduction. There was also evidence for certain sentences to be more sensitive to variation in speech intelligibility (e.g., ‘k’ versus ‘t’ or ‘s’ sentences for the jaw). Speaking conditions elicited distinct patterns of movements that were generally similar in direction between PD and control groups across all articulators. Movement size increased for all conditions relative to normal speech; faster average speeds were elicited during loud but not clear speech, and slower than normal average speeds were elicited during slow speech across the jaw, tongue blade, and tongue dorsum. Differences in movement size of the jaw and tongue blade between loud, clear, and slow conditions, however, varied between controls and speakers with PD.

2.4.2 Articulatory Impairment in PD: Evidence of Hypokinesia and Timing Disturbance

Existing literature commonly reports evidence of jaw/lip movement reduction (hypokinesia) in PD at the segmental level, (e.g., Forest et al., 1989; Walsh & Smith, 2012), while a single study observed this effect at the sentence level (Walsh & Smith, 2012). Our findings extended the sentence-level analysis to encompass movements of the tongue blade and dorsum. Our results, while agreeing with Walsh and Smith (2012) regarding movement reduction in the jaw, did not show changes in the tongue blade or tongue dorsum at the sentence level, indicating a pattern of differential impairment.

An early observational study of dysarthria in PD suggested a progression of impairment, from laryngeal symptoms early in the disease course to involvement of the tongue dorsum, tongue blade, and finally the lips (Logemann et al., 1978). Differential impairment of articulators in PD was later reported for the jaw and lips as well as for the jaw and tongue (Connor et al., 1989; Forrest et al., 1989; Yunusova et al., 2008). A greater magnitude of impairment for the jaw than the lower lip (Connor et al., 1989; Forrest et al., 1989) and for the tongue dorsum relative to the jaw and tongue blade (Yunusova et al., 2008) have been reported. In contrast to the vowel kinematic analysis of Yunusova et al. (2008), our present findings revealed a more prominent jaw than tongue impairment at the sentence level.

The pattern of differential impairment might be explained by physiological differences in the jaw and tongue musculature. Forrest et al proposed that the proprioceptive deficit leading to difficulties sensing jaw position in PD (Schneider et al., 1986) may be compensated for by holding the jaw in a fixed position during speech (Forrest et al., 1989), when the tongue, particularly the tongue blade, may be free to move more extensively. Post hoc, we explored the relationship between the jaw and tongue by statistically controlling for the contribution of the jaw to tongue movement (Shellikeri et al., 2016). The data revealed that when controlling for jaw movement, significantly faster movements of the tongue blade were observed for speakers with PD as compared to controls, suggesting a possible compensatory function of the tongue blade in response to the jaw deficit ($F(1, 32.17) = 4.80$, $p = .036$). No differences between groups were detected for the tongue dorsum when accounting for movements of the jaw. In order to more carefully assess the independent movement of articulators and examine patterns of compensation, tongue movements need to be decoupled from the jaw (Henriques & Van Lieshout, 2013; Westbury, Lindstrom, & McClean, 2002). Testing of a jaw-correction algorithm applicable to the NDI WAVE data, based on translational and rotational information, is currently in progress. Additionally, examination of the differential impairment longitudinally would be helpful in shedding light on the progression of PD across different articulators and muscle groups.

Interestingly, our data did not show group differences in average movement speed for any of the articulators. This finding contradicts previous reports of bradykinesia reported for jaw and tongue movements at the segmental and sentence levels (Ackermann, Konczak, et al., 1997; Forrest & Weismer, 1995; Forrest et al., 1989; Weismer et al., 2012). Only one study to date reported the reduction of jaw velocity in PD at the sentence level using a measure that included 80% of points in the velocity trajectory of an entire sentence (Walsh & Smith, 2012). In contrast to our study, the sentences in Walsh and Smith's study primarily contained bilabial consonants and required large movements of the jaw (e.g., "The boys and the pipers baked moist pumpkin pies"), and did not show differences in sentence durations between speakers with PD and controls. Our sentences had a more diverse phonetic composition, which may have led to the present results. Additionally, a reduction in movement size observed in our study coincided with shorter sentence durations, allowing for average speeds to be maintained. Notably, while articulatory movements may not have become slower on average during sentence production, subtle changes in the control of speed may have occurred throughout the movement trajectories associated with specific sounds (opening/closing gestures) that may not have been detected with our measure. Further studies examining articulatory movement speed across a range of speech tasks are needed to understand if and how bradykinesia manifests in speech articulators in PD.

2.4.3 The Effect of Speech Intelligibility on Articulatory Movements

The results of the current study pointed to a positive association between movement size of the jaw, tongue blade, and tongue dorsum and scaled intelligibility. Across articulators, smaller movements were associated with lower ratings of intelligibility. These findings are generally consistent with previous literature suggesting that more severely affected speakers produce smaller jaw movements at the segmental level (Forrest et al., 1989). A similar association, however, was not observed between movement speed and speech intelligibility, which has previously been reported for passage level data (Weismer et al., 2012).

The relationship between declining speech intelligibility and objective (acoustic or kinematic) measures of articulatory performance has been at the center of the dysarthria literature because it underlies the link between the movement disorder in PD and its relevance to speech communication. By establishing measures that are sensitive to variation in intelligibility, we can then use them to assess the degree of neuro-motor disease severity as well as set targets for treatment, with the overall goal of improving speech intelligibility. The finding of a significant association between articulatory movement size and perceived speech intelligibility impairment observed in this study highlights the important contribution of speech movement to communication in PD. This finding was most consistent across all sentences for the tongue, despite the most pronounced group differences associated with changes in the jaw. A reasonable target for treatment may, therefore, be to focus on the enlargement of tongue movement size, and may be addressed by using stimuli that specifically require relatively large movements size (see Yunusova et al., 2017).

2.4.4 Effect of Stimulus Materials

At the sentence level, our findings suggest that certain sentences might be more sensitive to disease-related changes in PD. This idea has been discussed in the past in both kinematic and acoustic literature (Kim et al., 2009; Rosen, Goozée, & Murdoch, 2008; Yunusova et al., 2008) in the context of developing a set of sensitive assessment materials as well as establishing efficient and effective therapy techniques for various dysarthria types. In this study, the sentence requiring the largest size of jaw movement ('k' sentence) and those requiring smaller, finer control of tongue ('s' and 't' sentences) were more sensitive to variation in speech intelligibility. These findings are important to consider in the selection of stimuli for assessment and treatment of hypokinetic dysarthria. The sentences in the current study, however, were not controlled for linguistic or motoric complexity, which might be important to consider in future studies.

2.4.5 Impact of Speaking Conditions on Jaw and Tongue Movements in PD

Speaking style manipulations are often used in the treatment of dysarthria with the overall goal to maximize intelligibility (Johnson & Pring, 1990; Park, Theodoros, Finch, & Cardell, 2016; Ramig et al., 1995; van Nuffelen et al., 2010). Without knowing the underlying mechanism of how these approaches work, however, it is difficult to assess why one approach is effective for some speakers but not for others. Previous research reported systematic changes in articulatory movements under various speaking conditions (Darling & Huber, 2011; Dromey, 2000; Goozée et al., 2011; Kleinow et al., 2001). While the previous studies have typically focused on the impact of a single speaking condition on a single articulator (i.e., lip or tongue) and measures of movement size and speed at the segmental level only, our study extended the previous findings reporting on multiple articulator performances at the sentence level.

When comparing the effect of different speaking styles across the same group of people, we could see that all conditions resulted in an increase in movement size across all of the articulators relative to normal habitual speech. Our results also suggested that loud speech resulted not only in the upscaling of movement size but also in increasing average speed for the jaw, tongue blade, and tongue dorsum. While loud speech appears to address both hypokinetic and bradykinetic signs in PD, it is important to consider that higher movement speeds observed in this condition may also be associated with greater articulatory effort (Perkell et al., 2002). Much of the research relating to loud speech intervention in PD has been conducted in the context of the Lee Silverman Voice Treatment (LSVT) (Ramig et al., 1995; Ramig et al., 2001), the most common behavioural treatment for hypokinetic dysarthria that trains the loudness strategy through a highly structured treatment program. LSVT is based on the premise that increased loudness results in increased movement size and speed, although neither measure has been used as an outcome measure in LSVT clinical trials. Poorer outcomes of LSVT, however, have been noted for speakers with significant articulatory/rate disorders (Fox et al., 2012). For these speakers, a strategy that results in an increase in articulatory movement size and speed may not be sufficient to achieve improvements in speech quality. Systematically examining changes in speech intelligibility under various conditions would be the next important step in this line of research.

Clear speech, on the other hand, led to an increase in movement size across articulators while maintaining speed of the jaw and slowing tongue blade and dorsum movement. The finding of maintained/slowed articulatory speeds during clear speech is in contrast to a previous study where lip movement speeds were reported to increase in clear speech tasks (Dromey, 2000). In addition to differences in speech material, this discrepancy may be explained by a difference in speaking instructions, which can have an effect on kinematic and acoustic measures of speech (Darling & Huber, 2011; Lam & Tjaden, 2013). In the study by Dromey, the instruction focused on exaggerating movements of the mouth, in contrast to 'making yourself understood in a noisy environment' in our study. While clear speech has been effective as part of a broader treatment program for dysarthria in PD (Johnson & Pring, 1990), studies examining clear speech as a structured treatment approach for hypokinetic dysarthria have not yet been conducted (see, however, Park et al., 2016). An increase in movement size and slower tongue speeds observed in our data may allow for greater articulatory precision for speakers with PD when using a clear speech strategy.

Slow speech in our study was characterized by an increase in movement size as well as slower speeds across articulators, which may have enabled speakers to achieve greater distinctiveness between articulatory targets (van Nuffelen et al., 2010). Measures of movement size and speed have not previously been reported for slow speech in PD; however, a study of lip movement showed increased variability when speaking at a slow rate of speech (Kleinow et al., 2001).

Treatments targeting a slow rate of speech have been widely used in dysarthria, including patients with PD, albeit with mixed results, (Yorkston, Hakel, et al., 2007). In this study, we elicited slow rate by encouraging speakers to prolong their speech sounds without inserting pauses in the current study resulting in changes in articulation. Future studies examining the effects of different slow rate instructions on both articulation and pausing would be helpful in determining optimal rate reduction strategies for dysarthria treatment.

Even though distinct patterns of movement were found for each speaking condition relative to normal speech, speakers with PD and control speakers used different control strategies to vary movement size between loud, clear, and slow conditions, as indicated by a number of significant condition-by-group interaction effects. Differential control strategies between groups have previously been reported at the segmental level (Darling & Huber, 2011; Goozée et al., 2011), and may reflect the property of motor equivalence, i.e., different control strategies employed to achieve the same acoustic goal (see review, Perrier & Fuchs, 2015). When speaking loudly in background noise, for example, speakers with PD increased their jaw displacement to a lesser extent than their peers (Darling & Huber, 2011). Our data agreed with the previous reports and showed that the speakers with PD did not achieve the same degree of change in movement size of the jaw and tongue dorsum as neurologically normal controls. These findings are particularly interesting considering both groups varied their rate and loudness in a similar pattern across conditions. In particular, our results highlighted that speakers with PD might need additional cues or feedback to achieve articulatory movements that are comparable to control speakers in these speaking conditions.

The current study examined the effect of a one-time instruction on articulatory movements, and direct parallels cannot be made to treatment studies targeting loud, clear, or slow speech. Nevertheless, experimental studies documenting the effect of speaking conditions can shed light on the underlying physiological changes that may occur during treatment, and as such, strengthen the scientific basis for dysarthria intervention. Future pre-post treatment studies should incorporate measures of articulatory movements to determine the physiological basis for treatment approaches in PD. Further, systematically relating these changes to changes in speech intelligibility will provide a comprehensive basis for dysarthria treatment in PD.

2.5 Conclusion

Studies of the effect of PD on sentence-level articulatory movement remain limited. Studying multiple articulators across a range of dysarthria severities allowed us to contribute a unique perspective on this debilitating disease and its impact on articulation, while sentence-level analyses increased the applicability of findings to stimuli used in speech interventions. From a clinical perspective, this study highlighted the underlying physiologic effects of common therapeutic approaches for speech rehabilitation in PD. Further work is required to understand the effect of these approaches when applied during intervention and to identify speech kinematic profiles of speakers who benefit from different treatment approaches.

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Chapter 3
Augmented Visual Feedback-Aided Interventions in Motor Rehabilitation in Parkinson's Disease: A Systematic Review

This chapter in its entirety is under review by Taylor & Francis for publication in the *Disability and Rehabilitation* journal: Kearney, E., Shellikeri, S., Martino, M., & Yunusova, Y. (under review). Augmented visual feedback-aided interventions in motor rehabilitation in Parkinson's disease: A systematic review.

3 Augmented Visual Feedback-Aided Interventions in Motor Rehabilitation in Parkinson's Disease: A Systematic Review

Abstract

Purpose: A systematic review was performed to (1) evaluate the effectiveness of augmented visual feedback-based treatment (AVFT) for motor rehabilitation in PD, and (2) examine treatment design factors associated with enhanced motor learning during AVFT.

Methods: Eight databases were searched up to January 2017 using the key terms PD and augmented visual feedback. Two independent raters screened the abstracts and full articles for inclusion using pre-specified criteria. Data of accepted articles were extracted and summarized, and methodological quality of accepted articles was assessed.

Results: Twenty articles were included in the review (two case studies, eight single group studies, 10 randomized control trials). AVFT resulted in improved outcomes post treatment for the majority of measures across impairment, activity, participation, and global motor function domains and these improvements were often superior to traditional rehabilitation/education programs. Enhanced treatment outcomes were observed in studies that provided large amounts and high intensities of treatment; gamified feedback; and provided knowledge of performance feedback in real-time on 100% of practice trials.

Conclusion: Augmented visual feedback appears to be a useful motor rehabilitation tool in PD; however, high-quality, rigorous studies remain limited. Future studies should consider factors that enhance rehabilitation outcomes when designing AVFT.

Keywords: Parkinson's disease, motor rehabilitation, augmented visual feedback, systematic review.

3.1 Introduction

Parkinson's disease (PD) is a progressive neurodegenerative disease characterized by four primary motor symptoms, namely resting tremor, rigidity, bradykinesia, and postural impairment (Jankovic, 2008). In spite of advances in pharmaceutical and surgical treatments in PD, individuals develop progressive motor impairments, resulting in complex gait dysfunction (i.e., freezing of gait, shuffling and festination), postural instability, dyskinesia, dystonia, micrographia, dysarthria, sialorrhea, and dysphagia (Hely, Morris, Reid, & Trafficante, 2005; Jankovic, 2008; Paul, Sherrington, Fung, & Canning, 2013). As a result, patients experience lack of independence, inactivity, social isolation, and ultimately a reduced quality of life (Karlsen, Tandberg, Årsland, & Larsen, 2000). Support for rehabilitation therapies in the area of motor impairment is growing (Gage & Storey, 2004; Nijkrake et al., 2007) to enhance personal wellbeing as well as to reduce the economic impact of the disease on society (Huse et al., 2005).

Physio-, occupational, speech, and swallowing therapies aim to reduce the burden of the motor impairments and maximize functional ability through rehabilitation. Clinical guidelines for professionals that deliver these therapies outline goals for best practice when addressing motor impairments in PD. Specifically, physiotherapy aims to normalize body posture, stimulate reaching and grasping movements, improve balance and gait, prevent inactivity, preserve or improve physical capacity (aerobic capacity, muscle strength, and joint mobility), improve transfers, and prevent falls (Keus, Bloem, Hendriks, Bredero-Cohen, & Munneke, 2007). Occupational therapy focuses on improving or maintaining hand and arm function (Sturkenboom et al., 2012). Speech-language therapy aims to improve patients' speech intelligibility as well as to remediate the impairments associated with swallowing, chewing, and saliva management (Kalf et al., 2010). Despite best practice guidelines, evidence for the effectiveness of rehabilitation therapies in PD remains limited.

Identifying treatment techniques and developing novel treatments is challenging in PD due to the complex disease pathophysiology (Abbruzzese et al., 2016). Among the most relevant deficits, individuals with PD experience a reduction in motor learning abilities due to the central role of the basal ganglia in motor learning (Doyon et al., 2009; Wu et al., 2010). While studies have shown that individuals with PD can successfully acquire or re-acquire motor skills, they do so at a slower rate than their healthy peers (Hayes et al., 2015; Siegert et al., 2006). Further, implicit motor learning mechanisms, which rely on motor practice rather than declarative memory, are particularly impaired in PD (Nieuwboer et al., 2009). As a result, patients with PD appear to benefit from explicit methods of motor learning and a lot of practice, particularly at the later stages of motor learning when skill transfer occurs (Abbruzzese et al., 2016).

One of the most challenging aspects of rehabilitation therapies is to motivate clients to perform an adequate number of trials during training to achieve sustainable improvements in their motor control. Motivation poses a significant challenge in individuals with PD, as the dopamine-dependent circuits for motivation are affected (Drui et al., 2014). Effective therapies need to be highly motivating in order to engage patients in the process of rehabilitation. Finally, individuals with PD become more dependent on external visual stimuli to learn motor patterns (Adamovich et al., 2001; Lewis et al., 2000; Schettino et al., 2006). The addition of visual information may help to compensate for proprioceptive deficits consistently observed in PD during motor tasks (Jobst et al.; Klockgether et al., 1995; Rickards & Cody, 1997).

Rehabilitation science turned to technology and paradigms based on augmented visual feedback to enhance learning, increase engagement and improve treatment outcomes (Barry et al., 2014). Augmented visual feedback has been shown to enhance motor learning in healthy and disordered populations (e.g., stroke; Molier et al., 2010). It engages visual sensory channels and can make the learning process more explicit by providing visual information regarding the treatment goal and movement characteristics (Lee et al., 1994). In PD, there has recently been a surge in a number of studies reporting novel therapies with augmented visual feedback, particularly in the domain of physiotherapy. The goal of this study is to comprehensively review this information and identify common factors leading to enhanced outcomes of augmented visual feedback-based treatments (AVFT) in PD.

A number of treatment design factors have been linked to enhanced motor learning and improved outcomes. These factors include (1) the amount of treatment (Lohse et al., 2014); (2) the intensity of treatment (i.e., frequency of treatment sessions) (Kwakkel et al., 1997); (3) gamification of feedback (Barry et al., 2014); (4) nature of feedback (i.e., information about the outcome of movement (knowledge of results, KR) vs. the quality of moment (knowledge of performance, KP)) (Young & Schmidt, 1992); (5) timing of feedback (e.g., real-time vs. delayed) (Schmidt & Wulf, 1997); and (6) frequency of feedback (e.g., every trial vs. summary of 5 trials)

(Winstein & Schmidt, 1990). Some of these factors have been examined directly when training patients with PD. For example, in a group of patients with PD with gait abnormalities, treadmill training programs showed better outcomes following low-to-medium intensity (2-3 times/week) than a high-intensity one (5 times/week) (Pelosin et al., 2016). Further, reduced frequency of feedback enhanced the retention of motor skills for both a hand-positioning task relative to a spatial target (Chiviacowsky et al., 2010) and a speech-timing task (Adams et al., 2002). While often not experimentally manipulated within studies, these factors are implicitly incorporated into the design of rehabilitation programs and are important to examine across studies as they may significantly affect the study outcomes.

The purpose of this systematic review of PD literature was to (1) evaluate the effectiveness of the AVFT approach across different types of motor rehabilitation in terms of motor impairment, function, and quality of life, and (2) examine the effect of treatment design factors associated with enhanced treatment outcomes. These findings provide future direction for the development and implementation of augmented visual feedback for motor rehabilitation in adults with PD.

3.2 Method

3.2.1 Operational Definitions

Operational definitions, determined a priori, guided the search and included: Augmented visual feedback, as movement-related information presented by an external source in the visual modality, including KR (information related to the outcome of movement) and/or KP (information related to the quality of movement) (Schmidt & Wrisberg, 2008); Motor rehabilitation, as any intervention that focused on the recovery of motor skill, including but not limited to, balance, gait, hand-writing, speech and swallowing.

3.2.2 Search Strategy

Eight databases were searched from their inception to January 11th 2017, including MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, Embase, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Allied and Complimentary Medicine Database (AMED), PsycINFO, Cochrane Database of Systematic Reviews (CDSR), and Cochrane Central Register of Controlled Trials (CENTRAL). The key search terms were Parkinson's disease combined with augmented visual feedback or associated terms (such as sensory feedback, visual feedback, KR, KP). The search terms were adapted for each database (for example, MeSH headings in MEDLINE vs. subject headings in CINAHL). See Appendix A for the search strategy used per database. Additionally, the reference lists of pertinent articles (i.e., related review articles and included studies) were examined to ensure all relevant articles were considered for review.

3.2.3 Inclusion and Exclusion Criteria

This review was limited to studies from peer-reviewed sources that examined the benefit of augmented visual feedback in motor rehabilitation in adults with a diagnosis of PD, regardless of outcome type. Studies were excluded if they (1) had no abstract; (2) targeted animal/ non-human subjects; (3) did not include treatment; (4) did not utilize augmented visual feedback; (5) did not compare performance either within subjects pre-post AVFT, or between experimental and control groups post treatment; or (6) were focused on instrument development or validation. Tutorials, educational reports, reviews, book chapters, bibliographies, study proposals, and commentaries were also excluded from the review.

Using these criteria, two raters (EK and SS) independently screened each title and abstract for inclusion. Each abstract was either coded as "accept" or "reject" with reason specified. The raters discussed and reached consensus on any differences in abstract coding. For all accepted abstracts, full articles were assessed using the same exclusion criteria.

3.2.4 Data Extraction

The first author (EK) conducted data extraction from accepted full-texts in order to characterize the included studies and identify study outcomes. The extracted data pertained to study design, participants (i.e., sample size, age, sex, disease duration, disease severity), intervention (i.e., setting, motor skill targeted, treatment schedule, description of intervention, augmented feedback modalities, and gamification, content, nature, timing and frequency of feedback), and timing of follow-up assessment (if applicable). In addition to these characteristics, all outcome measures reflecting motor impairment, motor function, quality of life and associated findings were recorded.

3.2.5 Critical Appraisal

Risk of bias was assessed following protocols developed a priori in accordance with the guidelines provided by the Cochrane Collaboration. Separate protocols were deemed necessary for different study designs. The included studies were classified as case studies or group design studies, where group designs included both single group and randomized designs. Case studies were assessed using the Single Case Experimental Design (SCED) scale (Tate et al., 2008), while group design studies were evaluated based on Cochrane's Grades of Recommendation, Assessment, Development, and Evaluation (GRADE) approach (Higgins, Altman, & Sterne, 2011). The key areas for single group studies were specifying clinical history (i.e., age, sex, aetiology, severity), blinding of outcome assessor, addressing incomplete outcome data (e.g., documenting and providing reasons for study attrition), selectively reporting outcomes (e.g., reporting data from all outcomes outlined in method), reporting point and variability measures (e.g., mean and standard deviation in table or graph form), conducting appropriate statistical analysis (e.g., conducting omnibus testing and correcting for multiple comparisons when necessary), and examining treatment generalization (i.e., examining functional utility of treatment beyond target behaviour, such as, activities of daily living (ADLs), quality of life, global motor function). In addition to these areas, randomized control trials (RCTs) were also examined for evidence of (1) sequence generation when randomizing participants into experimental and control groups; (2) allocation concealment to ensure that the person enrolling participants could not foresee group assignment; (3) equivalence of intervention groups at baseline on one measure of disease severity and one primary outcome measure; (4) following intention-to-treat principles, where all participants are included in the analysis and analyzed in the groups to which they were randomized; and (5) reporting results between intervention groups. Blinding of participants or treatment personnel was not considered possible, given the behavioural nature of the intervention under review. For both the SCED and GRADE approaches, key areas were rated as having high, low, or unclear risk of bias by two independent authors (EK, SS), and differences in ratings were discussed and resolved by consensus.

3.2.6 Data Analysis

Findings across studies were examined descriptively. First, outcome measures were classified according to the International Classification of Functioning, Disability, and Health framework (ICF; World Health Organization, 2001), and an additional category was included for measures examining change in global motor function. Then, in order to summarize outcome data in a manner that allowed for comparison across articles using heterogeneous measures, we calculated whenever possible effect sizes for each outcome using Cohen's *d* (Cohen, 1988), or extracted effect sizes that were provided. The comparisons targeted were: (1) within-subject and within-group effects for case studies and single group designs, respectively; and (2) between-group effects for RCTs. We operationalized a positive effect as $d > 0.2$, a negative effect as $d < -0.2$, and no effect as $d < |0.2|$ (Cohen, 1988).

3.3 Results

3.3.1 Study Identification

The search identified 773 articles related to the use of visual feedback in individuals diagnosed with PD. An additional 10 articles were identified for inclusion by manually checking reference lists of related studies. Following duplicate removal, 456 unique citations were screened using the inclusion/ exclusion criteria described above. Fifty-seven articles were accepted for full-text review, and a final 20 articles met all inclusion criteria (see figure 3-1). Percent agreement between the two independent raters on rejecting articles before reconciliation was 91% at the abstract level, and 81% for full-texts. All disagreements between raters were successfully discussed and resolved by consensus.

Two of the included articles analyzed data from the same dataset (dos Santos Mendes et al., 2012; Pompeu et al., 2012). The authors implemented different study designs (pre-post single group design vs. RCT) and focused on different outcome measures for both articles. The outcome data from both reports are summarized separately for this review.

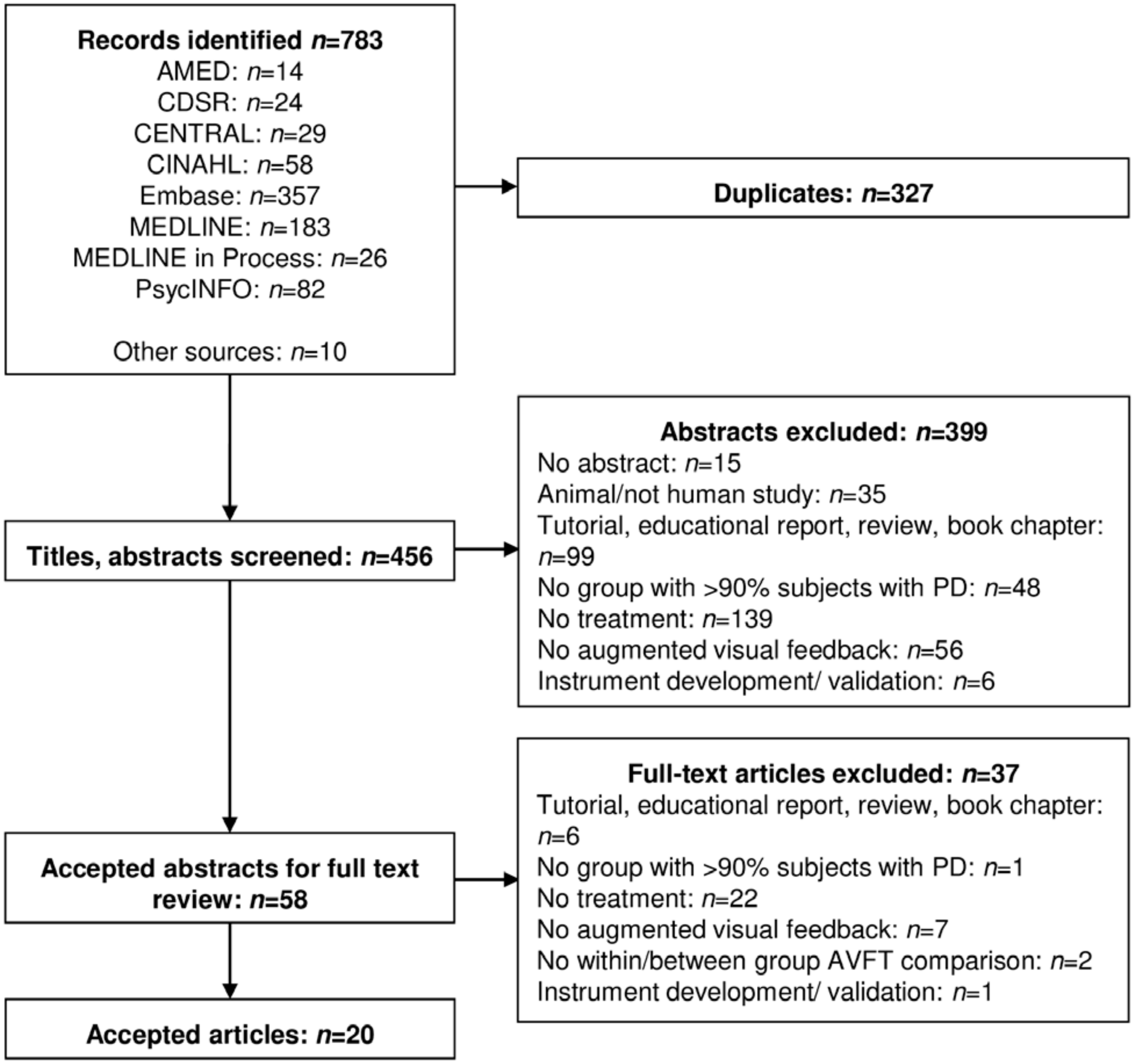

Figure 3-1. Flow chart illustrating search strategy and screening process.

3.3.2 Study Characteristics

Table 3-1 summarizes the study characteristics of the 20 included articles, stratified by study design.

3.3.2.1 Study Design

Two articles employed case study designs (Balci, Tonga, & Gulsen, 2013; Zettergren, Franca, Antunes, & Lavallee, 2011), eight articles used single group designs (Athukorala, Jones, Sella, &

Huckabee, 2014; dos Santos Mendes et al., 2012; Esculier, Vaudrin, Bériault, Gagnon, & Tremblay, 2012; Gonçalves, Leite, Orsini, & Pereira, 2014; Herz et al., 2013; Holmes, Gu, Johnson, & Jenkins, 2013; Mhatre et al., 2013; Zalecki et al., 2013), and the remaining ten articles were RCTs (Byl, Zhang, Coo, & Tomizuka, 2015; Lee, Lee, & Song, 2015; Liao, Yang, Wu, & Wang, 2015; Pedreira et al., 2013; Pompeu et al., 2012; Shen & Mak, 2014; Stern, 2009; van den Heuvel et al., 2014; Yang, Wang, Wu, Lo, & Lin, 2016; Yen et al., 2011). All RCTs included an active control group receiving traditional intervention or a comparable intervention without augmented visual feedback. Additionally, two RCTs included an inactive third control group who participated in a falls-prevention education program (Liao et al., 2015) or received no intervention (Yen et al., 2011).

3.3.2.2 Participants

Sample sizes across articles ranged from 1 to 51 individuals all with a diagnosis of PD, and included both male and female participants. In addition to individuals with PD, two articles included a healthy control group (dos Santos Mendes et al., 2012; Esculier et al., 2012), and one article included a group of stroke survivors (Byl et al., 2015). Across studies, the average age of participants with PD ranged from 61.1 to 71.5 years, and the average reported time since diagnosis ranged from 3.4 to 10.2 years. Eighteen of the included articles reported measures of disease severity, indexed by the Hoehn and Yahr scale (HY; Hoehn & Yahr, 1967) or by the motor part of the Movement Disorder Society - Unified Parkinson's Disease Rating Scale (MDS-UPDRS; Goetz et al., 2008). Disease severity on the HY scale ranged from unilateral involvement only to mild-moderate bilateral disease with some postural instability (average range: 1.5-3). On the UPDRS, average motor scores indicated mild to moderate impairment (average range: 15.9-28.5). The active nature of the majority of interventions excluded participants with more severe symptoms who were unable to ambulate specified distances (for example, 100 feet, or household distances). Most studies recruited participants with some range of disease severities, however, one study exclusively recruited participants with an HY score of 2 (Herz et al., 2013). Participants with PD were tested while in the "on" stage of their medication, although two studies did not report medication status (Byl et al., 2015; Lee et al., 2015).

3.3.2.3 Intervention

Thirteen articles provided information about the intervention setting; eight interventions were conducted in clinics (Athukorala et al., 2014; Byl et al., 2015; dos Santos Mendes et al., 2012; Mhatre et al., 2013; Pompeu et al., 2012; Stern, 2009; van den Heuvel et al., 2014; Yen et al., 2011), four were home-based (Esculier et al., 2012; Holmes et al., 2013; Yang et al., 2016; Zalecki et al., 2013), and a single study combined laboratory- and home-based interventions (Shen & Mak, 2014).

Balance was the most frequently targeted motor skill (n = 12), while the remaining articles targeted gait (Byl et al., 2015; Gonçalves et al., 2014); balance and gait (Shen & Mak, 2014; Zettergren et al., 2011); muscle strength, coordination and gait (Liao et al., 2015); swallowing (Athukorala et al., 2014); and general motor skills (Herz et al., 2013; Pedreira et al., 2013).

Interventions were conducted in 10-84 sessions (mean = 20.55, SD = 17.14) over 2-12 weeks (mean = 6.25, SD = 2.49), and testing in all studies was performed pre and post intervention. Additionally, 10 articles assessed maintenance of intervention effects from 2-52 weeks following intervention (Athukorala et al., 2014; dos Santos Mendes et al., 2012; Herz et al., 2013; Liao et al., 2015; Pompeu et al., 2012; Shen & Mak, 2014; Stern, 2009; van den Heuvel et al., 2014; Yang et al., 2016; Yen et al., 2011).

Visual feedback was provided by the Nintendo Wii in 12 articles (dos Santos Mendes et al., 2012; Esculier et al., 2012; Gonçalves et al., 2014; Herz et al., 2013; Holmes et al., 2013; Lee et al., 2015; Liao et al., 2015; Mhatre et al., 2013; Pedreira et al., 2013; Pompeu et al., 2012; Zalecki et al., 2013; Zettergren et al., 2011), custom-built software in four articles (Byl et al., 2015; van den Heuvel et al., 2014; Yang et al., 2016; Yen et al., 2011), the Smart Balance Master in two articles (Shen & Mak, 2014; Stern, 2009), the Myospace surface electromyography (sEMG) biofeedback device in one article (Athukorala et al., 2014), and the Tetraks Interactive Balance System in one article (Balci et al., 2013). In addition to visual feedback, the Nintendo Wii Fit provided auditory feedback, while the Nintendo Wii Sports provided both auditory and vibrotactile feedback. Two articles also incorporated verbal feedback during training (Mhatre et al., 2013; Shen & Mak, 2014). The majority of articles (n = 16) did not report details regarding the presentation of verbal feedback during training.

Feedback was gamified in most articles (*n* = 15), by using either commercially available games from Nintendo Wii (e.g., “Ski Slalom”, “Balance Bubble”) or custom-written software. Non-gamified feedback involved showing participants an sEMG signal regarding the time and amplitude of submental muscle contraction during swallowing (Athukorala et al., 2014); a kinematic signal regarding the timing, location, and amplitude of ground reaction forces during gait (Byl et al., 2015); or accuracy scores of a stepping or reaching task (Shen & Mak, 2014).

The nature of feedback was most commonly KP (*n* = 17). Information about accuracy of performance conveyed KR feedback only (Shen & Mak, 2014). Two articles did not provide information about gamification or the nature of feedback employed (Balci et al., 2013; Stern, 2009).

Visual feedback varied in timing of presentation and frequency across articles. Typically, visual feedback was presented in real-time while participants were practicing the motor skill (*n* = 16). The remaining articles used terminal feedback following the completion of each trial (Shen & Mak, 2014), delayed feedback after a few trials (Byl et al., 2015), or a combination of both real-time and terminal feedback (Stern, 2009). One article did not report the timing of feedback presentation (Balci et al., 2013). Details of feedback frequency were not explicitly stated for the studies using Wii technology, but the frequency was assumed to be 100% given the typical use of the technology. Examined across all articles, feedback was usually provided on 100% of practice trials (*n* = 17). Only one article reduced the frequency of feedback to approximately one-third of the treatment time (Byl et al., 2015), and two articles did not provide information regarding feedback frequency (Balci et al., 2013; Stern, 2009).

Table 3-1. Study Characteristics.

Study	Design	Participants					Intervention						
		N	**Sex (M/F)**	**Age (years, m ± SD)**	**PD Disease duration (years, m ± SD)**	**PD Disease severity, m ± SD)**	**Setting**	**Motor Skill Targeted**	**Treatment Schedule**	**Follow-up Assess ment (weeks)**	**Device/ Intervention Description**	**Feedback Modalities**	**Visual Feedback (gamification, content, nature, timing, frequency)**
Case Studies													
Balci et al., 2013	Case study	4	4/0	61.25 ± 6.70	7.25 ± 1.79	HY: 2.13 ± 0.74	NR	Balance	25 mins, 3 days/week , 5 weeks	NR	Tetraks Interactive Balance System	Visual	NR
Zettergren et al., 2011	Case study	1	1/0	69	NR	NR	NR	Balance, gait	40-60 mins, 2 days/week , 8 weeks	NR	Wii Fit balance board Stretching, balance + gait	Visual, auditory	Gamified; Sun Salutation, Half Moon, Chari, Rowing Squat, Torso Twist, Penguin Slide, Table Tilt, Balance Bubble, Free Step; KR/KP; real-time on 100% of trials
Single Group Designs													
Athukorala et al., 2014	Pre-post single group design	10	7/3	67.4 ± 8.6	6.6 ± 4.0	HY: 2.7 ± 0.4	Clinic	Swallowin g	60 mins, 5 days/week, 2 weeks	2	Myopace surface electromyography (sEMG), submental muscles Dry swallows	Visual	Not gamified; signal showing amplitude + timing; KR/KP; real-time on 100% of trials
dos Santos Mendes et al., 2012	Pre-post single group design, including compariso ns to healthy control group	**Exp:** 16 **Control:** 11	**Exp:** NR; **Control:** matched for gender	**Exp:** 68.6 ± 8.0 **Control:** 68.7 ± 4.1	**Exp:** 4.7 ± 5.4	**Exp:** HY: 1.86 ± 0.33	Clinic	Balance	30 mins (balance) + 30 mins (exercise), 2 days/week, 7 weeks	9	Wii Fit balance board + global exercise Static balance, dynamic balance + stationary gait	Visual, auditory	Gamified; Torso Twist, Single Leg Extension, Rhythm Parade, Table Tilt, Tilt City, Basic Step, Penguin Slide, Obstacle Course, Soccer Heading, Basic Run Plus; KR/KP; real-time on 100% of trials

Esculier et al., 2012	Pre-post single group design, including comparisons to healthy control group	**Exp:** 11 **Control:** 9	**Exp:** 6/5 **Control:** 5/4	**Exp:** 61.9 ± 11.0 **Control:** 63.5 ± 12.0	**Exp:** 8.5 ± 3.6	**Exp:** UPDRS (Motor III): 18.4 ± 5.4	Home	Balance	40 mins, 3 days/week, 6 weeks	NR	Wii Fit balance board + Wii Sports Balance, yoga + aerobics	Visual, auditory, vibro-tactile	Gamified; Golf, Bowling, Table Tilt, Ski Slalom, Balance Bubble, Ski Jump, Penguin Slide, Deep Breathing, Hula-Hoop; KR/KP; real-time on 100% of trials
Gonçalves et al., 2014	Pre-post single group design	15	8/7	68.70 ± 10.20	7.30 ± 3.70	HY: 2.10 ± 0.30 UPDRS (Motor III): 28.5 ± 9.91	NR	Gait	40 mins, 2 days/week, 7 weeks	NR	Wii Fit balance board + exercise Balance + aerobics	Visual, auditory	Gamified; Free Step, Rhythm Step, Slalom Skiing, Jump Skiing, Advanced Skiing, Header, Jump Rope, Segway Circuit, Advanced Circuit, Cycling, Advanced Cycling; KR/KP; real-time on 100% of trials
Herz et al., 2013	Pre-post single group design	20	13/7	66.7 ± 7.2	5.5 ± 4.3	HY: 2 ± 0	NR	Motor (unspecified)	60 mins, 3 days/week, 4 weeks	4	Wii Sport Balance, coordination + full-body motion training	Visual, auditory, vibro-tactile	Gamified; Bowling, Tennis, Boxing; KR/KP; real-time on 100% of trials
Holmes et al., 2013	Pre-post single group design	15	7/4	63.91 ± 12.05	8.45 ± 3.75	HY: 2.27 ± 0.39 UPDRS (Motor III): 25.18 ± 11.71	Home	Balance	30 mins, 3 days/week, 12 weeks	NR	Wii Fit balance board Balance	Visual, auditory	Gamified; Balance Bubble, Table Tilt, Soccer Heading, Tightrope Tension, Penguin Slide, Ski Slalom, Snowboard Slalom; KR/KP; real-time on 100% of trials
Mhatre et al., 2013	Pre-post single group design	10	4/6	67.1; Range: 44-91	6.7; Range: 1-14	HY: Range: 2.5-3	Clinic	Balance	30 mins, 3 days/week, 8 weeks	NR	Wii Fit balance board Balance	Visual	Gamified; unspecified marble, balance, bubble games; KR/KP; real-time on 100% of trials

Zalecki et al., 2013	Pre-post single group design	24	17/7	61.8 ± 1.9	9.21 ± 0.94	UPDRS (Motor II): 13.29 ± 0.47 UPDRS (Motor III): 22.42 ± 0.63	Home	Balance	20 mins, twice/day, 6 weeks	NR	Wii Fit balance board + Wii Sport Balance, flexibility, strength + coordination	Visual, auditory, vibro-tactile	Gamified; Ski Slalom, Balance Bubble, unspecified Wii Sport games; KR/KP; real-time on 100% of trials
RCT Group Designs													
Byl et al., 2015	RCT	**Exp:** PD: 7 Stroke: 5 **Control:** PD: 5 Stroke: 7	**Exp:** PD: 3/4 Stroke: 3/2 **Control:** PD: 4/1 Stroke: 2/5	**Exp:** PD: 68.5 ± 3.6 Stroke: 66.2 ± 5.0 **Control:** PD: 70 ± 2.9 Stroke: 60.8 ± 5.4	**Exp:** PD: 8.7 ± 4.4 Stroke: 10.4 ± 7.8 **Control:** PD: 11.6 ± 5.9 Stroke: 6.6 ± 3.6	**Exp:** PD: HY: Range: 1-3 Stroke: Fugl-Meyer: 14.5 ± 5.6 **Control:** PD: HY: Range: 1-3 Stroke: 14.9 ± 5.3	Clinic	Gait	90 mins, 12 session, 6-8 weeks	NR	**Exp:** Smart shoes with pressure sensors + smart pants with joint angle sensors Gait **Control:** Gait training	**Exp:** Visual **Control:** NR	Not gamified; signal showing timing, location + amplitude of ground reaction forces; KP; delayed schedule "after a few walking trials" for 1/3 of training session
Lee et al., 2015	RCT	**Exp:** 10 **Control:** 10	**Exp:** 5/5 **Control:** 5/5	**Exp:** 68.4 ± 2.9 **Control:** 70.1±3.3	NR	NR	NR	Balance	(1) 30 mins + (2) 30 mins + (3) 15 mins (FES), 5 days/week, 6 weeks	NR	**Exp:** (1) Wii, Dance (2) neurodevelopment treatment (3) functional electrical stimulation (FES) **Control:** Neurodevelopment treatment, FES	**Exp:** Visual, auditory, vibro-tactile **Control:** None	Gamified; K-pop Dance Festival; KR/KP; real-time on 100% of trials

Liao et al., 2015	RCT	**Exp:** 12 **Active Control:** 12 **Inactive Control:** 12	**Exp:** 5/7 **Active Control:** 6/6 **Inactive Control:** 6/6	**Exp:** 64.6 ± 8.6 **Active Control:** 65.1 ± 6.7 **Inactive Control:** 67.3 ± 7.1	**Exp:** 6.4 ± 3.0 **Active Control:** 6.9 ± 2.8 **Inactive Control:** 7.9 ± 2.7	**Exp:** HY: 1.9 ± 0.8 **Active Control:** HY: 2.0 ± 0.8 **Inactive Control:** HY: 2.0 ± 0.7	NR	Muscle strength, sensory integration, gait	45 mins (exercise) + 15 mins (treadmill training), 2 days/week, 6 weeks	4	**Exp:** Yoga, strengthening + balance exercise with Wii Fit balance board + Wii Sport + treadmill training **Active Control:** Traditional rehabilitation (stretching, strengthening + balance exercise) + treadmill training **Inactive Control:** No exercise + fall prevention education	**Exp:** Visual, auditory, vibro-tactile **Active Control:** NR **Inactive Control:** n/a	Gamified; Yoga (sun-salutation, modified lunges, chair pose, tree pose, table top in standing position), strengthening exercises, Football Game, Marble Balance, Ski Slalom, Bubble Balance; KR/KP; real-time on 100% of trials
Pedreira et al., 2013	RCT	**Exp:** 16 **Control:** 15	**Exp:** 11/5 **Control:** 11/4	**Exp:** 61.1 ± 8.2 **Control:** 66.2 ± 8.5	**Exp:** 8.6 ± 4.6 **Control:** 7.3 ± 6.6	**Exp:** HY: 2.5 ± 0.6 **Control:** HY: 2.4 ± 0.7	NR	Motor (unspecified)	10 mins (warm-up) + 40 mins (exercise), 3 days/week, 4 weeks	NR	**Exp:** Warm-up exercise + exercise training with Wii (unspecified) **Control:** Warm-up exercise + traditional physical therapy	**Exp:** Visual, auditory **Control:** NR	Gamified; Games NR; KR/KP; real-time on 100% of trials
Pompeu et al., 2012	RCT	**Exp:** 16 **Control:** 16	17/15 (NR by group)	**Exp:** 66.2 ± 8.3 **Control:** 68.6 ± 8.0	**Exp:** 5.2 ± 3.4 **Control:** 4.7 ± 5.4	HY 1.7 ± 0.5 (NR by group)	Clinic	Balance	30 mins (balance) + 30 mins (exercise), 2 days/week, 7 weeks	9	**Exp:** Static balance, dynamic balance + stationary gait training with Wii Fit balance board + global exercise **Control:** Traditional training (static balance, dynamic balance + stationary gait) + global exercise	**Exp:** Visual, auditory **Control:** None	Gamified; Torso Twist, Single Leg Extension, Rhythm Parade, Table Tilt, Tilt City, Basic Step, Penguin Slide, Obstacle Course, Soccer Heading, Basic Run Plus; KR/KP; real-time on 100% of trials

Shen & Mak, 2014	RCT	**Exp:** 26 **Control:** 25	**Exp:** 3/9 **Control:** 12/11	**Exp:** 63.3 ± 8.0 **Control:** 65.3 ± 8.5	**Exp:** 8.1 ± 4.3 **Control:** 6.6 ± 4.0	**Exp:** HY: 2.4 ± 0.5 **Control:** HY:2.5 ± 0.5	Lab-oratory / home	Balance, gait	Lab: 60 mins, 3 days/week, 8 weeks Home: 20 mins, 5 days/week, 4 weeks	12; 52	**Exp:** 1) Stepping + reaching exercise with computerized dancing system + Smart-Equitest Balance Master 2) Training for response to perturbation on treadmill **Control:** Lower limb strength training Session length: 60 mins (lab); 20 mins (home)	**Exp:** Visual, verbal **Control:** NR	Not gamified; accuracy of timing + amplitude of step + reaching; KR; terminally on 100% of trials
Stern, 2009	RCT	**Exp:** 10 **Control:** 10	**Exp:** 4/6 **Control:** 7/3	**Exp:** 66.1 ± 6.1 **Control:** 64.8 ± 7.3	**Exp:** 2.85 ± 1.55 **Control:** 4.0 ± 3.32	**Exp:** HY: 1.50 ± 0.33 **Control:** HY: 1.45 ± 0.37	Clinic	Balance	36 mins, 5 days/week, 2 weeks	4	**Exp:** Limits of stability + sit-to-stand training with feedback via Smart Balance Master System **Control:** Traditional rehabilitation (stretching, sitting + standing balance, gait + transfers)	**Exp:** Visual **Control:** NR	NR; related to weight-shifting on force plates; NR: real-time/ terminally, frequency NR
van den Heuvel et al., 2014	RCT	**Exp:** 17 **Control:** 16	**Exp:** 12/5 **Control:** 8/8	**Exp:** 66.3 ± 6.39 **Control:** 68.8 ± 9.6	**Exp:** Median: 9, IQR: 9.25 **Control:** Median: 8.8, IQR: 9	**Exp:** HY: Median: 2.5, IQR: 1.5 UPDRS (Motor III): Median: 30.8, IQR: 21.5 **Control:** HY: Median: 2.5, IQR: 1.0 UPDRS (Motor III): Median: 28.0, IQR: 17.88	Clinic	Balance	60 mins, 2 days/week, 5 weeks	6	**Exp:** Standing + dynamic training with feedback via forceplate + inertial sensors in custom software **Control:** Sitting + dynamic training	**Exp:** Visual **Control:** NR	Gamified; game corresponded to user's foot placement + upper leg orientation during body lean, stepping + sit-to-stand movement; KR/KP; real -time on 100% of trials
Yang et al., 2016	RCT	**Exp:** 11	**Exp:** 7/4	**Exp:** 72.5 ± 8.4	**Exp:** 9.4 ± 3.6	**Exp:** HY: Median: 3	Home	Balance	50 mins, 2 days/week,	2	**Exp:** Static posture +	**Exp:** Visual	Gamified; Star Excursion, Ball

		Control: 12	**Control:** 7/5	**Control:** 75.4 ± 6.3	**Control:** 8.3 ± 4.1	**Control:** HY: Median: 3			6 weeks		dynamic weight shifting with virtual reality balance training system (Cycling + Health Center of Taichung, Taiwan) **Control:** Traditional Rehabilitation (Static posture + dynamic weight shifting)	**Control:** Verbal	Maze, Table Tilt, Home Yoga, Cooking, Cloth Washing, Car Racing, Park Walking, Apple Catching; KR/KP; real-time on 100% of trials
Yen et al., 2011	RCT	**Exp:** 14 **Active Control:** 14 **Inactive Control:** 14	**Exp:** 12/2 **Active Control:** 12/2 **Inactive Control:** 9/5	**Exp:** 70.4 ± 6.5 **Active Control:** 70.1 ± 6.9 **Inactive Control:** 71.6 ± 5.8	**Exp:** 6.0 ± 2.9 **Active Control:** 6.1 ± 3.3 **Inactive Control:** 7.8 ± 4.2	**Exp:** HY: 2.6 ± .5 UPDRS (Motor III): 15.1 ± 3.2 **Active Control:** HY: 2.4 ± 0.5 UPDRS (Motor III): 15.9 ± 2.4 **Inactive Control:** HY: 2.6 ± 0.4 UPDRS (Motor III): 16.8 ± 5.5	Clinic	Balance	10 mins (warm-up) + 20 mins (training), 2 days/week, 6 weeks	4	**Exp:** Warm-up exercises + dynamic balance training with virtual reality balance training system (Cycling + Health Center of Taichung, Taiwan) **Active Control:** Conventional balance training (static stance, dynamic weight shifting, external perturbations) **Inactive Control:** No training	**Exp:** Visual **Active Control:** NR **Inactive Control:** None	Gamified; 3D Ball-Rolling Game, Indoor-outdoor Virtual Activities; KR/KP; real-time on 100% of trials

Note. M/F = Male/Female; Exp = Experimental Group; Control = Control Group; HY = Hoehn and Yahr Scale; NR = Not reported; PD = Parkinson's disease; RCT = Randomized Control trial; UPDRS = Unified Parkinson's Disease Rating Scale.

3.3.3 Methodological Quality

Two independent raters had good agreement in appraising methodological quality of studies, with 86% and 83% for case studies and group designs, respectively. All differences in ratings were discussed and successfully resolved by consensus.

3.3.3.1 Case Studies

The risk of bias assessment for case studies is shown in table 3-2. Both case studies provided clear descriptions of participants' clinical history, used precise and repeatable measures, and provided raw outcome measure data. One study reported independence of outcome assessor and conducted appropriate statistical analysis (Zettergren et al., 2011), and the other study replicated the treatment across four participants and assessed generalization of treatment effects (Balci et al., 2013). Three indicators of high risk of bias, however, were noted for both case studies: neither study clearly stated study design, adequately sampled data at baseline or during treatment, nor conducted statistical analysis.

Table 3-2. Critical appraisal of risk of bias (ROB) for single-subject design studies.

Study	Clinical history specified (age, sex, aetiology, severity)	Precise and repeatable measures	Type of design (e.g., ABA, multiple baseline) clearly stated	Minimum of 3 baseline points	Minimum of 3 treatment points	Raw data reported	Inter-rater reliability established for at least one measure	Independence of assessors	Statistical analysis	Replication across subjects, therapists, or settings	Evidence for generalization
Balci et al., 2013	✓	✓	✘	✘	✘	✓	-	-	✘	✓	✓
Zettergren et al., 2011	✓*	✓	✘	✘	✘	✓	-	✓	✓	✘	✘

Note.
✓ Low risk of bias (ROB)
✘ High ROB
- Unclear ROB
*Severity of symptoms described but not assessed with standard measure

3.3.3.2 Group Design Studies

The risk of bias assessment for group studies is shown in table 3-3. All single group studies provided point and variability measures for at least one outcome measure and reported data from all outcomes stated a priori. The majority of single group studies (n=7/8) also provided complete clinical history and assessed for evidence of generalization (Athukorala et al., 2014; Esculier et al., 2012; Gonçalves et al., 2014; Herz et al., 2013; Holmes et al., 2013; Mhatre et al., 2013; Zalecki et al., 2013). Only four of the eight single group studies clearly addressed study attrition (i.e., incomplete outcome data; Esculier et al., 2012; Herz et al., 2013; Holmes et al., 2013; Mhatre et al., 2013), only two studies implemented appropriate statistical analysis (Athukorala et al., 2014; Holmes et al., 2013), and none reported blinding of the outcome assessor.

For all RCTs, point and variability measures for at least one outcome measure as well as data from all outcomes were reported in the study methods. The majority of RCTs (*n* = 9/10) specified a complete clinical history of their participants (Byl et al., 2015; Liao et al., 2015; Pedreira et al., 2013; Pompeu et al., 2012; Shen & Mak, 2014; Stern, 2009; van den Heuvel et al., 2014; Yang et al., 2016; Yen et al., 2011). Eight of the ten RCTs adequately described their sequence generation process and reported blinding of the outcome assessor (Liao et al., 2015; Pedreira et al., 2013; Pompeu et al., 2012; Shen & Mak, 2014; Stern, 2009; van den Heuvel et al., 2014; Yang et al., 2016; Yen et al., 2011). Eight of ten RCTs also demonstrated that the intervention groups were equivalent at baseline and presented results for experimental and control groups (Byl et al., 2015; Lee et al., 2015; Liao et al., 2015; Pompeu et al., 2012; Shen & Mak, 2014; van den Heuvel et al., 2014; Yang et al., 2016; Yen et al., 2011). Seven studies reported reasons for study attrition and conducted appropriate statistical analyses, while six studies assessed for evidence of generalization (Byl et al., 2015; Liao et al., 2015; Pompeu et al., 2012; Shen & Mak, 2014; van den Heuvel et al., 2014; Yang et al., 2016; Yen et al., 2011). Only four RCTs, however, reported analyzing data using the intention-to-treat principles (Shen & Mak, 2014; van den Heuvel et al., 2014; Yang et al., 2016; Yen et al., 2011) and only three studies clearly described if and how allocation concealment was conducted (Liao et al., 2015; Shen & Mak, 2014; van den Heuvel et al., 2014).

Table 3-3. Critical appraisal of risk of bias (ROB) for all group designs (single group and RCTs).

Study	**Clinical history specified (age, sex, aetiology, severity)**	**Sequence generation**	**Allocation concealment**	**Groups equivalent at baseline**	**Blinding of outcome assessor**	**Incomplete outcome data addressed**	**Selective outcome reporting**	**Intention-to-treat analysis**	**Results between intervention groups reported**	**Point and variability measures reported for at least one outcome**	**Appropriate statistical analysis**	**Evidence for generalization**
Single Group Designs												
Athukorala et al., 2014	✓	n/a	n/a	n/a	✘	-	✓	n/a	n/a	✓	✓	✓
dos Santos Mendes et al., 2012	✘	n/a	n/a	n/a	-	-	✓	n/a	n/a	✓	-	✘
Esculier et al., 2012	✓	n/a	n/a	n/a	-	✓	✓	n/a	n/a	✓	✘	✓
Gonçalves et al., 2014	✓	n/a	n/a	n/a	-	-	✓	n/a	n/a	✓	✘	✓
Herz et al., 2013	✓	n/a	n/a	n/a	-	✓	✓	n/a	n/a	✓	✘	✓
Holmes et al., 2013	✓	n/a	n/a	n/a	-	✓	✓	n/a	n/a	✓	✓	✓
Mhatre et al., 2013	✓	n/a	n/a	n/a	✘	✓	✓	n/a	n/a	✓	✘	✓
Zalecki et al., 2013	✓	n/a	n/a	n/a	-	-	✓	n/a	n/a	✓	✘	✓
RCT Group Designs												
Byl et al., 2015	✓	-	-	✓	-	✓	✓	-	✓	✓	✓	✘
Lee et al., 2015	✘	-	-	✓	-	-	✓	-	✓	✓	✘	✓
Liao et al., 2015	✓	✓	✓	✓	✓	✓	✓	-	✓	✓	✓	✘

Pedreira et al., 2013	✓	✓	-	✘	✓	✘	✓	-	✘	✓	✘	✓
Pompeu et al., 2012	✓	✓	-	✓	✓	✓	✓	-	✓	✓	✓	✓
Shen & Mak, 2014	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Stern, 2009	✓	✓	-	✘	✓	-	✓	-	✘	✓	✘	✘
van den Heuvel et al., 2014	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Yang et al., 2016	✓	✓	-	✓	✓	✓	✓	✓	✓	✓	✓	✓
Yen et al., 2011	✓	✓	✘	✓	✓	✓	✓	✓	✓	✓	✓	✘

Note.
✓ Low risk of bias (ROB)
✘ High ROB
- Unclear ROB
n/a Not applicable to non-randomized control trials

3.3.4 Summary of Findings

3.3.4.1 Classification of Outcome Measures

Figure 3-2 shows the distribution of outcome measures by type across articles, classified by the core levels of the ICF (impairment, activity, and participation) (World Health Organization, 2001) and global motor function (i.e., UPDRS motor score). The case studies captured change at the impairment, activity and global motor function levels (Balci et al., 2013; Zettergren et al., 2011). A similar distribution in outcome measure classification was observed for all group studies (single group and RCT). Activity-level measures were the most prevalent, captured in 17/18 group articles (Athukorala et al., 2014; Byl et al., 2015; dos Santos Mendes et al., 2012; Esculier et al., 2012; Gonçalves et al., 2014; Herz et al., 2013; Holmes et al., 2013; Lee et al., 2015; Liao et al., 2015; Mhatre et al., 2013; Pompeu et al., 2012; Shen & Mak, 2014; Stern, 2009; van den Heuvel et al., 2014; Yang et al., 2016; Yen et al., 2011; Zalecki et al., 2013). Half of the group articles examined change at the impairment level (9/18; Athukorala et al., 2014; Byl et al., 2015; Herz et al., 2013; Holmes et al., 2013; Lee et al., 2015; Liao et al., 2015; Mhatre et al., 2013; Pompeu et al., 2012; van den Heuvel et al., 2014), while participation level measures were rarely examined (4/18; Athukorala et al., 2014; Herz et al., 2013; Pedreira et al., 2013; Yang et al., 2016). Measures of global motor function were assessed in 6/18 group design articles (Gonçalves et al., 2014; Herz et al., 2013; Pompeu et al., 2012; van den Heuvel et al., 2014; Yang et al., 2016; Zalecki et al., 2013).

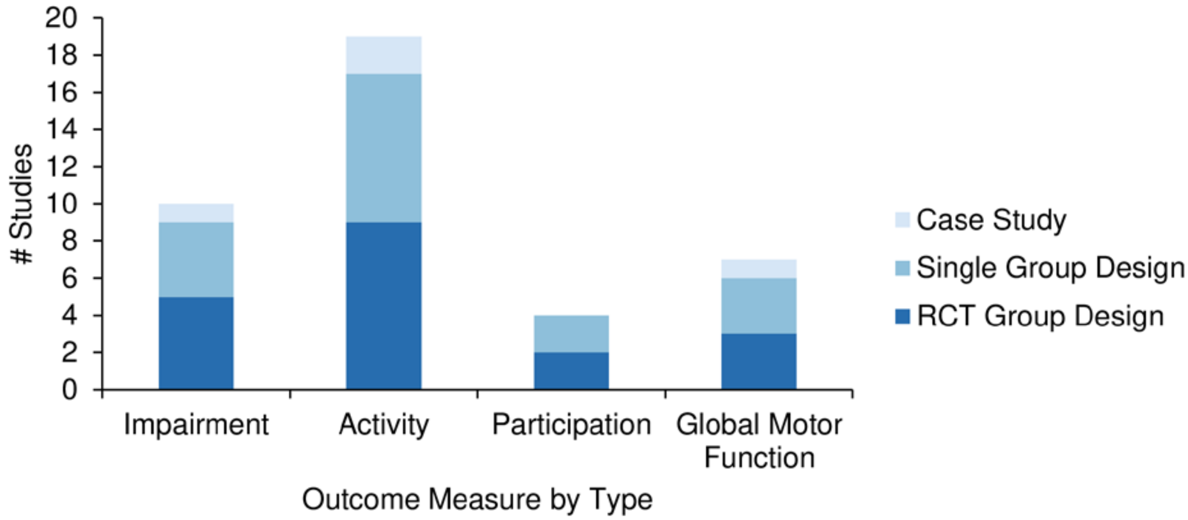

Figure 3-2. Distribution of outcome measures by type across all studies. Outcome measures are classified by the core levels of the International Classification of Functioning, Disability, and Health (ICF), and global motor function.

3.3.4.2 Treatment Effect

The treatment outcomes of the studies are summarized in tables 3-4 – 3-6. Fifteen articles provided effect sizes or raw data from which effect sizes could be derived. The total number of measures by category is shown in column 2 (table 3-4 and 3-5), and outcome measures with effect sizes ($d > |0.2|$) are included in column 3. All effect sizes are reported with positive or negative signs indicating improvement ("+") or decline ("-") in performance for within-subject/group effects, and enhanced ("+") or reduced ("-") benefit of AVFT compared to control treatment for between-group effects. Figures 3-3 and 3-4 provide a summary of the effect of AVFT immediately post treatment (figure 3-3) and at follow-up (figure 3-4).

3.3.4.2.1 Studies reporting within-Subject/Group Effect (Case Studies and Single Group Designs)

Six of 10 articles reporting within-subject/group effects included sufficient data to estimate the magnitude of effect size (table 3-4). Above threshold improvements were observed for 79% of all measures (figure 3-3), including measures of impairment (i.e., balance centre of pressure) and activity (i.e., static and dynamic balance; mobility; gait; upper extremity speed and coordination;

fall risk) (Balci et al., 2013; Herz et al., 2013; Holmes et al., 2013; Mhatre et al., 2013; Zalecki et al., 2013). Generalization of treatment effects was also observed for measures of ADLs, participation (i.e., quality of life) and global motor function (Balci et al., 2013; Gonçalves et al., 2014; Herz et al., 2013; Holmes et al., 2013; Mhatre et al., 2013; Zalecki et al., 2013). One measure of depression showed a decline in rating post treatment (Mhatre et al., 2013). The remaining measures (18%) capturing change at the activity level did not meet the threshold for change post intervention; these measures typically examined performance in areas that were not directly targeted during intervention, including upper extremity dexterity (Herz et al., 2013), balance confidence (Holmes et al., 2013; Mhatre et al., 2013), and balance centre of pressure with eyes closed and feet together (Holmes et al., 2013).

Only one of the articles examined performance four weeks post intervention (figure 3-3) and showed maintenance of treatment effects on measures of impairment, activity, participation and global motor function (Herz et al., 2013). At the follow-up time point, performance in ADLs had returned to pre-treatment levels.

Table 3-4. Summary of within-group findings (case studies and single group designs).

Study	Classification of Measures (n)	Outcome Measures	Effect Size Post Intervention	Effect Size at Follow-Up
Balci et al., 2013	Activity (6)	Activity		
	Global Motor Function (1)	*Berg Balance Scale*	+1.81	n/a
		Single Leg Stance – right	+0.39	
		Single Leg Stance - left	+1.27	
		Timed Up and Go	+0.56	
		Functional Reach Task	+1.32	
		Fall risk	+1.50	
		Global Motor Function		
		UPDRS	+0.96	
Gonçalves et al., 2014	Activity (2)	Activity		
	Global Motor Function (1)	*Shwab & England ADL scale*	+1.30	n/a
		Functional Independence Measure	+1.49	
		Global Motor Function		
		UPDRS	+1.45	
Herz et al., 2013	Impairment (1)	Impairment		
	Activity (10)	*Hamilton Rating Scale for Depression*	+0.98	+1.10
	Participation (1)	Activity		
	Global Motor Function (1)	*Nottingham Extended ADL Scale*	+0.37	
		9-hole peg test - right	+0.31	
		Purdue Pegboard Test – left	+0.51	+0.38
		Purdue Pegboard Test – both	+0.30	
		Purdue Pegboard Test – alternating		+0.30
		Timed tapping test – right	+0.38	+0.28
		Timed tapping test – left		+0.27
		Timed Up and Go	+0.61	+0.21
		Participation		
		Parkinson's Disease Questionnaire-39	+0.39	+0.22
		Global Motor Function		
		UPDRS	+0.25	+0.32
Holmes et al., 2013	Impairment (4)	Impairment		
	Activity (1)	*Balance Centre of Pressure – eyes open, feet apart*	+0.20	n/a
		Balance Centre of Pressure – eyes open, feet together	+0.20	
		Balance Centre of Pressure – eyes closed, feet apart	+0.20	
Mhatre et al., 2013	Impairment (1)	Impairment		
	Activity (5)	*Geriatric Depression Scale*	-0.35	n/a
		Activity		
		Berg Balance Scale	+0.37	
		Dynamic Gait Index	+0.98	
		Sharpened Romberg Test – eyes open	+0.28	
		Sharpened Romberg Test – eyes closed	+0.57	
Zalecki et al., 2013	Activity (1)	Activity		
	Global Motor Function (1)	*Timed Up and Go*	+2.59	n/a
		Global Motor Function		
		UPDRS	+10.35	

Note. The total number of measures by category is shown in column 2. Only data from outcome measures with small ($d \geq .2$), medium ($d \geq .5$) or large effect sizes ($d \geq .8$) shown; ' + ' indicates improvement in performance, and ' – ' indicates decline in performance.
n/a = not applicable; UPDRS = Unified Parkinson's Disease Rating Scale; ADL = Activities of Daily Living.

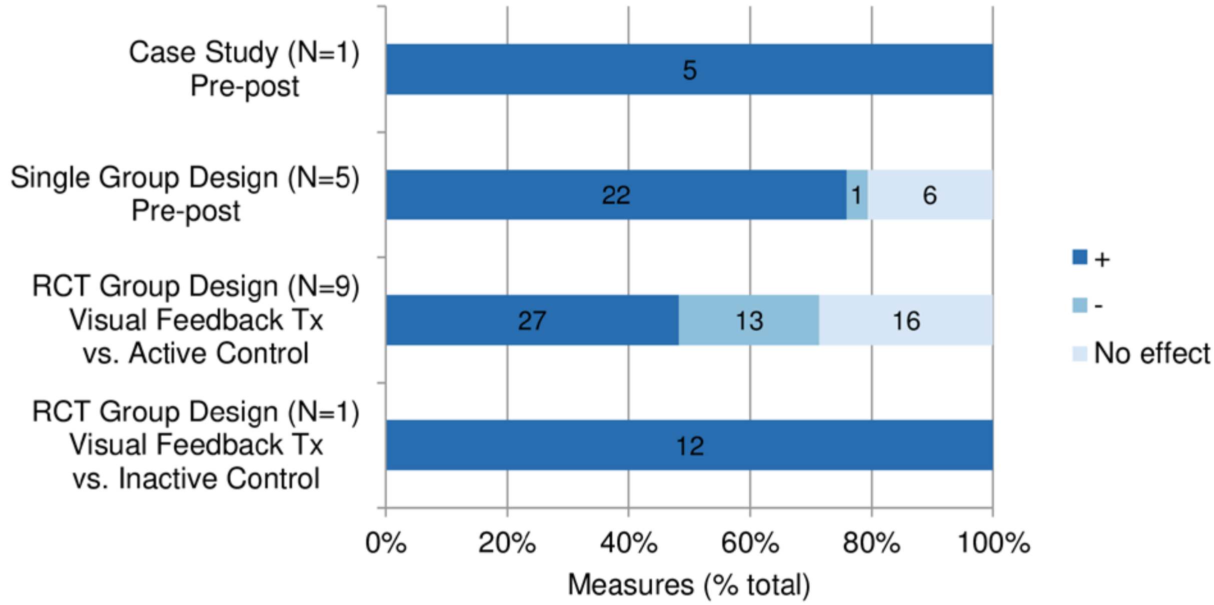

Figure 3-3. The summary of measures showing positive (+), negative (-), or no effect immediately after treatment. Case studies and single group studies show effect pre-post treatment; RCT studies show effect compared to (1) active control groups, and (2) inactive control groups. The number of studies with available effect size data is shown in parentheses following study design, and the number of included measures is indicated on each bar.

3.3.4.2.2 Studies reporting between-Group Effect (RCTs)

Nine of 10 RCTs provided data to calculate the magnitude of treatment effect between AVFT and active control groups (table 3-5). Approximately half of all measures (48%) indicated an enhanced benefit of AVFT immediately post intervention (figure 3-4). The remaining measures showed reduced (23%) or equivocal benefit of AVFT (29%). Inconsistent results (enhanced and reduced benefit) were reported across studies and muscle groups for impairment level measures, such as muscle strength and range of movement (Byl et al., 2015; Liao et al., 2015). Similarly, study-dependent findings were reported for measures of activity; enhanced, reduced and equivocal findings were found for measures of static and dynamic balance, mobility and gait (Byl et al., 2015; Lee et al., 2015; Liao et al., 2015; Pompeu et al., 2012; Shen & Mak, 2014; Stern, 2009; van den Heuvel et al., 2014; Yang et al., 2016). Generalization of treatment effect to ADLs, cognition, fatigue, quality of life and global motor function was either enhanced for the

AVFT group, or similar to the control group (Lee et al., 2015; Pedreira et al., 2013; Pompeu et al., 2012; van den Heuvel et al., 2014; Yang et al., 2016).

Six articles examined the maintenance of treatment effects, with the majority of effects being maintained from 2-12 weeks post intervention (Liao et al., 2015; Pompeu et al., 2012; Shen & Mak, 2014; Stern, 2009; van den Heuvel et al., 2014; Yang et al., 2016), while one study showed maintenance on activity-level measures 12 months post intervention (Shen & Mak, 2014) (figure 3-4). Reports of both enhanced and reduced benefit of AVFT, however, were reported for global motor function when assessed at follow-up (Pompeu et al., 2012; van den Heuvel et al., 2014; Yang et al., 2016).

Table 3-5. Summary of between-group findings (RCTs: AVFT vs. active control group).

Study	Classification of Measures (n)	Outcome Measures	Effect Size Post Intervention	Effect Size at Follow-up
Byl et al., 2015	Impairment (4) Activity (8)	Impairment		
		Muscle strength – affected side	-0.30	n/a
		Muscle strength – unaffected side	-0.30	
		ROM – affected side	-0.56	
		ROM – unaffected side	-0.76	
		Activity		
		Step length	-0.27	
		Tinetti Gait Assessment	-0.32	
		6 min walk	-0.94	
		Dynamic Gait Index	+0.23	
		Timed Up and Go	+0.86	
		Berg Balance Scale	-0.89	
Lee et al., 2015	Impairment (1) Activity (2)	Impairment		
		Beck Depression Index	+0.99	n/a
		Activity		
		Berg Balance Scale	+0.62	
		Modified Barthel Index	+0.91	
Liao et al., 2015	Impairment (6) Activity (6)	Impairment		
		Muscle strength		
		- hip flexors (f) + extensors (e)	-0.29 (f) +0.44 (e)	-0.51 (f) +0.29 (e)
		- knee f + e	-0.23 (f) +0.24 (e)	-0.31 (f)
		- ankle dorsiflexors (d)+ plantarflexors (p)	-0.23 (d) +0.31 (p)	+0.31 (p)
		Activity		
		Gait velocity	+0.32	+0.30
		Stride length		+0.28
		Functional gait assessment	+0.48	+0.54
		Sensory Organization Test (somatosensory)	+0.47	
		Sensory Organization Test (vision)	+0.56	+0.46
		Sensory Organization Test (vestibular)	+0.76	+0.67
Pedreira et al., 2013	Participation (1)	Participation		
		Parkinson's Disease Questionnaire-39	+0.72	n/a
Pompeu et al., 2012	Impairment (1) Activity (3) Global Motor Function (1)	Activity		
		Unipedal Stance Test (eyes open)	+0.23	+0.23
		Global Motor Function		
		UPDRS		-0.22
Shen & Mak, 2014	Activity (6)	Activity		
		Activities-Specific Balance Confidence Scale		+0.35 (4 weeks); +0.38 (52 weeks)
		Limits of Stability – velocity	+0.38	
		Limits of Stability – end-point excursion	-0.32	+0.59 (4 weeks); +0.24 (52 weeks)
		Gait velocity	-0.23	
		Stride length	+0.61	+0.38 (4 weeks); +0.50 (52 weeks)
Stern, 2009	Activity (2)	Activity		
		Timed Up and GO	+0.58	+1.12
		Functional Reach Task	+0.40	+0.94
van den Heuvel et al., 2014	Impairment (4) Activity (8) Global Motor Function (1)	Impairment		
		Hospital Anxiety and Depression Scale – anxiety	-0.21	+0.28
		Hospital Anxiety and Depression Scale – depression	-0.42	+0.34
		Activity		
		Functional Reach Test		0.39
		Berg Balance Scale	+0.28	0.48
		Single Leg Stance – preferred	+0.23	
		Single Leg Stance – non-preferred	+0.31	
		Gait speed	+0.51	
		Gait step length	+0.55	0.22
		Falls Efficacy Scale		0.36
		PDQ-39 (mobility subscore)		0.27
		Global Motor Function		
		UPDRS	+0.29	0.22
Yang et al., 2016	Activity (3) Participation (1) Global Motor Function (1)	Activity		
		Dynamic Gait Index	+0.45	
		Global Motor Function		
		UPDRS	+0.46	-0.40

Note. Only outcome measures with small (d ≥ .2), medium (d ≥ .5) or large effect sizes (d ≥ .8) shown; ' + ' indicates experimental group performance was enhanced compared to active control group, and ' – ' indicates experimental group performance was reduced relative to active control group.
n/a = not applicable; UPDRS = Unified Parkinson's Disease Rating Scale.

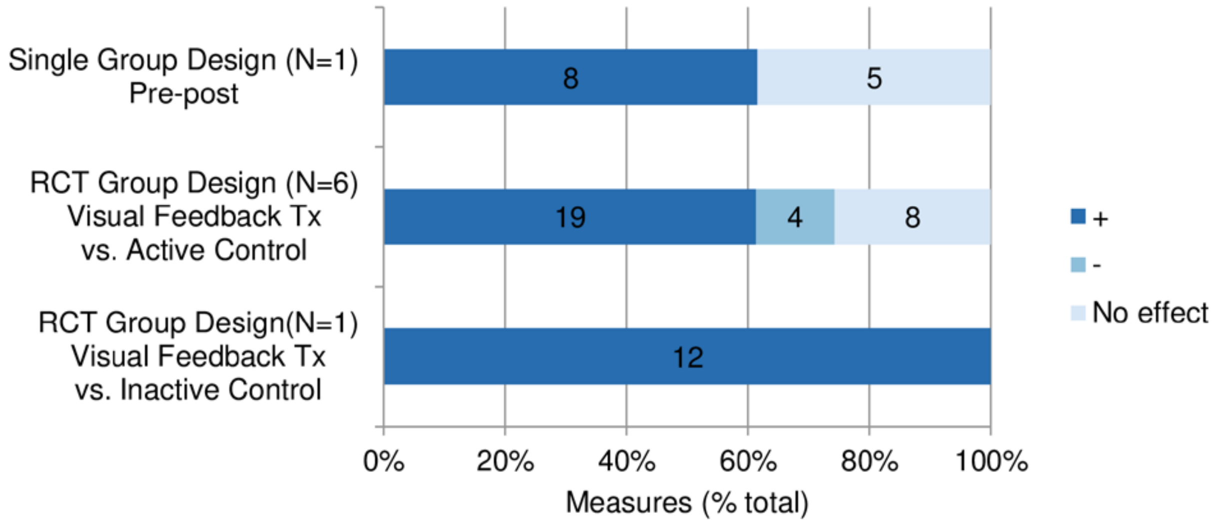

Figure 3-4. The summary of measures showing positive (+), negative (-), or no effect immediately at follow-up. The measures are grouped by positive (+), negative (-), or no effect. Case studies and single group studies show effect pre-treatment to follow-up; RCT studies show effect for visual feedback-based treatment compared to (1) active control groups, and (2) inactive control groups. The number of studies with available effect size data is shown in parentheses following study design, and the number of included measures is indicated on each bar.

One study provided data to calculate the magnitude of treatment effect between AVFT and an inactive control group who received falls prevention education (table 3-6). Post-intervention measures of impairment (i.e., muscle strength) and activity (i.e., balance, gait) were enhanced in the AVFT group (Liao et al., 2015). At follow-up assessment four weeks post intervention, the benefit of AVFT was maintained for all measures.

Table 3-6. Summary of Between-group Findings (RCTs: AVFT vs. Inactive Control Group).

Study	Classification of Measures (n)	Outcome Measures	Effect Size Post Intervention	Effect Size at Follow-up
Liao et al., 2015	Impairment (6) Activity (6)	Impairment		
		Muscle strength		
		- hip flexors (f) + extensors (e)	+0.68 (f) +1.07 (e)	+0.71 (f) +0.76 (e)
		- knee f + e	+0.61 (f) +1.13 (e)	+0.57 (f) +0.91 (e)
		- ankle dorsiflexors (d)+ plantarflexors (p)	+1.16 (d) +1.21 (p)	+1.31 (d) +1.05 (p)
		Activity		
		Gait velocity	+1.06	+0.75
		Stride length	+0.97	+0.96
		Functional gait assessment	+1.86	+1.83
		Sensory Organization Test (somatosensory)	+0.58	+0.66
		Sensory Organization Test (vision)	+1.34	+1.29
		Sensory Organization Test (vestibular)	+1.67	+1.43

Note. Only outcome measures with small (d ≥ .2), medium (d ≥ .5) or large effect sizes (d ≥ .8) shown; ‘ + ’ indicates experimental group performance was enhanced compared to inactive control group, and ‘ – ‘ indicates experimental group performance was reduced relative to inactive control group.

3.3.4.3 Analysis of Treatment Design Factors in RCTs

Figure 3-5 summarizes the analysis of treatment design factors in RCTs comparing AVFT to active control groups. For continuous measures (amount and intensity of treatment), the distribution of data was examined to identify clusters (figure 3-6). Studies were then categorized as having small (≤20 hours) or large (>20 hours) amounts of treatment, and low (≤3 sessions/week) or high (>3 sessions/week) treatment intensities. One RCT did not provide details that pertained to gamification, nature, or timing of feedback, and was excluded from those analyses (Stern, 2009).

The majority of RCTs used a small amount of treatment time at a low intensity. Six of the seven studies that implemented a small amount of treatment also delivered the treatment at a low intensity. Studies with large amounts and high intensities of treatment showed a trend for greater benefits of AVFT as compared to treatments delivered in small amounts and at low intensities.

Most RCTs also implemented gamification of feedback and provided KP information in real-time and on 100% of practice trials. Gamification of feedback resulted in a higher proportion of enhanced benefits, compared to studies with non-gamified feedback. A trend for greater benefits was also observed for studies providing KP information, relative to a single study that provided KR. Real-time feedback, either alone or combined with terminal feedback, led to a greater proportion of enhanced benefits, compared to providing only terminal or delayed feedback. Additionally, studies implementing 100% feedback frequency showed a larger percentage of measures with enhanced benefits than a study with a reduced feedback schedule.

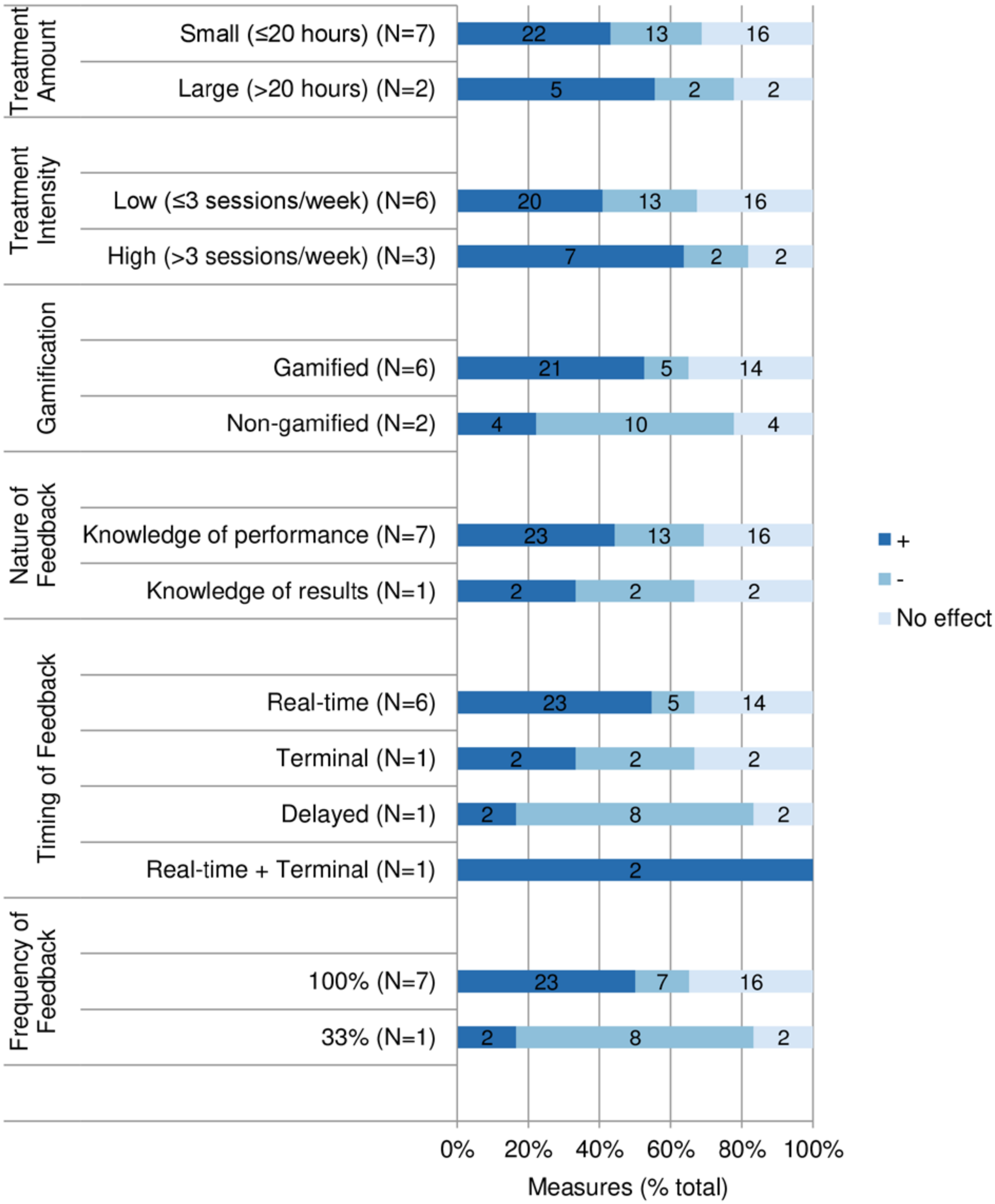

Figure 3-5. The summary of measures in RCT studies comparing augmented visual feedback-based treatment to active control intervention immediately after treatment. Measures are grouped by the direction of the effects (positive (+), negative (-), no effect). The number of included measures is indicated on each bar.

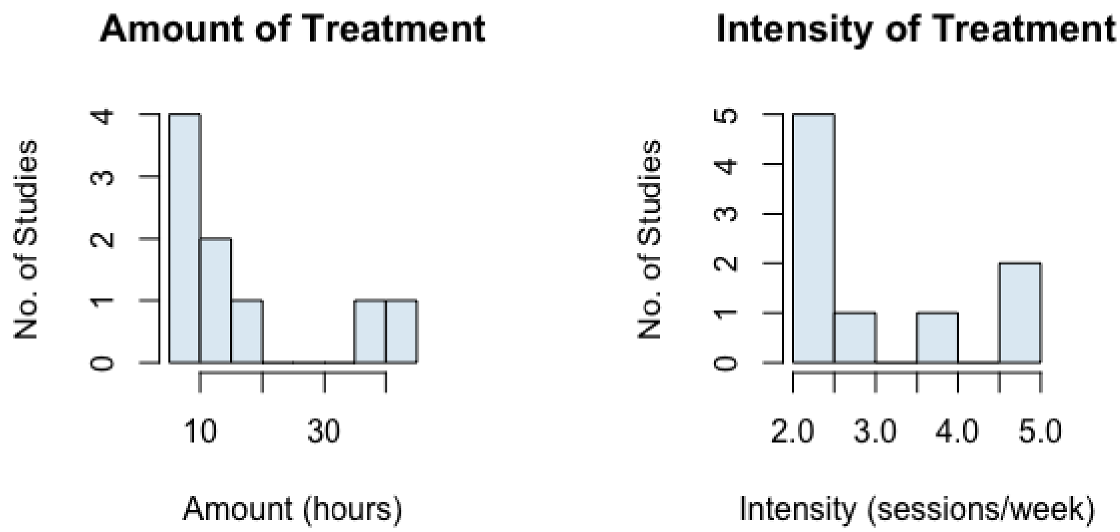

Figure 3-6. Distribution of treatment amount and intensity across RCT studies.

3.4 Discussion

The overall aim of this study was to examine the effectiveness of AVFT on motor rehabilitation in Parkinson's disease and to identify the factors that might be associated with better treatment outcomes. A detailed analysis of the data from 15 published articles of various methodologies (from case studies to RCTs) revealed that AVFT led to improved outcomes post treatment that were often superior to outcomes of traditional rehabilitation and education programs. A further five articles reported positive results for measures of swallowing, balance, and gait following AVFT; however, it was not possible to estimate the magnitude of treatment effect.

The case studies and single group studies showed improvements post treatment across measures of impairment, activity, and participation, as well as in global motor function. The RCTs often showed superior outcomes of AVFT when compared to traditional rehabilitation (active control treatments), although instances of enhanced, reduced and equivocal benefits of AVFT were also reported. These mixed results were apparent across all levels of measurement – impairment, activity, participation, and global motor function. Additionally, one RCT showed enhanced impairment- and activity-level outcomes of AVFT when compared to a falls prevention education program (inactive control treatment).

Many of the included studies were rated, however, as having a high or unclear risk of bias on key areas of methodological quality. Only two RCTs were rated as having a low risk of bias for all key areas, and their results showed enhanced, reduced and equivocal benefit of AVFT on measures of impairment, activity and global motor function compared to traditional rehabilitation (Shen & Mak, 2014; van den Heuvel et al., 2014). The effectiveness of AVFT approaches needs to be considered in relation to the characteristics of the participants in the included studies, as well as the implementation of different treatment factors. Examining the outcome data in this way can lead to recommendations for treatment candidacy as well as identifying which factors are important in promoting enhanced treatment outcomes.

3.4.1 Participant Characteristics

Both the presentation and progression of symptoms in PD are notably variable across patients (Jankovic, 2008), yet the participants in the included studies represented a relatively homogenous group of patients in terms of age and disease severity. Most studies recruited those with mild-moderate disease severity without cognitive impairment. Noteworthy is one RCT study that included older, more severely impaired participants (i.e., moderate impairment) and showed an enhanced benefit of AVFT over traditional rehabilitation on the UPDRS immediately post treatment (Yang et al., 2016). Patients in the later stages of PD have greater difficulties with implicit motor learning and may benefit to a greater extent from augmented visual feedback to improve their control of movement (Abbruzzese et al., 2016).

In general, more male than female participants took part in the studies, which likely reflects the fact that males are at a greater risk of developing PD than females (van Den Eeden et al., 2003). The RCT studies, however, rarely sex-matched experimental and control groups, or statistically controlled for sex in the analyses, even though previous studies suggested sex differences in the clinical presentation of PD (Haaxma et al., 2007; Lubomski, Rushworth, Lee, Bertram, & Williams, 2014; Miller & Cronin-Golomb, 2010). In particular, women are more likely to present with milder symptoms in the early stages of the disease (Haaxma et al., 2007), yet are also more likely to experience dyskinesias and deficits in visuospatial cognition than their male counterparts (Martinez-Martin et al., 2012; Miller & Cronin-Golomb, 2010). In contrast, rigidity of movement and daytime sleepiness are more prevalent in men (Martinez-Martin et al., 2012).

These differential symptoms may have affected participants' performance during treatment as well as treatment outcomes.

3.4.2 Treatment Design Factors

A number of factors have been identified as influencing the outcomes of rehabilitation. Among these factors are the amount and intensity of therapy, the use of engaging and motivating games, and the nature, timing, and frequency of augmented visual feedback.

3.4.2.1 Amount and Intensity of Treatment

Generally, studies that provided large amounts of treatment did so at a high intensity, and therefore, in the context of this review, it is not possible to delineate the effect of these two treatment factors independently. When AVFT was provided in large amounts at high intensities, more enhanced benefits of treatment were observed compared to AVFT provided in small amounts at low intensities. Although intense programs with many treatment hours may place greater demands on participants' energy levels, when the patients are already susceptible to fatigue (Karlsen, Larsen, Tandberg, & Mæland, 1999), these programs did not seem to have negative consequences on treatment outcomes in our review. This finding is in contrast to a previous study of treadmill training in PD (without augmented visual feedback) that showed better outcomes at lower treatment intensities (Pelosin et al., 2016). The amount of treatment in Pelosin et al.'s study, however, was small (i.e., 10 hours). It is possible that a high intensity of treatment might be most effective when combined with a large amount of treatment.

3.4.2.2 Gamification of Feedback

One aspect of the feedback systems that varied greatly across studies was whether the visual feedback was gamified as in a video game, or simply presented as information during or post performance. The majority of RCTs used gamified AVFT - via the Wii or custom-built software - and showed enhanced benefit compared to traditional rehabilitation. In contrast, inconsistent results were found for the non-gamified approaches (Byl et al., 2015; Shen & Mak, 2014). When feedback was not gamified, it was presented as a time history either of muscle contraction during swallowing or ground reaction forces during gait, or as an accuracy score. This information may be limiting for a non-expert user who may have difficulty applying the information from the time history plot to their motor skill, or may not know how to increase their accuracy. Further, non-gamified approaches may lack the engagement of a game that has intuitive representations of movement and structured levels of difficulty. These early results indicate that gamification is a beneficial factor of the visual feedback systems, and may promote greater treatment adherence and potentially better outcomes than traditional rehabilitation (Barry et al., 2014).

3.4.2.3 Nature of Feedback

The majority of studies provided KP feedback during various treatments and showed a benefit of these treatments over a single intervention which provided KR feedback. The complex nature of the motor skills targeted in the reviewed studies may have necessitated KP feedback to convey information about the multiple components of movement at once. Differences in the effect of KP versus KR on motor learning have previously been investigated in healthy populations, with KP showing a benefit over KR, particularly during the early stages of skill acquisition, when the goal of a task is unclear (Swinnen, Walter, Lee, & Serrien, 1993). Over time it may be possible to shift the nature of feedback from KP to KR as patients develop a stronger internal representation of the movement pattern required to successfully complete the task.

3.4.2.4 Timing of Feedback

Real-time or concurrent feedback has been shown to be beneficial to motor learning in healthy adults when it provides an external focus of attention (Hodges & Franks, 2001; Shea & Wulf, 1999). However terminal or delayed feedback can allow for greater intrinsic processing of feedback and thus, better retention of motor skill (Schmidt & Wulf, 1997). The majority of studies implemented real-time feedback in their design and showed better outcomes than the terminal or delayed feedback studies. Real-time feedback may have a dual effect in facilitating motor learning in PD; as the visual information is always present, patients may be benefitting from cueing of movement, as well as from the feedback about how the movement was performed. Only two RCTs implemented delayed or terminal feedback without real-time feedback, and showed mixed results post intervention (Byl et al., 2015; Shen & Mak, 2014). Notably, the same two studies used non-gamified visual feedback as discussed above and thus these two design factors may have interacted.

3.4.2.5 Frequency of Feedback

Even though most studies provided feedback 100% of the time during training, gains were still apparent post intervention when feedback was removed, suggesting that participants were not dependent on the feedback in order to carry out the motor skill (see Guidance Hypothesis; Salmoni, Schmidt, & Walter, 1984). In contrast, a study that provided feedback on a reduced schedule (for approximately one third of the treatment session) showed reduced benefit of AVFT when compared to traditional rehabilitation on measures of impairment, and inconsistent benefits on measures of activity. The advantage of high frequency over low frequency feedback differs from previous studies of novel motor skill learning in PD (Adams et al., 2002; Chiviacowsky et al., 2010). Video games - outside of the rehabilitation context- however, are typically played with feedback available 100% of the time, and we speculate that reducing feedback frequency may seem unnatural and demotivating for the game players. While feedback frequency was not experimentally manipulated during the studies, the significant benefits in studies with 100% feedback frequency suggest that individuals with PD can transfer their learning to non-feedback contexts.

3.4.3 Limitations of Existing Studies and Recommendation for Future Works

The majority of identified studies were in the physiotherapy domain, targeting motor skills such as balance, gait and muscle strength. Even though the search aimed to identify studies relevant to all rehabilitative disciplines, only one study examined the effect of AVFT for the rehabilitation of swallowing. A number of studies examining writing and speech in PD either did not study these skills in the context of rehabilitation (e.g., Potgieser, Roosma, Beudel, & de Jong, 2015), or augmented visual feedback was incorporated as a small component of a wider treatment program in a single group study (e.g., Scott & Caird, 1984). This finding may be unsurprising as a systematic review of rehabilitative therapies in PD also identified a greater number of RCTs for physiotherapy (n = 25) compared to occupational therapy (n = 4) and speech-language pathology (n = 10) (Gage & Storey, 2004) highlighting the immediate need for studies of AVFT in those areas.

Almost all studies summarized in this review demonstrated a high or unclear risk of bias. Only two studies (both RCTs) were rated as having a low risk of bias for all key areas. This highlights the need for more rigorous design, particularly paying attention to blinding of the outcome assessor, following intention-to-treat principles during analysis, and conducting appropriate statistical analyses. Almost half of the group studies failed to implement adjustments for multiple comparisons, which inflated the chance of finding significant findings due to chance alone and therefore weakening the interpretation of results. For this reason, our summary focused only on the magnitude of effect sizes, rather than on the significance of findings. Future studies, and in particular RCTs, would benefit from following the Consolidated Standards of Reporting Trials (CONSORT) guidelines when designing studies and disseminating results (Schulz, Altman, & Moher, 2010).

Even though the aim of all studies was to assess the effect of an intervention, methodological descriptions of the interventions were often not detailed enough to be replicated by another research group. Furthermore, many of the interventions involved multiple components (e.g., a variety of video games), or included additional training tasks that were supplementary to AVFT/traditional rehabilitation for the experimental and control groups, respectively. As a result, it was difficult to assess which components were effecting change, or whether AVFT alone was effective. It is plausible that certain games or exercises are more effective than others, which may be investigated by examining performance during the individual treatment components (e.g., dos Santos Mendes et al., 2012).

The majority of studies aimed to capture change in activity-based clinical measures. While these measures often show strong and important relationships to functional change for participants, they don’t capture the underlying change at a physiological level. The inclusion of physiological measures would allow researchers to develop a theoretical basis for why these clinical outcomes occur. Similarly, only four studies examined change at the participation level, even though a number of valid PD-specific instruments are available to measure quality of life in this population, such as the Parkinson’s Disease Questionnaire-39 item version (PDQ-39; Jenkinson, Fitzpatrick, Peto, Greenhall, & Hyman, 1997) or the Parkinson's disease quality of life questionnaire (PDQL; de Boer, Wijker, Speelman, & de Haes, 1996). The inclusion of these measures would offer a broader social perspective on the potential effects of AVFT for patients with PD.

A number of participant factors may have played a role in treatment outcomes in the included studies. For example, socioeconomic status and education level have been shown to impact motor recovery in individuals post stroke (Putman et al., 2007), but were not reported in the included studies. Additionally, increased familiarity with technology prior to treatment onset may have benefitted participants in their treatment outcomes, yet only three studies considered this factor by excluding participants who had prior experience with the Wii. While intact vision is a pre-requisite of using visual feedback systems, only half of the studies specified normal or corrected-to-normal vision as an inclusion criterion. Finally, when assessing balance parameters in an older population, it is pertinent to remember that hearing loss occurs in 45% of adults over 60 years of age, and is associated with an increased risk of balance impairment and falls (Jiam, Li, & Agrawal, 2016). The balance impairment, therefore, may be confounded by comorbid hearing impairment. Three studies excluded participants with auditory impairment, but did not document how the participants were screened (for example, by patient report or audiometric testing). Improved participant descriptions are needed to control for confounding factors and to assess the applicability of study results.

3.5 Conclusion

The findings from this systematic review showed that high-quality, rigorous studies of the effect of AVFT for motor rehabilitation in PD are limited, however, this area is a growing topic of research in PD. Clinically, this review indicates that augmented visual feedback may be beneficial for individuals with mild-moderate PD symptoms. When designing visual feedback-based intervention, the following factors should be considered: large amounts and high intensities of treatment, gamification of feedback, knowledge of performance feedback, real-time feedback, and a high frequency of feedback. Further high-quality research is needed to understand the physiological mechanisms underlying changes in clinical outcomes following treatment, and to assess the effect of AVFT in the rehabilitation of fine motor, speech and swallowing skills.

Acknowledgements

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Chapter 4
Treating Speech-Movement Hypokinesia in Parkinson's Disease: Does Size Matter and to What Extent?

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4 Treating Speech-Movement Hypokinesia in Parkinson's Disease: Does Size Matter and to What Extent?

Abstract

Purpose: This study evaluates the effects of a novel speech therapy program that uses a verbal cue and augmented visual feedback regarding tongue movements to address articulatory hypokinesia during speech in individuals with Parkinson's disease (PD).

Method: Five participants with PD participated in an ABA single-subject design study. Treatment aimed to increase tongue movement size using a combination of a verbal cue and augmented visual feedback and was conducted in 10 45-minute sessions over five weeks. The presence of visual feedback was manipulated during treatment. Articulatory working space (AWS) of the tongue was the primary outcome measure and was examined during treatment as well as in cued and uncued sentences pre and post treatment. Changes in AWS in response to a verbal cue were examined with respect to paired-comparison ratings of speech intelligibility for the same stimuli.

Results: During treatment, 4/5 participants showed a benefit of visual feedback in increasing their tongue AWS. Following treatment, 4/5 participants used larger tongue movements when cued, relative to their pre-treatment performance, however, none of the participants generalized the effect to the uncued sentences. Intelligibility of cued sentences was judged as better pre-treatment for 3/5 participants, post treatment for one participant, and the same pre-post treatment for the final participant.

Conclusions: This study demonstrated that augmented visual feedback may be helpful in addressing articulatory hypokinesia in individuals with PD when combined with a verbal cue. The optimal degree of articulatory expansion required to elicit benefits in speech intelligibility, however, requires further investigation.

Keywords: Parkinson's disease, dysarthria, augmented visual feedback, speech kinematics, speech therapy.

4.1 Introduction

Parkinson's disease (PD) is the second most common degenerative disease of neurological origin, caused primarily by a loss of dopaminergic neurons in the basal ganglia (Bertram & Tanzi, 2005). Motor manifestations of PD include the classic symptoms of hypokinesia, bradykinesia, tremor, rigidity, and postural instability, and these symptoms can lead to functional impairments during motor tasks (Jankovic, 2008). The majority (~90%) of individuals diagnosed with PD develop a motor speech disorder as the disease progresses (Ho et al., 1998). The most common speech disorder associated with PD is hypokinetic dysarthria, characterized by symptoms in the phonatory, prosodic and articulatory domains, leading to decreased speech intelligibility (Weismer et al., 2001). As a result, hypokinetic dysarthria can limit participation in everyday activities, and patients may experience social isolation and a reduced quality of life (Dykstra, Hakel, & Adams, 2007; Pinto et al., 2004).

A relatively small number of treatment options exist to remediate dysarthria in individuals with PD, and the existing approaches have primarily focused on the phonatory/prosodic aspects of speech production. The Lee Silverman Voice Treatment program (LSVT; Ramig et al., 1995; Ramig et al., 2001), which aims to address the reduced vocal loudness associated with hypokinetic dysarthria, is the most commonly prescribed treatment. Other approaches include the Pitch Limiting Voice Treatment (PLVT; de Swart et al., 2003), treatment using the SpeechVive device (Richardson et al., 2014), Speech Rate and Intonation Therapy (SPRINT; Martens et al., 2015), prosodic exercises (Scott & Caird, 1984), and rate reduction techniques (Lowit, Dobinson, Timmins, Howell, & Kröger, 2010). While these approaches have shown positive treatment effects (Herd et al., 2012), they have not been designed to directly address the underlying articulatory movement disorder, experienced by up to 45% of individuals with PD (Logemann et al., 1978).

4.1.1 The Articulatory Disorder and Intelligibility in Individuals with PD

Studies of articulatory movements in individuals with PD have indicated that hypokinesia and bradykinesia are observed in movements of the jaw (Darling & Huber, 2011; Forrest et al., 1989; Walsh & Smith, 2012), lips (Ackermann, Konczak, et al., 1997) and, possibly, the much less studied tongue (Weismer et al., 2012; Yunusova et al., 2008). These findings have been reported in a variety of speech tasks from syllable production to passage reading.

Articulatory movements during sentence-level tasks are of particular interest because it is at this level of speech complexity that individuals with PD experience communication difficulties due to a reduction in speech intelligibility (Kempler & Van Lancker, 2002; Weismer et al., 2001). At the sentence level, smaller and slower jaw movements have been observed in individuals with PD (Walsh & Smith, 2012). Kearney et al. (in press) recently showed a positive association between speech intelligibility and articulatory movement size of the jaw, tongue blade, and tongue dorsum across a group of speakers with PD, who exhibited a range of speech intelligibility deficit. In this study, the movement-intelligibility association was more consistently found across a range of sentences for the tongue blade as compared to sentence-specific findings for the jaw and tongue dorsum.

Existing therapies based on increasing vocal loudness, such as LSVT and PLVT, or improving prosody may indirectly result in increased articulatory movement size. For example, studies examining the effect of a one-time loud-speech instruction on speech kinematics in individuals with PD showed larger and faster movements of the jaw and tongue (Darling & Huber, 2011; Dromey, 2000; Kearney et al., in press). These effects, however, have not been examined empirically over a long period of time, e.g., pre and post treatment. Further, those with articulatory deficits, such as a perceived fast rate of speech, have shown relatively poor outcomes post-LSVT (Fox et al., 2012).

These findings suggest that direct articulatory intervention might be beneficial in addressing hypokinesia in PD. Current theoretical models (e.g., Directions Into Velocities of Articulators, DIVA; Guenther, 1995; Guenther, Hampson, & Johnson, 1998) and empirical data (e.g., Tremblay, Shiller, & Ostry, 2003) also support the idea of articulatory targets and assign an important role to somatosensory information during speech production.

Training speakers with hypokinesia to focus on their articulatory movement patterns and to increase their articulatory movement size may presumably be conducted by cueing a patient with a simple verbal prompt or by providing augmented visual feedback (AVF) regarding the relevant movement parameters. Because it is challenging for a clinician to judge spatial properties of orofacial movements (Simione, Wilson, Yunusova, & Green, 2016), we chose to use a combination of a verbal cue and AVF for this purpose.

4.1.2 Using Augmented Visual Feedback in the Treatment of Movement Abnormalities in Individuals with PD

AVF (also known as visual biofeedback) is an external source of feedback that can be used in speech therapy to supplement an individual's own somatosensory and auditory feedback. This treatment modality is highly suitable to the underlying nature of the motor disorder in individuals with PD. AVF capitalizes on the strength of patients with PD in using visual information during motor tasks to compensate for the proprioceptive deficit associated with the disease (Klockgether et al., 1995; Rickards & Cody, 1997). When incorporated into engaging games, AVF provides a means for designing highly motivating therapies (Barry et al., 2014). This aspect of AVF is important because patients with PD require a greater amount of practice than their healthy peers when acquiring novel motor skills (Nieuwboer et al., 2009), yet their motivation can be reduced due to the effect of the disease on dopamine-dependent motivation circuits in the brain (Drui et al., 2014). AVF has been successfully applied for the remediation of various motor skills in individuals with PD including balance, gait, and swallowing (Athukorala et al., 2014; Lee et al., 2015; Pompeu et al., 2012).

Technologies such as ultrasound, electropalatography, and electromagnetic articulography have been used to visualize speech movement patterns in the past, and studies have revealed positive results of visual feedback-based treatments in both pediatric and adult populations (e.g., Gibbon et al., 2001; Mauszycki et al., 2016; McNeil et al., 2010). To the best of our knowledge, only two previous studies provided acoustic-based AVF as part of speech rehabilitation programs in individuals with PD (Johnson & Pring, 1990; Scott & Caird, 1984). Johnson and Pring used AVF regarding pitch and intonation contours of phrases. Other components of their treatment, such as breathing and articulation exercises, did not incorporate visual feedback. Scott and Caird provided AVF regarding vocal loudness and showed comparable results between the experimental group and a control group who received similar treatment without visual feedback.

To date, the effect of AVF regarding articulatory movements has not been examined during speech therapy for individuals with PD.

4.1.3 Movement-Based Augmented Visual Feedback System for Individuals with PD

Our group recently developed and tested feasibility of an AVF system that provides information about articulatory movements and aims to remediate articulatory hypokinesia in individuals with PD (Haworth, Kearney, Baljko, Faloutsos, & Yunusova, 2014; Shtern, Haworth, Yunusova, Baljko, & Faloutsos, 2012; Yunusova et al., 2017). The system is based on electromagnetic articulography (WAVE, Northern Digital Inc., Canada) and provides visual information regarding movements of a single sensor attached to the tongue blade. Yunusova et al.'s (2017) feasibility study showed that, following a single training session where articulatory working space of the tongue during sentences was visualized in the form of a game, individuals with PD were able to increase articulatory movement size. Further, the effects of training were evident at a retention session 24 hours later. This system has not yet been examined in the context of a structured treatment program, and the improvements in hypokinesia have not been assessed with respect to changes in speech intelligibility.

In the current study, we conducted a Phase 1 clinical-outcome research study in order to identify the therapeutic effects of a 10-session articulatory-treatment program using a verbal cue and AVF for individuals with PD (Robey, 2004). Given the articulatory nature of the intervention, tongue movement size was the primary outcome measure and was evaluated in a series of analyses. First, we examined articulatory movements in three baseline sessions to assess the stability of articulatory performance prior to treatment. Second, we examined the effect of a simple verbal cue on tongue movement size before treatment to answer the question whether and to what extent a verbal cue alone resulted in changes in movement size. Third, we evaluated the effect of AVF (+ verbal cue) on tongue movement size during treatment as compared to trials with the verbal cue alone in order to establish the direct effect of AVF on articulatory kinematics. Fourth, the effects of treatment were evaluated via the following analyses: (1) The effect of the cue on trained sentences pre and post treatment was examined to assess if treatment was effective in teaching participants to use the large movement cue; (2) The effect of the cue on the untrained sentences was assessed in order to determine the generalization of cueing from trained to untrained sentences; and (3) The generalization from treatment to untrained (uncued) sentences was assessed to judge whether the “large movement” strategy was habituated to novel sentences. Finally, changes in speech intelligibility for sentences produced with a verbal cue were examined pre-post treatment to address the question of whether increases in tongue movement size corresponded to improvements in speech intelligibility.

We hypothesized that articulatory movements would be stable at baseline. Further, we expected that the response to the verbal cue prior to treatment would be limited, and that AVF (+ verbal cue) would result in a greater increase in tongue movement size during treatment compared to trials with verbal cues alone. Additionally, we hypothesized that individuals with PD would be able to increase their tongue movement size in response to a verbal cue post treatment, and that the effect would generalize to untrained cued sentences as well as uncued sentences. Finally, we hypothesized that increases in tongue movement size in response to a verbal cue would correspond to improvements in speech intelligibility.

4.2 Methods

4.2.1 Ethics

Ethical approval for this project was granted by the University Health Network–Toronto Rehabilitation Institute Research Ethics Board and the Health Sciences Research Ethics Board at the University of Toronto. All participants provided informed written consent before starting the study.

4.2.2 Participants

Five adults, diagnosed with PD and native speakers of English, were recruited from a larger study of speech kinematics and speech intelligibility in individuals with PD (N = 21, Kearney et al., in press). Exclusion criteria were a history of other neurological disorders or conditions affecting speech as well as uncorrected vision impairment and hearing loss. Only participants who exhibited clear evidence of hypokinetic dysarthria with reduced articulatory movement size, based on the original kinematic study, and a speech intelligibility deficit were recruited for the current study. A further exclusion criterion for the current study was enrollment in speech therapy at the time of the study.

Demographic, clinical, and speech characteristics of the participants are provided in Table 4-1. All participants in the study were male, with a mean age of 75.45 years (*SD* = 8.71). On average, participants were diagnosed with PD 3.14 years (*SD* = 1.55) prior to the study, and their Hoehn and Yahr scores were between 1 and 2, indicating a relatively early stage of the disease. Performance on the Montreal Cognitive Assessment (MoCA) indicated an absence of dementia (Nasreddine et al., 2005). All participants reported that they were on medication to alleviate PD-related symptoms, and their medications did not change for the duration of the study. The study sessions were scheduled when the participants felt optimally medicated and at a consistent time in their medication cycle throughout the study.

Previous history of speech therapy was negative in the majority of cases. One participant (PD30) reported previously attending some speech therapy sessions approximately four years before the study but was unable to recall the details of the therapy. All participants reported normal or corrected-to-normal vision. 4/5 had pure tone thresholds of 40dB or better in at least one ear at 1000, 2000, and 4000Hz (Ventry & Weinstein, 1983). One participant (PD25) presented with high-frequency hearing loss bilaterally[1] and wore hearing aids during the screening session; however, he did not wear the hearing aids for the remainder of the study due to potential interference with the electromagnetic recording equipment.

Baseline intelligibility ratings were obtained using a sentence transcription task (Sentence Intelligibility Test; Yorkston, Beukelman, et al., 2007) and a scaled intelligibility task from our previous study (direct magnitude estimation task with modulus; Kearney et al., in press). All participants showed intelligibility impairment at baseline on at least one of the intelligibility measures.

Perceptual characteristics of dysarthria were judged by two speech-language pathologists (SLPs) independently. The SLPs listened to recordings of *My Grandfather* passage by each speaker using headphones (BOSE QuietComfort 15) in a quiet room and identified prominent deviant perceptual characteristics. The SLPs were provided with a list of the most commonly associated perceptual characteristics of hypokinetic dysarthria (Darley et al., 1969a) and were encouraged to

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[1] PD25 was recorded as part of the original kinematic study but his data were excluded from the group analysis. He was included in the current study as the analysis was conducted at the individual level.

record other perceptual characteristics if noted (McRae et al., 2002). The perceptual ratings revealed that all participants presented with articulatory symptoms (e.g., imprecise consonants, change in rate) in addition to phonatory or prosodic symptoms (e.g., monoloudness, reduced stress). Perceptual characteristics identified by both SLPs are indicated in bold in Table 4-1.

ID	Age / Sex	PD Onset (y)	HY	Medication	MoCa	Previous Speech Therapy	Baseline SIT (%)	Baseline Scaled Speech Intelligibility (Z score)	Perceptual Characteristics
PD14	90 / M	5	2	Levodopa	25	None	94.55	-0.77	**Audible inspiration,** short phrases, voice stoppages, intermittent breathy voice, variable rate, monoloudness, monopitch, reduced stress
PD25	73 / M	2	1	Levodopa-carbidopa, pramipexole	30	None	96.36	-1.81	**Monopitch, monoloudness, imprecise consonants,** short rushes of speech, reduced stress, harsh voice, hypernasality
PD27	72 / M	3	1	Levodopa	29	None	96.36	-1.24	**Reduced stress, monopitch, monoloudness,** imprecise consonants, low pitch
PD28	77 / M	0.6	1	Levodopa	28	None	99.09	-1.13	**Increased rate overall, monoloudness, repeated phonemes**/ phrases**,** pitch breaks, breathy voice, short rushes of speech, monopitch, imprecise consonants
PD30	63 / M	4	-	Levodopa, pramipexole	30	4 years prior; details unknown	94.55	-2.14	**Imprecise consonants, repeated phonemes, breathy voice, monopitch, monoloudness,** short rushes of speech, pitch breaks, audible inspiration, increased rate overall, reduced stress

Note. PD = Parkinson's disease; HY = Hoehn and Yahr score; MoCA = Montreal Cognitive Assessment; SIT = Sentence Intelligibility Test; Scaled speech intelligibility scores are expressed as Z scores relative to healthy control speakers from larger study (Kearney et al., in press); Perceptual characteristics in bold were observed by both speech-language pathologists.

Table 4-1. Participant demographic and clinical characteristics.

4.2.3 Instrumentation and Signal Processing

Tongue movements were recorded during assessment and treatment sessions using the Wave Speech Research System (WAVE; Northern Digital Inc., Canada), a 3D electromagnetic tracking system with sub-millimeter accuracy (Berry, 2011). Movement data were used to assess performance, as well as to provide visual feedback during treatment. A 6 degree-of-freedom (DOF) sensor attached to a headband was placed on the forehead, and a 5-DOF sensor was attached to the tongue blade using non-toxic dental glue (PeriAcryl®90, Glustitch). The tongue sensor was placed at midline, approximately 10 millimeters from the tongue tip (mean = 10.26mm, *SD* = 1.54). Movement data were acquired at a sampling rate of 100Hz, and were post-processed to subtract head movement and to filter the data using a median filter (window size = 3) in real time (Haworth, Kearney, Faloutsos, Baljko, & Yunusova, submitted).

To provide visual feedback, tongue movement data during each sentence recording were accessed using the Wave Real Time Application Interface (RTAPI) and transferred to a visualization computer using the Wave proxy server. Visual feedback regarding tongue movement size (see Measurements section below) was provided in a game format using Unity3D v4.6.5p1 game engine technologies (Unity Technologies Inc, 2015). Games were displayed on a 24" 24-bit colour LCD monitor. Participants sat approximately 140cm from the monitor, positioned at eye-level.

Simultaneously, acoustic data were recorded via a lapel microphone (Countryman B3P4FF05B) positioned 15 cm from the participant's mouth and digitized at 22kHz, 16-bit resolution on the hard drive of a computer.

4.2.4 Experimental Design

An ABA single-subject design was used to evaluate the effects of treatment for each participant in the study. Multiple baseline measures were taken during the first 'A' phase to establish the stability of articulatory performance before beginning treatment (Kazdin, 2011) and to evaluate the effect of a verbal cue alone. Additionally, data from the 'B' (treatment) phase was used to examine the effect of AVF on articulatory movements. Finally, measures taken pre and post treatment were used to examine the treatment and generalization effects on articulatory movements and to assess if changes in articulatory movements corresponded to changes in speech intelligibility.

4.2.5 Assessment and Treatment Schedule and Procedures

All assessment and treatment sessions were conducted by the third author, who was not involved in the design of the study or analysis of the data. Figure 4-1 shows a flowchart of the assessment and treatment schedule. Following recruitment, participants attended three baseline assessment sessions, 10 treatment sessions, and a single post-treatment assessment session.

4.2.5.1 Assessment

During the first three baseline sessions, participants read six sentences, repeated four times (uncued: 'Sally sells seven spices', 'Show Shelley the shady shoe shine', 'Take today's tasty tea on the terrace', 'The nightly news is never nice', 'You used the yellow yoyo last year', 'Clever Kim called the cat clinic'). The participants followed the instruction to read the sentences at their 'normal rate and loudness.' The goal of these recordings was to assess the stability of participants' articulatory performance before beginning treatment.

At the third baseline session, a further four sentences were recorded with the goal to assess how participants responded to a verbal cue to 'use large speech movements' (cued: 'Jimmy worked on a crossword puzzle', 'Show Shelley the shady show shine', 'That's my favourite Italian restaurant', 'Clever Kim called the cat clinic'). The cued sentences were first recorded in the habitual style, followed by the cued production. Two of the cued sentences were subsequently trained during treatment, while two remained untrained. Both the uncued and cued stimuli were selected to represent a range of lingual consonants, and both high and low vowels to elicit large articulatory movements. Following treatment, the assessment procedures were identical to the third baseline session in order to evaluate the effects of treatment. All of the assessment stimuli were recorded in the absence of AVF.

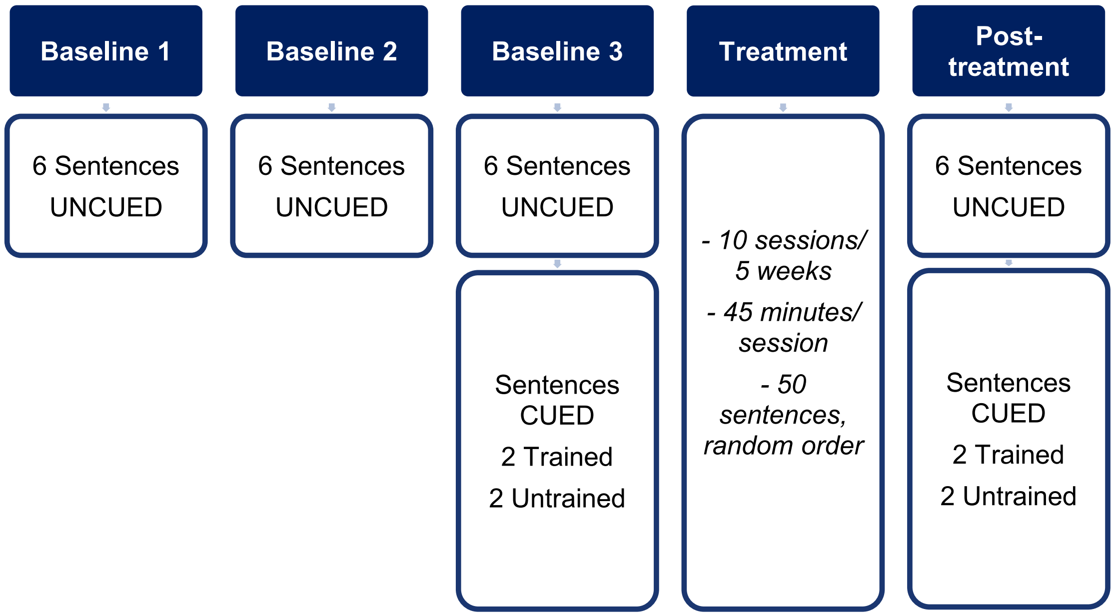

Figure 4-1. Flowchart of the assessment and treatment schedule.

4.2.5.2 Treatment

Treatment began immediately following the third baseline assessment. All sessions were conducted on an individual basis in a speech laboratory. The goal of treatment was to increase AWS of the tongue during sentence production when prompted with a verbal cue.

4.2.5.2.1 Schedule and Stimuli

All participants attended 10 treatment sessions lasting approximately 45 minutes. Median treatment intensity was 1.5 sessions per week (*IQR* = 1.2-1.9). Throughout treatment, 50 functional sentences (five per session) were trained in random order (Appendix B). The range of sentences was used to ensure that the "large movement" strategy was implemented across phonetic contexts and sentence types.

4.2.5.2.2 Protocol

Training of each sentence was conducted in three distinct phases: calibration, acquisition and test phases (Figure 4-2).

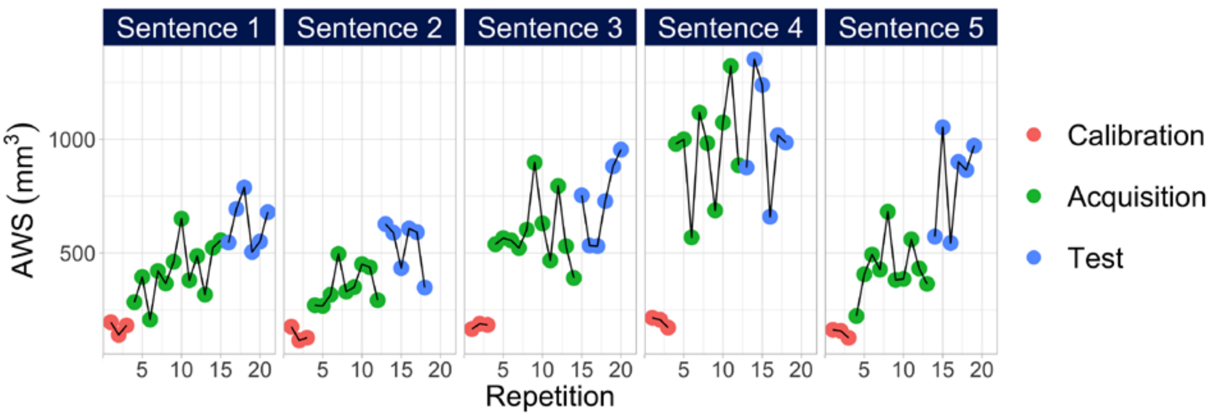

Figure 4-2. Sample data from a single treatment session for one participant (PD30).

The goal of the calibration phase was to set speaker and sentence specific AWS targets for training and to calibrate these targets within the AVF-game space. This phase was necessary due to anatomical differences between speakers and phonetic differences between sentences. To establish the target AWS, participants produced the target sentence three times in their habitual style (uncued) and without AVF.

The acquisition phase aimed to train the participants to expand their articulatory movement relative to the calibration movement size and to sustain this expansion across repetitions. An initial target was specified as a 45% (±10%) increase in AWS from the median of the three calibration productions. Data from our previous pilot study indicated that a 45% increase was a reasonable target for the majority of speakers to attain (Yunusova et al., 2017). Participants were verbally cued to use large tongue movements, and terminal feedback regarding the target and achieved AWSs was provided following each sentence. As such, the feedback corresponded to both knowledge of results (above or below target) and knowledge of performance (magnitude of movement size). Terminal feedback was selected over a real-time display of feedback, as participants were required to read the treatment stimuli from the screen, and paying attention to feedback at the same time would have increased the attentional demands of the task (e.g., O'Shea, Morris, & Iansek, 2002).

Following the initial target set at a 45% increase in AWS, target setting depended on the participant's performance, and adapted based on the running mean of the previous three repetitions: 1) if the running mean was on target, the target level remained the same; 2) if the running mean exceeded the target, the target increased to the running mean (±10%); 3) if the running mean was less than the target, the target decreased by 15% (±10%). These reference values were empirically determined during our previous research (Yunusova et al., 2017). The acquisition phase was complete when participants successfully produced five repetitions of the target AWS. Alternatively, if performance did not stabilize by the 20th repetition, participants automatically progressed to the test phase.

The goal of the test phase was to encourage participants to use the verbal cue without depending on visual feedback. The final target (AWS) setting, obtained in the acquisition phase, was carried forward to the test phase. Participants were cued to use large tongue movements for six repetitions, and feedback was provided on a reduced schedule (50% of trials). Participants selected the three trials to receive visual feedback on, in order to increase motivation and engagement with the learning process (Chiviacowsky, Wulf, Lewthwaite, & Campos, 2012). Performance on the trials that followed the selection of feedback (or no feedback) allowed an evaluation of the effect of AVF on tongue movement size during treatment. Summary feedback regarding performance during the test phase was shown at the end of the phase (e.g., 4/6).

4.2.5.2.3 Visual Feedback During Treatment

Two games that were developed in-house (Haworth, 2016) – one representing a “dragon world” and one a “fish world” – were used on alternating treatment days (Figure 4-3). In the dragon world, the extent of fire breathed by a dragon, corresponding to the AWS of the tongue, was shown as well as the location of a target object to burn. Similarly, in the fish world, a fishing net corresponded to the size of the tongue AWS, and the target was indicated by different types of fish. Each world had five levels, and participants progressed from one level to the next after each session. At the end of each session, a cumulative score from all test phases was shown on a “high score board.” Participants were able to see the scores from all players (anonymized) on the scoreboard.

Figure 4-3. Visual feedback in the form of two video games ("dragon world", "fish world") showed articulatory working space (AWS) of the tongue blade relative to a target AWS.

4.2.6 Speech Intelligibility Rating and Procedures

Five naïve listeners (F = 5; mean age 24.72 ± 4.16) were recruited to rate intelligibility before and after treatment. Given the subjective nature of perceptual ratings, multiple listeners were required to provide an overall estimate of speech intelligibility. All listeners passed a pure-tone hearing screen at 20dB HL for frequencies ranging from 250-8000Hz bilaterally. The listeners were native speakers of English, had at least a high school diploma, and reported no history of speech or language disorders.

The audio recordings were post-processed prior to intelligibility rating using Goldwave Version 6 software (Goldwave Inc, 2015); non-speech high-frequency noise attributed to the WAVE was removed from the signal (high-pass filter at 9800Hz), and the recordings were equated for root mean square amplitude to minimize intelligibility effects due to audibility (Tjaden et al., 2014). The stimuli were then mixed with speech-shaped noise at a signal-to-noise-ratio (SNR) of -5dB (van Engen et al., 2014), in order to avoid a ceiling effect in the data and to create a listening environment that more closely resembles everyday communication situations.

The listeners performed paired-comparison ratings of intelligibility of the two cued-trained sentences from pre and post treatment sessions (Park et al., 2016; Wenke, Theodoros, & Cornwell, 2011). The purpose of this task was to assess if increases in tongue movement size corresponded to improvements in speech intelligibility following treatment. As such, the post-treatment samples were selected based on a minimum increase of 1*SD* in tongue movement size from the pre-treatment mean.

One repetition of each sentence pre and post treatment was randomly selected for each speaker. Each pair of speech samples was presented to listeners in both pre-post and post-pre combinations in random order. Each pair, therefore, was rated twice by each listener. The listeners were required to decide whether the first or second sample of each pair was easier to understand, or if there was no perceptible difference between them (they sounded the same). The task instructions were adapted from previous studies that used paired-comparison ratings of intelligibility (Park et al., 2016; Wenke et al., 2011). The listeners were blinded to the assessment time of the recordings (i.e., pre vs. post). The recordings were presented once through headphones (BOSE QuietComfort 15) in a sound-attenuated booth (Industrial Acoustics Co.) using E-Prime 2.0 experiment software (Psychology Software Tools Inc, 2012). Before completing the experimental task, the listeners practiced rating five pairs of audio recordings that were not part of the current study to ensure that they understood the requirements of the task. As each pair of pre-post speech samples was rated twice by each listener, a total of 100 ratings were obtained (5 speakers x 2 sentences x 2 presentation orders x 5 listeners).

All ratings were assessed for intra-rater reliability using Cohen's kappa and inter-rater reliability using Fleiss' kappa for multiple raters. The reliability coefficients were interpreted using benchmarks proposed by Landis and Koch (1977). The intra-rater reliability analysis revealed kappa (k) coefficients ranging from .62 to .77 (mean = .68, SD = .06), indicating substantial agreement within listeners. The inter-rater reliability analysis showed a k value of .22, indicating a fair agreement between listeners.

4.2.7 Outcome Measures

Two measures were employed in this study to examine tongue movement size and speech intelligibility. Tongue movement size was indexed using a measure of articulatory working space (AWS), indicative of the size of the articulatory movement during an entire sentence. AWS was chosen because, in previous research, it showed sensitivity to disease-related change in individuals with PD (Kearney et al., in press; Weismer et al., 2012) and the effect of training (Yunusova et al., 2017). AWS was calculated as the volume of a convex hull fit to the movement trajectory of each sentence using a MatLab function *convhull*. Figure 4-4 shows an example AWS for a single sentence ('Jimmy worked on a crossword puzzle") produced by PD28 pre and post treatment. The measure is shown in two-dimensional (2D) space for simplification; however, the measurements were conducted in 3D.

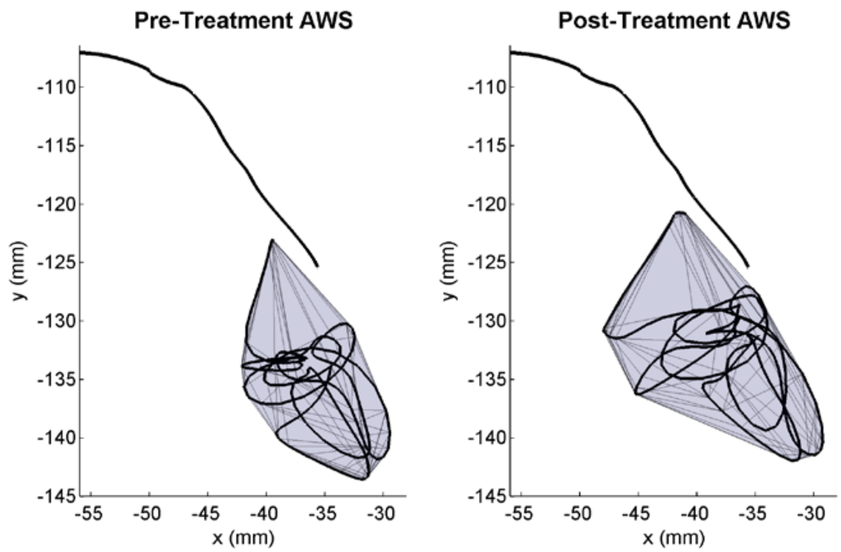

Figure 4-4. Articulatory working space (AWS) of the tongue blade during the sentence ‘Jimmy worked on a crossword puzzle” for a speaker with PD (PD28) pre and post treatment, indicating a 99.1% increase in AWS from pre to post treatment.

Paired-comparison ratings of speech intelligibility were used to assess if participants were easier to understand before or after treatment, or if there was no difference between the two time points. The percentage of ratings categorized as being easier to understand pre or post treatment, or as being the same pre-post treatment, was calculated out of the total number of ratings per speaker (n = 20).

4.2.8 Data Analysis

Visual analysis of the uncued sentences across the three baseline sessions was conducted to assess the stability of articulatory performance (via AWS) prior to treatment. Before obtaining the mean and standard deviations across sentences, AWS data were mean-centered to account for the inherent differences in movement size between sentences. Additionally, effect sizes were calculated to evaluate participants’ response to the verbal cue alone before treatment, compared to the uncued condition. The magnitude of effect was determined using a variation of Cohen’s d statistic, which pools an individual’s standard deviation across conditions ($d2$) (Busk & Serlin, 1992). Currently, there is no empirically established bench-mark for interpreting effect sizes for AWS data. With this limit, effect sizes greater than 1 were interpreted as a clinically significant difference. An effect size greater than 1 indicates that the difference between mean values exceeds the pooled standard deviation (Maas & Farinella, 2012).

Data from the test phase (after acquisition) of the treatment sessions were visually analyzed to assess the effect of AVF on articulatory movements during treatment. Specifically, articulatory performance on the trials that followed feedback was compared to the trials that did not follow feedback. Percent change in AWS was calculated for the feedback and no feedback trials from the calibration (uncued) to test (cued) phase of each sentence. Average percent change values for the feedback and no feedback trials were then computed per session and plotted as time series. The visual analysis was supplemented with the two-standard deviation (2SD) band analysis method (Bloom, 1975; Nourbakhsh & Ottenbacher, 1994).

The magnitude of treatment and generalization effects for AWS data pre-post treatment was determined using effect sizes, as described above. Three effects sizes of interest were calculated pre-post treatment for each participant: (1) cued-trained sentences to assess treatment effect; (2) cued-untrained sentences to assess generalization from trained to untrained sentences; and (3) uncued sentences to assess generalization to habitual speech.

Paired-comparison ratings of speech intelligibility for the cued-trained sentences were examined descriptively. All statistical and graphical analyses were conducted in R version 3.3.2 (R Core Team, 2016).

4.3 Results

4.3.1 Articulatory Working Space

4.3.1.1 Baseline Performance

Figure 4-5 shows mean-centered AWS data across the three baseline sessions for each participant in their habitual style (uncued). Four participants (PD14, PD25, PD28, PD30) were judged to demonstrate a stable AWS measure across sentences prior to treatment. One participant (PD27) showed variable performance, but visual inspection did not suggest either a rising or falling trend. It was noted that when prompted to say the stimuli in his habitual rate and loudness, PD27 “spoke more slowly and deliberately”, which was not representative of his habitual style. Therefore, treatment results for PD27 should be interpreted with caution.

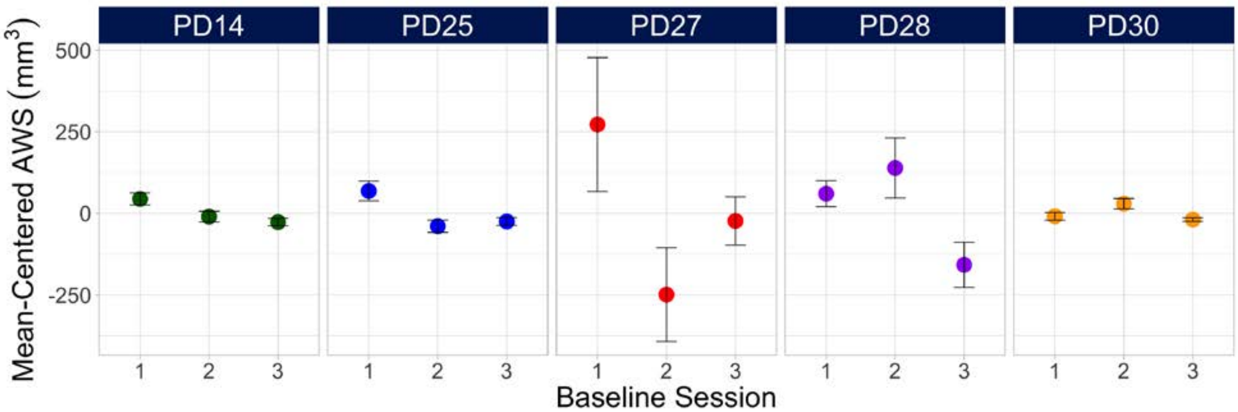

Figure 4-5. Mean and standard deviation of baseline measures of AWS for all uncued stimuli.

Figure 4-6 shows box and whisker plots of participants’ response to a verbal cue alone at baseline, expressed as percent change in AWS relative to their uncued performance. Table 4-2 shows the corresponding effect sizes. One participant (PD25) showed a large and clinically significant effect size in response to the verbal cue alone before treatment. Two participants (PD28, PD30) showed small effect sizes, and two participants (PD14, PD27) had difficulty applying the large movement instruction to their articulatory performance and were unable to increase their AWS.

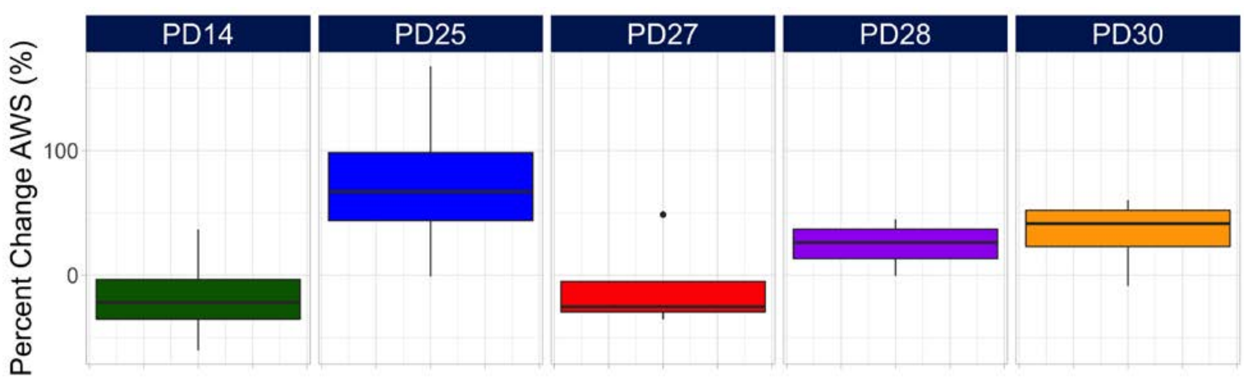

Figure 4-6. Box and whisker plots of percent change in AWS for cued (relative to uncued) stimuli at baseline.

Table 4-2. Baseline effect sizes showing participants' response to the verbal cue alone (uncued-cued).

Participant ID	**Uncued-cued effect size Feedback**
PD14	-0.54
PD25	1.05*
PD27	0.01
PD28	0.44
PD30	0.24

Note. * *d*>1.0, clinically significant difference from uncued-cued.

4.3.1.2 Effect of Augmented Visual Feedback During Treatment

Figure 4-7 shows average percent change in AWS for sentences produced during treatment, with and without visual feedback. A line representing 2*SD* above the pre-treatment mean was added to the time series; two consecutive treatment points above this line indicates a significant improvement in performance.

Four of five participants showed improved performance during the trials following feedback by increasing their AWS to a greater extent than their pre-treatment (cued) levels for at least two consecutive sessions. The same participants also exceeded this threshold for the majority of the sessions (PD14, 6/10 sessions; PD25, 8/10 sessions; PD27, 9/10 sessions; PD30, 10/10 sessions). In comparison, only one participant improved their performance during the trials following no feedback, performing above the threshold for 7/10 sessions (PD27).

The extent of increase in AWS varied considerably across participants, particularly in the feedback condition (Table 4-3). On average, PD28 showed the smallest percent increase in AWS (Feedback, 46%; No feedback, 27%) and PD30 showed the largest percent increase in AWS (Feedback, 770%; No feedback, 83%).

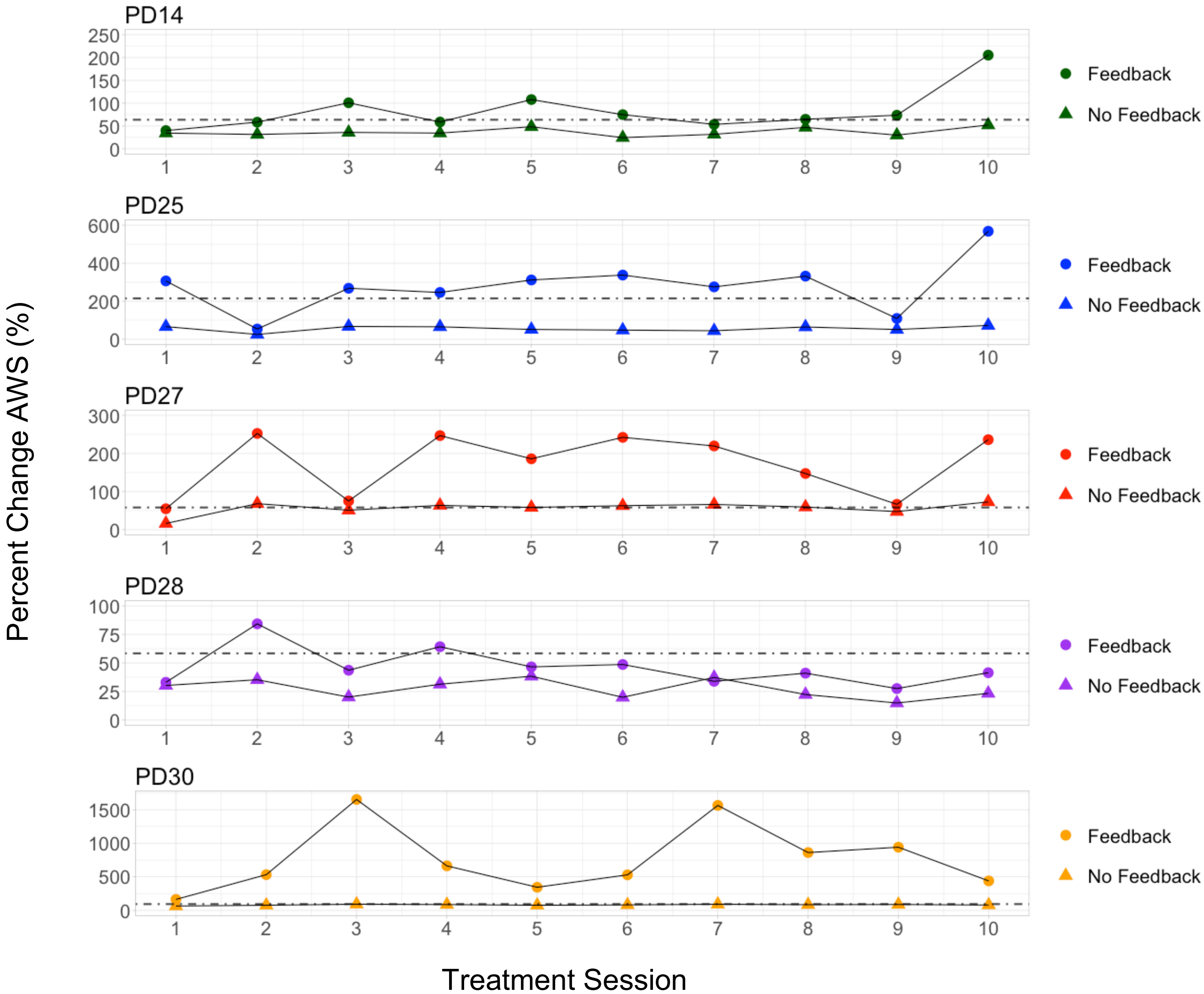

Figure 4-7. Percent change in AWS for cued sentences produced during treatment with and without visual feedback. The dot-dashed line indicates 2*SD* above pre-treatment mean.

Table 4-3. Mean and *SD* of percent change in AWS for cued sentences across treatment sessions with and without visual feedback.

Participant ID	**Percent Change AWS (*SD*)**	
	Feedback	**No Feedback**
PD14	83.84 (47.43)	37.10 (9.02)
PD25	280.95 (138.34)	55.79 (14.28)
PD27	172.83 (80.64)	56.63 (16.10)
PD28	46.46 (16.70)	27.34 (8.25)
PD30	769.55 (498.01)	82.62 (8.21)

4.3.1.3 Treatment Effect

Effect sizes representing change in AWS from pre to post treatment are shown for all participants in Table 4-4. The majority of participants responded to treatment, showing large and clinically significant effect sizes for cued-trained sentences (*n* = 4). Two of five participants generalized the effect of treatment to cued-untrained stimuli. No evidence of generalization to uncued sentences was observed for any participant post treatment.

Table 4-4. Effect sizes pre-post treatment for cued-trained, cued-untrained, and uncued sentences.

Participant		**Pre-post effect size**	
ID	**CUED-trained**	**CUED-untrained**	**UNCUED**
PD14	1.07*	0.28	0.04
PD25	1.13*	-0.53	-0.02
PD27	1.67*	1.26*	-0.33
PD28	0.40	-0.92	-0.45
PD30	1.64*	1.05*	-0.90

Note. * *d*>1.0, clinically significant change from pre-post treatment.

4.3.2 Speech Intelligibility

Table 4-5 shows the percentage of paired-comparison ratings for each participant that were judged as easier to understand pre or post treatment, or as being the same pre-post treatment, for cued-trained sentences. Three participants were rated as being more intelligible pre-treatment when cued to used larger speech movements for the majority of their ratings (PD14, PD25, PD30), in comparison to one participant (PD28) who was rated as being more intelligible post treatment. The final participant (PD27) was rated as being the same between pre and post recordings for the majority of his ratings.

Table 4-5. Percentage of paired-comparison ratings rated as being more intelligible or the same pre and post treatment for cued-trained sentences.

Participant	**Percentage of Ratings**		
ID	**Pre**	**Post**	**Same**
PD14	70	10	20
PD25	75	0	25
PD27	30	30	40
PD28	15	55	30
PD30	50	25	25

4.4 Discussion

4.4.1 Summary of Findings

The present study investigated the effects of using a verbal cue and AVF to treat articulatory hypokinesia in five individuals with PD. At baseline, four of the five participants demonstrated stable articulatory performance measured using AWS. Additionally, at baseline participant responses to the verbal cue to increase speech movements were relatively limited in four out of five patients. The training results revealed a substantial effect of AVF on articulatory kinematics during treatment and showed that AVF was effective in increasing tongue movement size for 4/5 participants beyond their baseline response to a verbal cue alone. Following treatment, 4/5 participants demonstrated an ability to use the verbal cue for trained sentences. Two of these participants successfully generalized the ability to use the cue to untrained sentences. None of the participants, however, applied the strategy to their habitual style of speech, when the verbal cue was removed. Changes in speech intelligibility examined in cued sentences pre and post treatment did not correspond to observed increases in articulatory movement size. Optimal increases in movement size to address articulatory hypokinesia and the speech intelligibility deficit in individuals with PD remain to be identified. These findings are discussed below with respect to the future design of speech therapy in PD and theoretical implications regarding articulatory targets for speech production training.

4.4.2 The Role of AVF in Training Larger Speech Movements

Based on the results of our previous work, the premise of this study was that hypokinesia or smaller movement is a contributing factor to the speech impairment exhibited by the individuals with PD (Kearney et al., in press). We set to evaluate whether and how articulatory movement size can be changed in a therapeutic context and whether this change would have a positive effect on speech intelligibility. Because a verbal cue alone had a limited effect on articulatory kinematics, and monitoring of spatial features is difficult in a clinical setting without the help of instrumentation (Simione et al., 2016), instrumentation-based AVF treatment was employed.

During treatment, AVF was more effective than a verbal cue alone in reducing articulatory hypokinesia. This finding is unsurprising given the reported success of AVF in enhancing motor learning and treatment outcomes for individuals with PD (see reviews, Kearney, Shellikeri, Martino, & Yunusova, submitted; Nieuwboer et al., 2009). AVF may have been particularly important in the current treatment approach because conceptualizing articulatory movement size is not a typical process in normal speech production, and may be even more difficult for patients with PD who experience deficits in sensorimotor integration required for speech (Mollaei et al., 2013). AVF regarding articulatory movement size seemed to facilitate this conceptualization by providing a reference for performance over the course of the treatment. In subsequent trials, the participants were able to apply a corrective response in planning their next movements, which may help to strengthen their feedforward control of movement when AVF is no longer available (Perkell, 2012).

4.4.3 The Effect of Larger Speech Movements on Speech Intelligibility

Although AVF appears to be beneficial in teaching participants to increase their articulatory movements, this increase had varied effects on speech intelligibility, with three participants rated as having better intelligibility before treatment, one after treatment, and one the same pre-post treatment. The reverse patterns observed in the intelligibility and AWS data suggest that the target setting in the current treatment paradigm may not have been optimal. In the present design, as long as patients were able to increase their movement size, the target setting adapted to their performance, with no upper limit set. Therefore, participants may have increased their movement size to the maximum they could achieve within their anatomical constraints, regardless of the effect on the acoustic signal.

Interestingly, the participant with the smallest increase in AWS (PD28) showed improved speech intelligibility post treatment. His average increase in AWS was 36.9% over the course of the treatment. These data suggested that above a certain point, movement increases might result in speech sounding less natural and more difficult to understand and, therefore, movement size needs to be monitored carefully in the context of auditory perceptual effects.

These findings stress the importance of assessing speech intelligibility in treatment studies, which is not a trivial problem (Kent, 1996; Miller, 2013). Here we employed untrained, naive listeners that attempted a global judgement through comparisons of sentence pairs (Park et al., 2016; Wenke et al., 2011). Transcription-based methods by highly trained listeners may show greater sensitivity to sound-specific changes that occur in articulation post treatment (Miller, 2013) and may be more appropriate in the context of treatment studies.

Relating changes in speech intelligibility to underlying changes in physiology has a great importance in treatment research. Without a physiological understanding of how treatments work, we are unable to establish treatment candidacy and properly assess patients' response to therapy.

4.4.4 Generalization of Treatment Effects to Untrained and Uncued Contexts

The goal of treatment in speech disorders is to promote generalization to untrained stimuli and other contexts (Ballard, 2001). Limited generalization in the current study may indicate a need to modify some aspects of the treatment design to enhance motor learning.

A recent systematic review of AVF-based treatments for motor rehabilitation in individuals with PD (Kearney et al., submitted) showed that AVF is most beneficial when gamified, relates to knowledge of performance, is provided in real-time and at a high frequency of delivery. The current design of AVF was based on these recommendations; however, AVF was presented terminally, or immediately after the sentence was executed, due to the visual demands of sentence reading. Real-time feedback may have produced different results (Shea & Wulf, 1999).

A further factor to consider is the treatment schedule and whether 10 sessions over five weeks was a sufficient amount or intensity of practice to facilitate generalization of treatment effects. Previous studies have indicated that individuals with PD experience significant difficulties at the automatization stage of learning and require extended practice to achieve this level of motor skill (Nieuwboer et al., 2009). Treatments targeting loud speech in individuals with PD have established a treatment schedule of 16 sessions over four weeks (Martens et al., 2015; Ramig et al., 1995), which may be required for generalization of effects to occur. Such a schedule would be facilitated by home-based practice. The high hardware and software requirements for the current treatment set-up would make it difficult to implement in a clinic or home setting. Our group, however, are currently investigating the validity of alternative technologies, such as facial tracking, that could be used in the future implementation of this treatment (Bandini, Namasivayam, & Yunusova, 2017).

Finally, motor learning is considered to be specific to the conditions of training (specificity of practice; Proteau, 1992), and this principle of motor learning may explain why none of the participants habituated the "large movement" strategy to uncued sentences following treatment. During treatment, the participants were always cued to use large articulatory movements. As a result, the effect of treatment was observed for cued sentences post treatment, but not for the uncued sentences. Refining the protocol to include practice opportunities without a verbal cue may encourage participants to apply the large movement strategy to their habitual speaking style.

4.4.5 Theoretical Considerations

The targets of speech production have been grossly classified as acoustic or somatosensory, and the importance of both domains has been debated in a number of studies (Perkell et al., 1997; Saltzman & Munhall, 1989) with a current consensus on the importance of both (Houde & Jordan, 1998; Nasir & Ostry, 2008; Tourville, Reilly, & Guenther, 2008; Tremblay et al., 2003). Little attention, however, has been given to targets in the context of speech therapy. There is an expectation that a global auditory target, such as speaking louder, would have an effect on the articulatory domain, serving as a key mechanism behind remediating the speech disorder (Sapir, Spielman, Ramig, Story, & Fox, 2007). Given the underlying sensorimotor disorder in PD, we posited that directly addressing an articulatory goal would improve the execution of articulatory movements and subsequently speech intelligibility. As mentioned above, the results showed a reversed pattern of response – the largest movements appeared to have resulted in worsening of speech intelligibility. The suggestion that an optimal range of movement increase may exist, with regards to effects on speech intelligibility, can be theoretically rooted in the DIVA model of speech production (Guenther, 1995). Guenther (1995) proposed that target ranges exist along which articulatory movements can vary while still producing the same target phoneme. In addition to established target ranges for the production of specific vowels and consonants (Perkell, 1996; Yunusova, Rosenthal, Rudy, Baljko, & Daskalogiannakis, 2012), the current data also suggest that a target range may exist for articulatory movement size at the sentence level. Articulatory movements above or below this range appear to be associated with reduced intelligibility. In the development of an articulatory-expansion treatment, it is now crucial that we establish methods for identifying this range. Examining within-person change in speech movement size with respect to changes in speech intelligibility in a larger sample size may be a plausible way of identifying target ranges for therapy.

4.4.6 Limitations

In addition to the aforementioned limitations (having no upper limit target during treatment and factors regarding treatment design), a few further limitations need to be considered when interpreting the results and designing future treatment studies in this population. First, the assessment of performance during treatment was conducted across different stimuli in every session. In order to compare across sessions, we examined percent change in movement size from uncued to cued productions; however, we were unable to account for phonetic differences across sentences that may have facilitated (or hindered) AWS expansion. For example, sentences that contained a greater number of low vowels may have been more responsive to an increase in movement size, than sentences with primarily high vowels. The same may be true for speech intelligibility, which is often stimulus-specific and may interact with certain combinations of sounds and sound classes. Future studies of this treatment would benefit from the use of probe lists with the same items administered at regular intervals throughout treatment.

Given the small sample size in the current study, the results provide preliminary evidence in support of using AVF to increase tongue movement size; however, the generalizability of findings may be limited. In addition, variability in treatment responsiveness was observed but cannot be fully explained in this very small group of participants. Future studies examining physiological changes in articulation pre-post treatment will require a larger group of participants to generalize findings and delineate factors associated with treatment candidacy.

The modest inter-rater reliability results for the paired-comparison ratings of speech intelligibility may indicate that a clear distinction was not present between pre and post treatment recordings. When samples are relatively homogenous, it is difficult to establish reliability (De Vet, Terwee, Mokkink, & Knol, 2011; Streiner, Norman, & Cairney, 2015), and a consensus may not have been reached across listeners. Some of the listeners commented that the recordings sometimes varied in rate/intonation but that these differences did not make a recording easier to understand. Establishing reliable methods of assessing within-subject change due to treatment is pertinent to understanding the effect of treatment on speech intelligibility, and linking changes in intelligibility to underlying changes in articulatory movements. Transcription-based methods by highly trained listeners may show greater sensitivity to sound-specific changes that occur in articulation post treatment (Miller, 2013).

4.5 Conclusion

Treatment approaches that directly address the articulatory impairment in individuals with PD remain limited. The present study is an initial step in the programmatic evaluation of a movement-based intervention using AVF for speech rehabilitation in individuals with PD. AVF may be particularly beneficial in the early stages of speech therapy in PD to train participants how to increase their articulatory movement size and maintain their articulatory function. Further modifications to target specification, however, are required to optimize the effects of treatment on speech intelligibility.

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Chapter 5
Discussion

5 Overview of Findings

The three studies in this dissertation contribute new and important knowledge to the literature on the articulatory movement disorder in individuals with PD and the treatment of the articulation disorder using AVF. The findings lay the groundwork for expanding evidence-based treatment options for the individuals with PD who experience an articulation disorder and the associated consequences of impaired intelligibility and reduced quality of life. The novel findings of this dissertation are:

1. Jaw movements at the sentence level in individuals with PD are significantly smaller in size, but similar in their average speed, relative to those produced by age-matched control speakers (Chapter 2);
2. Tongue movements at the sentence level in individuals with PD are comparable in size and average speed to normal movements but highly vary across individuals with PD (chapter 2); these movements appear to be smaller at more advanced stages of the speech disorder (chapter 2).
3. Smaller movement size of the jaw, tongue blade, and tongue dorsum in individuals with PD is significantly associated with lower ratings in speech intelligibility, and this association is most consistent across different sentences for the tongue blade (chapter 2);
4. Although speaking styles, such as increasing vocal loudness or clarity, or reducing speaking rate, result in similar patterns of change in articulatory movements for speakers with PD as compared their age-matched peers, the degree of change in movement size is not always comparable between groups. Specifically, increases in movement size of the jaw and tongue blade are significantly smaller for the speakers with PD, relative to the controls (chapter 2);
5. AVF is an effective tool for the rehabilitation of motor skills, such as balance and gait, in individuals with PD and often leads to superior outcomes compared to control groups trained without AVF or without treatment (chapter 3);
6. The design of rehabilitation using AVF can be optimized by providing treatment in large amounts at high intensities, by gamifying feedback, and by presenting feedback that

relates to knowledge of performance, in real-time, and at a high frequency of delivery (100% frequency compared to 33%) (chapter 3);

7. AVF regarding tongue movement size has a positive effect on the size of tongue movements in individuals with PD, compared to a verbal cue alone, in addressing articulatory hypokinesia; however, the effect on speech intelligibility appears varied. Further investigation into the optimal degree of articulatory movement expansion is required to elicit improvements in speech intelligibility (chapter 4).

This chapter compiles the findings across the studies to comprehensively characterize the nature of the articulatory disorder during sentence production in individuals with PD, as well as to identify movement-intelligibility correlates that can be used to guide the development of movement-based interventions in this population. Furthermore, this chapter integrates results to provide support and recommendations for the continued development of motor interventions that use AVF for individuals with PD across a range of motor skills in the speech therapy (e.g., swallowing, speech) and physiotherapy (e.g., gait, balance) domains. Finally, possible limitations of the studies are discussed, and future directions of research are proposed.

5.1 Characterizing Sentence-Level Speech Kinematics in Parkinson's Disease

PD is a movement disorder that affects orofacial musculature. Existing studies reported smaller and slower jaw, lip, and tongue movements (e.g., Forrest et al., 1989; Weismer et al., 2012); yet, studies reporting sentence-level changes and tongue results have been very limited. Notably, only one study, to the best of our knowledge, reported sentence-level kinematics in the jaw (Walsh & Smith, 2012) and studies have rarely considered the relationship between articulatory kinematics and speech intelligibility in the assessment and treatment of the articulatory movement disorder in individuals with PD. In chapter 2, we reduced the existing gaps by assessing sentence-level movements of the jaw and tongue with respect to speech intelligibility. We focused on jaw and tongue movements and omitted the lips because of the limits of our sensor array.

The current findings corroborate a previous report of smaller jaw movement size, but not average speed, at the sentence level in individuals with PD, as reported by Walsh and Smith (2012). This finding may suggest that hypokinesia is a more prominent feature than bradykinesia in the articulatory movement disorder in individuals with PD. A differential response of motor symptoms to medication may help to explain this pattern; in a study of limb movements 'on' and 'off' medication, symptoms of bradykinesia were more responsive to treatment than hypokinesia (Espay et al., 2011). All of the participants in the current study were on medication for the recording, which may have reduced the effect of the disease on movement speed, although not on movement size to the same extent. Additionally, levodopa may have worsening effects on rigidity and associated hypokinesia of the jaw and lips during speech (Chu et al., 2015). However, this statement is purely speculative as the relationship between rigidity and bradykinesia of the oral musculature, and with respect to medication, has not yet been examined.

The lack of group differences for the measures of average speed may have an alternative explanation. In Walsh and Smith's (2012) study showing slow jaw movement in individuals with PD, the calculation of velocity range was based on 80% of points in the velocity trajectory, and may not be directly comparable to the measure of average speed across the whole trajectory in the current study. Further, their participants had similar sentence durations relative to control participants, whereas the smaller movement size in our study coincided with shorter sentence durations, thus allowing for average speeds to be maintained. These differences in durational findings may be explained by the stimuli examined in the two studies. The sentences in Walsh and Smith's (2012) study were relatively long (11 and 17 syllables) and focused on bilabial consonants that required large movements of the jaw. In contrast, our sentences were shorter (7-9 syllables) with a more diverse phonetic composition. Further, while articulatory movements were not slower on average, there may have been subtle changes in the control of movement speed associated with specific sounds/gestures, as reported in the past (Ackermann, Konczak, et al., 1997; Forrest & Weismer, 1995; Forrest et al., 1989) but not captured with the current measure. More investigations of articulatory movement speed in individuals with PD are needed to identify if bradykinesia affects oral articulators, and whether it is associated with a global slowing of movements or a sound/gesture-specific difference in movement speed.

5.2 Differential Impairment of Articulators

Jaw and tongue musculature appeared to be differentially impaired in individuals with PD, with the jaw appearing to be affected to a greater degree than the tongue. The finding of differential impairment of articulators aligns with previous reports at the segmental level that highlighted a greater magnitude of impairment for jaw compared to the lower lip, and tongue dorsum relative to the tongue blade and jaw (Connor et al., 1989; Forrest et al., 1989; Yunusova et al., 2008).

Physiological differences in jaw and tongue musculature have been suggested as a potential explanation of the differential impairment (Forrest et al., 1989). Muscles controlling closing-movement of the jaw contain a large number of muscle spindles, which play a role in detecting changes in position and providing proprioceptive feedback (Cooper, 1960; Kubota & Masegi, 1977). The muscles of the tongue, in comparison to jaw muscles, are not rich in muscle spindles and do not show a clear pattern of stretch reflexes, suggesting that the muscle spindles in the tongue may not respond to sensory information in the same way as the jaw (Anderson, 1956; Cooper, 1960). As the basal ganglia play an important role in proprioception, substantial difficulties controlling jaw movement may be directly related to the proprioceptive deficit in PD (Schneider et al., 1986). It has been suggested that to compensate for difficulties sensing jaw position, the jaw may be held in a fixed position (Forrest et al., 1989), when the tongue may be free to move more extensively. Although the proprioceptive response of muscle spindles in the tongue is unclear (Takayuki, 2015), the non-uniform density of muscle spindles across regions of the tongue – with most observed in the front one-third of the tongue (Cooper, 1953) – may also offer insight into differences between the sensitivity of the tongue blade and tongue dorsum to the articulatory impairment.

There are two possibilities of the evolution of the differential impairment between the jaw and tongue in individuals with PD. The first is that articulatory impairment in PD develops over time, affecting the jaw earlier in the disease, and the tongue during the later stages – an idea that was first proposed in an early observational study by Logemann and colleagues (1978). In our data, smaller jaw movements were observed consistently across speakers with PD, however, tongue movements were only affected in speakers who were rated as having lower speech intelligibility. The opposite pattern (impaired tongue movement with jaw movement within normal range) was not observed in our data, which provides preliminary support for the progression of articulatory impairment over time. An alternative explanation is that sub-groups of patients exist that present with varying clusters of motor speech symptoms; for example, some patients may only experience deficits in their jaw movements, whereas others present with an overall more involved articulatory system. Recently, the issue of heterogeneity in disease presentation and progression has been discussed in motor literature, and studies have identified clusters of patients with distinct neuropathology, for instance, based on tremor-dominant versus akinetic-rigid or mixed presentations (Eggers, Kahraman, Fink, Schmidt, & Timmermann, 2011; van Rooden et al., 2011). Measures of speech in studies of clinical subtyping have typically been captured by speech items on the Unified Parkinson's Disease Rating Scale (UPDRS), which provides limited information relating to the nature of the speech disorder and, as of yet, cannot be used to directly interpret the current findings. Clinical subtypes are likely to share similar pathology and genetics, and if identified, may provide direction for optimal pharmaceutical, surgical, and behavioural treatment strategies in the future (Foltynie et al., 2002; van Rooden et al., 2011). Similarly, identifying patients with greater articulatory involvement would be helpful in determining candidacy for speech treatments aimed at addressing the articulatory disorder in individuals with PD, something that we built on in chapter 4.

5.3 Articulatory Movement-Intelligibility Correlates

Identifying correlates of speech intelligibility decline has been a central focus of dysarthria research in the past number of decades as it underlies the relationship between the speech disorder and its relevance to speech communication. The majority of studies have determined the acoustic correlates of speech intelligibility primarily among measures of vowel formants, their rate of change, and overall extent of the acoustic vowel space (e.g., McRae et al., 2002; Weismer et al., 2001). At the level of speech movement, only two studies examined the association between articulatory movements and speech intelligibility; specifically, for movement size and speed of the lower lip at the segmental level (Forrest et al., 1989), and tongue body movement speed at the passage level (Weismer et al., 2012). Our results in chapter 2 agree that between-speaker variation in speech movements is associated with variations in speech intelligibility; however, the significant associations were detected for movement size across the jaw, tongue blade, and tongue dorsum, rather than for movement speed. Further, the findings were most consistent for the tongue blade when examined across sentences. Establishing movement size-intelligibility correlates provided a rationale for targeting tongue blade movements in speech therapy.

We tested the link between these measures in the context of treatment in chapter 4 but did not observe an expected effect of increasing movement size on intelligibility. A number of factors may explain the effects on speech intelligibility following treatment. First, the adaptive target setting in the game (without an upper limit set) may have encouraged participants to continually increase their articulatory movement size as much as possible within anatomical constraints. The resulting increase in movements was likely beyond a range required to achieve a benefit in intelligibility. Additionally, the central focus of the treatment on speech movements may have reduced the speakers' attention on the resulting acoustic signal. Further, self-monitoring of the resulting acoustic signal may be difficult for individuals with PD who experience deficits in auditory processing (Kwan & Whitehill, 2011), and therefore specific movement targets are needed. These results highlight the need to further examine the limits of speech movement space and the within-speaker association between articulatory movement size and speech intelligibility.

5.4 Stimulus Materials for the Assessment and Treatment of Dysarthria

Developing sensitive assessment materials is essential to the effective assessment and treatment of the articulatory movement disorder in individuals with PD. The idea of certain stimuli being more sensitive to disease-related change in articulation has been discussed before in both the kinematic and acoustic literature regarding patients with dysarthria secondary to PD, amyotrophic lateral sclerosis, and multiple sclerosis (Kim et al., 2009; Rosen et al., 2008; Yunusova et al., 2008). Previous studies have suggested that stimuli requiring larger movement extents and rapid changes in F2 were more sensitive than stimuli requiring smaller movements and slower changes in F2. Our findings in chapter 2 provide additional support for the differential sensitivity of certain sentences to disease-related change in individuals with PD, and contributed novel evidence that the sensitive stimuli can vary by articulator. For example, the sentence requiring largest jaw movement was most sensitive to variation in speech intelligibility, compared to the sentences requiring smaller, finer control of the tongue dorsum. This further illustrates the differential impact PD has on the jaw and tongue articulators, and underlies the need to tailor assessment procedures to capture potential deficits across articulators.

5.5 Dysarthria Treatment for Individuals with Parkinson's Disease

Behavioural treatments remain central to the remediation of dysarthria in patients with PD with the overall aim to improve speech intelligibility and maintain functional communication for as long as possible (Weismer et al., 2012). During treatment, cueing can provide a reference, target, or external trigger for movement generation (Nieuwboer et al., 2007) and can improve movement execution by compensating for deficits in internal cueing in PD (Lim et al., 2005). The use of verbal cues in this dissertation included prompts to speak in different speaking styles and use larger articulatory movements. In chapter 2, we showed that cues to speak louder, with greater clarity, or at a slower rate showed a direct effect on movement size and speed in both healthy controls and patients with PD, and the patterns of change were similar across articulators for both groups. Specifically, speaking loudly was associated with larger, faster movements; speaking clearly was associated with larger movements; and speaking slowly was associated with larger, but slower movements. These findings are consistent with previous research suggesting that individuals with PD can respond to external cues to make adjustments to their speech (e.g., Goberman & Elmer, 2005; Tjaden et al., 2014), and that the varying of speaking styles results in systematic changes in articulatory movements (Darling & Huber, 2011; Dromey, 2000; Goozée et al., 2011; Kleinow et al., 2001). A number of significant interactions between group and condition in the analyses of tongue and jaw movement size, however, indicated that the magnitude of increase for individuals with PD was not always as great as for their healthy peers.

Recent findings by Yunusova and colleagues indicated that speakers with PD who have impaired intelligibility show a low response to verbal cues to speak louder or more clearly (Yunusova et al., 2017). In chapter 4, we attempted to directly cue individuals who presented with a clear articulation deficit to use larger speech movements, and again, the results showed a limited ability to do so prior to treatment. These limited responses to external cues in adjusting articulatory movements may be explained by auditory perception and proprioceptive deficits experienced by individuals with PD (Ho et al., 2000; Konczak et al., 2009). For example, a number of studies have shown that when asked to speak at a louder volume, individuals with PD have difficulty estimating their perceived volume increase compared to healthy controls (Adams et al., 2006; Dromey & Adams, 2000; Ho et al., 2000; Kwan & Whitehill, 2011). Additionally, as previously mentioned, studies have shown that patients with PD have difficulty sensing the position of oral articulators, especially the muscle spindle-rich jaw (Cooper, 1960; Schneider et al., 1986).

Taken together, the findings from chapter 2 and 4 suggest that verbal cueing alone may not be an adequate strategy for some speakers with PD to achieve a range of articulatory motion that is within normal limits. This idea is important when developing criteria for treatment candidacy and identifying patients who require additional strategies to support the remediation of their articulation disorder. Clinical or demographic characteristics in the current studies, however, did not explain why some participants responded better to verbal cues than others. If cueing does not elicit an adequate response – pointing more towards difficulty integrating sensory information – augmented feedback may offer a solution by supplementing an individual's own feedback with additional specific movement information.

The use of AVF in speech therapy appeared to more effectively support individuals with PD in learning how to increase their tongue movement size during speech, compared to cueing alone prior to treatment. This finding suggests that AVF may be useful in complementing the internal auditory and somatosensory feedback that is central to the production of speech (Guenther, 1995), particularly when the internal feedback loops are disrupted due to neurological disorders such as PD. In this way, AVF may help establish compensatory mechanisms to improve speech production, for example, by strengthening the speech motor plan instead of relying on internal feedback.

Results from imaging studies of motor learning in individuals with PD may offer insight into the neural compensation that underlies the (re)acquisition of motor skill in this population. Compared to healthy controls, individuals with PD recruit more neural resources as well as different neural networks during motor learning (Nieuwboer et al., 2009). Particularly, previous studies have reported that patients had four times as much brain activation and show a more prominent bilateral activity than controls (Mentis et al., 2003; Wu & Hallett, 2005). These findings suggest that individuals with PD have the potential for brain plasticity to compensate for neurodegeneration. Establishing effective methods to optimize neural compensation may be key to dysarthria therapy for individuals with PD.

5.6 Treatment Design for Individuals with Parkinson's Disease

In the introduction of this dissertation, we proposed that the use of AVF during motor rehabilitation may be particularly suited to address the difficulties experienced by individuals with PD, including proprioception loss (Konczak et al., 2009), impaired motor learning (Nieuwboer et al., 2009), and reduced motivation (Drui et al., 2014). In chapter 3, we collectively analyzed the results of 20 articles and showed that AVF-based treatments led to improved outcomes following intervention that were often superior to outcomes of traditional rehabilitation and education programs. Additionally, we identified six key treatment design factors that were associated with enhanced outcomes of treatment; namely, large amounts and high intensity of treatment, gamified feedback, knowledge of performance feedback, real-time feedback, and a high-frequency (100%) of feedback. Synthesizing this information was critical to implementing and optimizing a speech therapy program using AVF in chapter 4. Of the six identified factors, we implemented three: we gamified feedback, provided knowledge of performance feedback, and delivered feedback at a high frequency. Subsequently, the post-treatment results indicated that 4/5 participants were able to more effectively use a cue to increase their articulatory movements compared to before treatment, however, limited generalization was observed for untrained sentences or when the verbal cue was removed. The combination of treatment design factors may have played a role in supporting the participants achieve these results. Future iterations of the treatment program, incorporating more of the optimal design factors, may help to support the generalization of treatment results to other stimuli and other contexts.

In the review studies, large amounts (>20 hours) and high intensities (>3 sessions/week) of practice were often facilitated by home-based interventions, allowing for easy and frequent access to the treatment (e.g., Zalecki et al., 2013). For our treatment, a small amount of treatment (i.e., 7.5 hours) was delivered at a low intensity (i.e., 2 sessions/week), as the hardware and software requirements of the set-up necessitated participants to attend therapy on site, and may not have been sufficient to establish automatization of movement patterns. Increasing the amount and intensity of practice may be made feasible by the future implementation of tablet-based technologies, such as facial tracking (Bandini et al., 2017). Such technologies would be useful in examining the effect of variations in treatment schedule on AVF-based speech therapy outcomes.

During speech therapy, terminal feedback was selected over real-time feedback, as patients were required to read target sentences from the screen; paying attention to AVF at the same time would have significantly increased the attentional demands of the task. In contrast, none of the review studies required participants to read from a visual display while practicing motor tasks, which were most commonly related to gait and balance. While our system has been technically developed to provide feedback in real-time (Haworth, 2016), careful consideration needs to be given to the implementation of real-time feedback when participants are required to attend to two different parts of the screen to complete the task.

5.7 Limitations of Studies

When interpreting the results of these studies, a number of limitations need to be considered. First, tongue movements in chapters 2 and 4 were not decoupled from movements of the jaw, and as a result, the findings reflect the contribution of jaw movements to the tongue. Independent assessment of articulators longitudinally is needed to further refine our understanding of the articulatory movement profile in individuals with PD, and to make stronger inferences regarding compensatory mechanisms between articulators and identify potential sub-groups of patients.

Second, we acknowledge that the motor behaviours targeted in the reviewed studies in chapter 3 (i.e., primarily gait and balance) have different neuro-anatomical and physiological underpinnings to motor speech, and findings from non-speech studies may not be directly applicable to speech rehabilitation. Nevertheless, given the lack of comparable evidence in the speech rehabilitation literature, the motor limb literature can offer insights into how to enhance the (re)learning and organization of the speech motor system.

Third, the experimental design in chapter 4 did not include a control condition that would have facilitated the examination of AVF versus no AVF approaches. While the results are suggestive that AVF may be helpful in altering articulatory movements, they do not provide support for the use of AVF over traditional rehabilitation methods. More rigorous studies designed to explicitly elucidate the role of AVF in this treatment are needed.

5.8 Future Research

The findings of these studies generated a number of hypotheses that warrant further investigation to advance our understanding of the articulatory movement disorder in individuals with PD and to extend the evidence base for its rehabilitation.

First, longitudinal investigation of the articulatory movement disorder in patients diagnosed with PD is needed to delineate the nature of the differential impairment between the jaw and tongue. Whether this pattern of impairment is representative of disease progression or different sub-groups of patients cannot be inferred from data corresponding to a single time point. This information would have important implications in determining different patient profiles and identifying optimal individualized treatment strategies for the management of the articulatory movement disorder.

Second, improved articulatory treatment design requires refinement of the target setting as well as the treatment protocol (e.g., treatment schedule, presentation of AVF). Investigating the within-speaker association between articulatory movements and speech intelligibility will allow the identification of specific targets for movement-based interventions. Further, empirical studies examining the effect of treatment design factors in AVF-based speech therapy will help delineate the key “active ingredients” associated with enhanced treatment outcomes. Effective and efficient treatments have the potential to not only benefit our patients but also to reduce the economic impact of the disease on society.

While a central focus of this dissertation was furthering our understanding of the role of hypokinesia underlying the speech movement disorder in individuals with PD, other physiological mechanisms, such as deficits in sensorimotor integration, warrant further study. This dissertation has set out a systematic way of studying underlying mechanisms of speech movement deficits that will guide future work; first identifying an outcome measure that reflects the physiological mechanism; second, studying the association between the measure and speech intelligibility both across and within speakers; and finally, assessing the effect of treatment on the measure. Aligning the underlying mechanism of the disorder with treatment would allow us to develop testable hypotheses regarding the mechanism of treatment action and to identify when treatment is (or is not) working.

Finally, as articulatory treatments are further developed for individuals with PD, a crucial line of research is to identify predictors of treatment success. This investigation will ultimately inform treatment candidacy and match individuals to their optimal treatment program at each stage of the disease.

5.9 Conclusion

Existing speech therapy options for individuals with PD who present with an articulation disorder are currently limited. This dissertation contributes to our understanding of the articulatory movement disorder in individuals with PD and how it relates to their speech intelligibility deficit, thereby laying the groundwork for establishing articulation treatments for this population. Tongue hypokinesia, in particular, is associated with worsening speech intelligibility. We have shown that it may be possible to increase tongue movement size in speech therapy that uses AVF. The effect of treatment on speech intelligibility, however – at least when the movement size target is not precisely specified – may be undesirable.

The results of this dissertation pertain not only to the rehabilitation of the speech movement disorder for individuals with PD but also to the rehabilitation of motor skills more generally. Specific recommendations are made regarding the design of motor rehabilitation programs that use AVF and can be incorporated to enhance the outcomes of treatment for a range of motor impairments associated with PD.

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Appendices

Appendix A. Search strategies by database

Ovid MEDLINE ®.

#	Searches	Results
1	Parkinson disease/	60706
2	(parkinson disease or parkinson* or PD).mp,kw.	155517
3	Feedback, Sensory/	2354
4	sensory feedback.mp,kw.	1668
5	(visual adj5 (feedback or biofeedback)).mp,kw.	4310
6	(visual and knowledge of performance).mp,kw.	24
7	(visual and knowledge of results).mp,kw.	249
8	1 or 2	155517
9	3 or 4 or 5 or 6 or 7	7423
10	8 and 9	183

Ovid MEDLINE ® In-Process and Other Non-Indexed Citations.

#	Searches	Results
1	Parkinson disease/	1084
2	(parkinson disease or parkinson* or PD).mp,kw.	26494
3	Feedback, Sensory/	88
4	sensory feedback.mp,kw.	220
5	(visual adj5 (feedback or biofeedback)).mp,kw.	613
6	(visual and knowledge of performance).mp,kw.	4
7	(visual and knowledge of results).mp,kw.	19
8	1 or 2	26494
9	3 or 4 or 5 or 6 or 7	866
10	8 and 9	26

Embase Classic and Embase

#	Searches	Results
1	Parkinson disease/	128842
2	(parkinson disease or parkinson* or PD).mp.	2258170
3	visual feedback/	2448
4	sensory feedback.mp.	3142
5	(visual adj5 (feedback or biofeedback)).mp.	6168
6	(visual and knowledge of performance).mp.	30
7	(visual and knowledge of results).mp.	146
8	1 or 2	2258170
9	3 or 4 or 5 or 6 or 7	9012
10	8 and 9	357

Cumulative Index to Nursing and Allied Health Literature (CINAHL)

#	Searches	Results
S1	MH ("Parkinson Disease")	14,360
S2	parkinson disease OR parkinson* OR PD	25,246
S3	MH ("Biofeedback")	2,927
S4	sensory feedback	197
S5	(visual n5 (feedback OR biofeedback))	820
S6	visual AND knowledge of performance	58
S7	visual AND knowledge of results	175
S8	S1 OR S2	25,246
S9	S3 OR S4 OR S5 OR S6 OR S7	3,993
S10	S8 AND S9	58

Allied and Complementary Medicine (AMED)

#	Searches	Results
1	Parkinson disease/	1339
2	(parkinson disease or parkinson* or PD).mp.	1745
3	feedback/	370
4	sensory feedback.mp.	80
5	(visual adj5 (feedback or biofeedback)).mp.	292
6	(visual and knowledge of performance).mp.	2
7	(visual and knowledge of results).mp.	13
8	1 or 2	1745
9	3 or 4 or 5 or 6 or 7	674
10	8 and 9	14

PsychINFO

#	Searches	Results
1	Parkinson disease/	0
2	(parkinson disease or parkinson* or PD).mp.	35523
3	visual feedback/	1533
4	sensory feedback.mp.	2158
5	(visual adj5 (feedback or biofeedback)).mp.	3483
6	(visual and knowledge of performance).mp.	25
7	(visual and knowledge of results).mp.	210
8	1 or 2	35523
9	3 or 4 or 5 or 6 or 7	5543
10	8 and 9	82

Cochrane Central Register of Controlled Trials

#	Searches	Results
#1	MeSH descriptor: [Parkinson Disease] explode all trees	2610
#2	"parkinson disease" or parkinson or PD (Word variations have been searched)	35867
#3	MeSH descriptor: [Feedback, Sensory] explode all trees	150
#4	"sensory feedback"	87
#5	"visual" near/5 ("feedback" or "biofeedback")	644
#6	"visual" and "knowledge of performance"	7
#7	"visual" and "knowledge of results"	46
#8	#1 or #2	35867
#9	#3 or #4 or #5 or #6 or #7	818
#10	#8 and #9 In Trials	29

Cochrane Database of Systematic Reviews

#	Searches	Results
#1	MeSH descriptor: [Parkinson Disease] explode all trees	2610
#2	"parkinson disease" or parkinson or PD (Word variations have been searched)	35867
#3	MeSH descriptor: [Feedback, Sensory] explode all trees	150
#4	"sensory feedback"	87
#5	"visual" near/5 ("feedback" or "biofeedback")	644
#6	"visual" and "knowledge of performance"	7
#7	"visual" and "knowledge of results"	46
#8	#1 or #2	35867
#9	#3 or #4 or #5 or #6 or #7	818
#10	#8 and #9 In Cochrane Reviews (Reviews only)	24

Appendix B. Training stimuli

1. The girl wore her hair in two braids
2. The door slammed down on my hand
3. My shoes are blue with yellow stripes
4. The mailbox was bent and broken
5. I found a gold coin on the ground outside
6. The chocolate chip cookies smelled good
7. The church was white and brown
8. I went to the dentist the other day
9. The box was small and wrapped in paper
10. My pen broke and leaked blue ink
11. That guy has been talking forever
12. My daughter made the honour roll
13. I love a hot cup of coffee
14. Did you hear that song on the radio?
15. Don't sit on the broken chair
16. The movie was coming out on videotape
17. He likes cheese and crackers for lunch
18. Could you please pass the jam
19. That's my favourite Italian restaurant
20. Pick me up from the bank at eleven.
21. John planted the tree in the front yard.
22. He scored the winning touchdown
23. Sam loves the smell of fresh bread
24. Do you speak any other languages?
25. The family had their picture taken
26. The subway was running late tonight
27. We should have made a right turn.
28. How much does that chocolate cost?
29. The photographer is in the darkroom
30. He had a talent for writing music

31. She grows flowers in the greenhouse
32. Life in the country is relaxing
33. Jen adopted a new baby kitten
34. Ryan dropped his keys down the grate.
35. Remember to pay rent this month
36. Show me how to change the locks
37. The coat needs a new zipper
38. Luke went to college in England
39. We went on a road trip to Vegas
40. I always need my midnight snack
41. He'll clear the snow with a snow plow
42. Can we stop at the next gas station?
43. Have you seen my new painting?
44. Please don't stop telling me the story
45. Tell the neighbours to turn it down
46. Make a list before you go shopping
47. The plant needs more sun and water
48. Jimmy worked on a crossword puzzle
49. Using chopsticks is a real challenge
50. That was quite a strong argument