PERIORAL BIOMECHANICS, KINEMATICS, AND ELECTROPHYSIOLOGY IN PARKINSON'S DISEASE

BY

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IN PARKINSON'S DISEASE

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Abstract

This investigation quantitatively characterized the orofacial biomechanics, labial kinematics, and associated electromyography (EMG) patterns in individuals with Parkinson's disease (PD) as a function of anti-PD medication state. Passive perioral stiffness, a clinical correlate of rigidity, was sampled using a face-referenced OroSTIFF system in 10 mildly diagnosed PD and 10 age/sex-matched control elderly. Labial movement amplitudes and velocities were evaluated using a 4-dimensional computerized motion capture system. Associated perioral EMG patterns were sampled to examine the characteristics of perioral muscles and compensatory muscular activation patterns during repetitive syllable productions.

This study identified several trends that reflect various characteristics of perioral system differences between PD and control subjects:

1. The presence of high tonic EMG patterns after administration of dopaminergic treatment indicated an up-regulation of the central mechanism, which may serve to regulate orofacial postural control.
2. Multilevel regression modeling showed greater perioral stiffness in PD subjects, confirming the clinical correlate of rigidity in these patients.
3. Similar to the clinical symptoms in the upper and lower limb, a reduction of range of motion (hypokinesia) and velocity (bradykinesia) was evident in the PD orofacial system. Administration of dopaminergic treatment improved hypokinesia and bradykinesia.
4. A significant correlation was found between perioral stiffness and the range of labial movement, indicating these two symptoms may result in part from a common neural substrate.

5. As speech rate increased, PD speakers down-scaled movement amplitude and velocity compared to the control subjects, reflecting a compensatory mechanism to maintain target speech rates.
6. EMG from orbicularis oris inferior (OOI*m*) and depressor labii inferioris (DLI*m*) muscles revealed a limited range of muscle activation level in PD speakers, reflecting the underlying changes in motor unit firing behavior due to basal ganglia dysfunction.

The results of this investigation provided a quantitative description of the perioral stiffness, labial kinematics, and EMG patterns in PD speakers. These findings indicate that perioral stiffness may provide clinicians a quantitative biomechanical correlate to medication response, movement aberrations, and EMG compensatory patterns in PD. The utilization of these objective assessments will be helpful in diagnosing, assessing, and monitoring the progression of PD to examine the efficacy of pharmacological, neurosurgical, and behavioral interventions.

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CHAPTER I: INTRODUCTION

Neurophysiology of Parkinson's disease (PD)

Parkinson's disease (PD) is a progressive degenerative neurological movement disorder affecting more than one million Americans with 40,000 new cases diagnosed each year (Liotti et al., 2003). PD affects approximately 1 percent of the population over the age of 65, and 2 percent of those over 85 (Bennett et al., 1996; Burn, 2000). As the population ages and life expectancies continue to rise, the prevalence and incidence of PD increases. The central pathology of PD is the progressive depletion of the neurotransmitter dopamine in the substantia nigra pars compacta of the basal ganglia circuit, resulting in rigidity, bradykinesia, tremor, postural instability, impoverished gait control and reduced speech intelligibility (DeLong & Wichmann, 2007).

Normal Function of the Basal Ganglia (BG) Circuitry

The primary role of the BG circuit is to control postural adjustments, regulate muscle tone, and assist in the learning, selection, and initiation of movements. The basal ganglia, a group of subcortical nuclei located in the basal telencephalon, consists of four interconnected structures: the striatum (caudate nucleus, putamen, ventral striatum), the subthalamic nucleus (STN), the globus pallidus (internal segment or GPi, and external segment or GPe), and the substantia nigra (pars compacta or SNc, and pars reticulate or SNr) (Mink, 2003), all of which connect directly and indirectly to the cortex via the thalamus. The striatum is the major recipient of input to the BG and serves to modulate the efferent activity of the BG (DeLong, 2000). The striatum receives information from the sensory, motor, and limbic areas of the primary motor and premotor areas, as well as from the thalamus and brainstem. In addition, the striatum projects to

the globus pallidus and substantia nigra structures and transmits information back to the cortex via the thalamus or the cerebellum (Hikosaka, 2007). The globus pallidus and subthalamic nucleus account for the major output projection from the BG and primary efferents from the substantia nigra project to the frontal cortex and striatum (Kandel, Schwartz, & Jessell, 2000). In general, the BG circuit comprises a complex feedback system that originates and returns to the cortex by the following pattern: pallidum-thalamus-cortex, and terminates in the spinal cord (corticospinal tract) or brainstem (corticobulbar tract).

Pathology of Parkinson's disease

PD is a model of the disruption of the BG circuit and demonstrates aberrant patterns of movement such as hypokinesia and bradykinesia, which are commonly observed in hypokinetic dysarthria. The primary cause for the neurodegenerative process associated with PD is the degeneration of dopaminergic neurons of the substantia nigra pars compacta, resulting in a reduced activity in the striatum (DeLong & Wichmann, 2007). This leads to an excessive inhibition in the thalamocortical projection accompanied by a reduced drive to the pedunculopontine nuclei (PPN) in the brainstem. As a result, patients may exhibit tremor at rest, rigidity, akinesia (no movement), bradykinesia (slowness of movement), and postural instability. Two subtypes of PD have been proposed by Iacono et al. (1995): 1) excessive globus pallidus internal outflow to the venterolateral thalamus contributes to hyperkinetic PD (Type A) with symptoms such as tremor, rigidity, and dyskinesia, 2) excessive globus pallidus internal output to the brainstem resulted in akinetic PD (Type B) symptoms with akinesia, frozen gait, postural instability, and stooped posture (Barlow & Hammer, 2008; Barlow, Iacono, Paseman, Biswas, & D'Antonio, 1998).

Speech Motor Control in PD

PD affects both spinal nerve systems involved in limb, gait, and respiratory functions (DeLong, 2000; Solomon & Hixon, 1993), and cranial nerve systems involved in mastication, facial expressions, and speech motor control (Duffy, 2005). Hypokinetic dysarthria (HKD), a motor speech disorder that affects the clarity of speech by reducing mobility of the respiratory, phonatory, resonatory, and articulatory systems is commonly associated with PD. An altered speech rate in PD patients could be caused by an increased rigidity and hypokinesia of the speech production system (Solomon & Hixon, 1993). Clearly, multiple subsystems of speech can be negatively affected by PD, resulting in an overall reduction of speech intelligibility (Sewall, Jiang, & Ford, 2006). HKD affects between 60-90% of patients with PD and generally increases in severity with disease duration (Logemann, Fisher, Boshes, & Blonsky, 1978). The cardinal characteristics associated with HKD are reduced loudness, restricted pitch range, monoloudness, a variable rate which has been attributed to a reduced range of articulatory movements (Darley, Aronson, & Brown, 1969), and a breathy and hoarse voice quality resulting in an overall reduction of speech intelligibility (Ackermann, Hertrich, Daum, Scharf, & Spieker, 1997; Adams & Dykstra, 2008; Darley, Aronson, & Brown, 1975; Fox & Ramig, 1997). Collectively, these disturbances in neuromotor control severely affect patient mobility, speech, and social interaction skills (Nijhawan et al., 2009).

Orofacial Muscular Influence on Speech Production

Rigidity, a clinical correlate of stiffness, has been hypothesized to play a significant role in movement, including the regulation of end-point accuracy, force recruitment, and velocity scaling among articulatory systems for speech production (Gracco, 1994; Shaiman & Gracco, 2002). Measurements of jaw and lip stiffness reinforce the important role of muscle

biomechanics in speech and nonspeech movements. Measurements of jaw stiffness during speech and nonspeech tasks have demonstrated the importance of considering both postural and voluntary control of jaw stiffness in the presence of external loads (Shiller, Houle, & Ostry, 2005). For example, up-regulation of jaw stiffness has been shown to decrease kinematic variability during speech (Shiller, Laboissiere, & Ostry, 2002). Jaw perturbation during speech production indicated that passive properties (stiffness) of the lips and jaw could contribute as a compensatory mechanism for accomplishing speech tasks (Gomi, Honda, Ito, & Murano, 2002; Ito, Gomi, & Honda, 2000). Precise regulation of lip stiffness is essential for accurate production of fricative sounds such as [f] and [v] (Ito, Gomi, & Honda, 2004). Stiffness regulation appears to play a central role for speech motor learning and adaptation (Tremblay, Houle, & Ostry, 2008).

Central Mechanism of Stiffness in PD

Stiffness in the musculoskeletal system is defined as the resistance to an imposed stretch, due in part, to the inherent mechanical properties of muscle fibers, connective tissue, and tonic innervations from descending pathways (Struppler, 1993). Healthy muscle systems have an internal stiffness representation in the brain, which relays in the ventroposterolateral (VPL) and ventroposteromedial (VPm) nuclei of the thalamus, primary somatosensory and motor cortices, and lateral hemispheres of the cerebellum in order to achieve predictive motor control. Because stiffness can be modulated by peripheral (i.e., Golgi tendon organs, mechanoreceptors, muscle spindles) and central neural systems (i.e., basal ganglia circuitry, sensorimotor cortex, and cerebellum), impairments in central regulatory mechanisms of tonic descending inputs can alter muscle stiffness and affect coordination. An increase in centrally-mediated tonic drive on lower motor neurons yields an increase in muscle stiffness, which clinically is identified as “muscular

rigidity" in PD. The clinical characteristic of PD rigidity is often described as lead pipe by patients, such that the resistance to prevent a movement is independent of the velocity of the movement (Burke, Hagbarth, & Wallin, 1977).

The precise mechanism of PD rigidity is unclear. The classic explanation of stiffness in PD includes increased gamma motor drive to muscle spindles (Burke, Andrews, & Lance, 1972; Dietrichson, 1971; Rushworth, 1964) and loss of recurrent inhibition (Magladery, 1964). However, there is no evidence of any malformation in the gamma motor drive. Burke (1977) found that hyperactivity of the gamma motor drive (also known as fusimotor system) also exists in healthy adults using vibratory stimulation, without elicit rigidity. The mechanism and significance of the gamma motor control on the muscles innervated by the cranial nerves are still open to debate. The mechanism underlying muscle stiffness is complex since the muscle system of the face, which does not have muscle spindles, also manifests rigidity and impairment in motor control. For instance, Leanderson, et al.(1972) reported that hypertonic EMG activities in the labial levator depressor muscles of PD patients were similar to rigidity in the limbs. This hypertonic EMG activity reduced after administration of Levodopa (Leanderson, Meyerson, & Persson, 1971). Therefore, hyperactivity of the fusimotor system does not appear to explain the main cause of PD rigidity.

Another hypothesis suggests that co-activation of antagonistic muscle groups during movement reflects the rigidity and restricted structural movement (Burke, et al., 1977). Studies of limb motor control in individuals with PD suggest that these individuals exhibit movement with an overall reduction in amplitude and velocity in addition to difficulty in planning and initiating movements (Morris, Iansek, Matyas, & Summers, 1994; Viviani, Burkhard, Chiuve, Corradi-Dell'Acqua, & Vindras, 2009; Weiss, Stelmach, & Hefter, 1997). A key feature of the

PD limb system is the impairment in rate and range of motion during voluntary and automatic movements, mainly due to excessive contraction of antagonistic muscle groups (Burke, et al., 1977). For example, movement of the arm is impaired in rate and range of motion in reaching an object if both bicep and tricep muscle groups co-contract simultaneously. Such rigidity and hypokinesia are also present in respiratory (Solomon & Hixon, 1993), laryngeal (Barlow & Abbs, 1986), and supralaryngeal (Hunker, Abbs, & Barlow, 1982) musculature of speech motor subsystems, resulting in diminished speech intelligibility (Forrest & Weismer, 1995).

Orofacial Muscular Influence on PD Speech Production

Perioral stiffness was found to be positively correlated with electromyography activity levels (EMG) in select muscles of the lower face and inversely related to the magnitude of lip movement during speech, thereby providing some evidence for a relationship between facial rigidity and labial hypokinesia (Hunker, Abbs, & Barlow, 1982). The excessive muscle rigidity observed in PD patients may lead to a limited excursion of articulators, resulting in movements that are slow and reduced in amplitude.

Most of the previous works in measuring limb and jaw stiffness have focused on active stiffness sampled during dynamic motor tasks. In order to determine the differences between active and passive (i.e., non-participatory) perioral stiffness, Müller and colleagues (1985) sampled perioral span-tension and force-velocity relations over a displacement of 20 mm imposed horizontally and tangential to the oral angle. A perpendicular orientation of the displacement and load sensitive transducers was found to be a significant main effect in order to facilitate sampling and more accurately reflect force vectors and soft-tissue properties of this complex muscle system. A follow-up study derived active and passive stiffness coefficients by sampling perioral force over a displacement range spanning 25–70 mm using an interangle

actuator (Barlow & Müller, 1991). Gender was a significant main effect for active force. Using a digitally-controlled linear servo motor to produce a lateral tangential stretch of the oral angle, a highly significant positive relation was observed between perioral stiffness and imposed displacement in female (Seibel & Barlow, 2007) and male (Chu, Barlow, & Lee, 2009) adults.

Although biomechanical studies of limb rigidity have provided valuable insight into the neural regulation of locomotor and movement disorders (Sepehri et al., 2007), similar applications to the orofacial system have been tenuous primarily due to inadequate methods of transduction of the perioral muscle complex. Given that impairments in the central regulatory mechanisms of tonic descending inputs in PD alter muscle stiffness (Leanderson, Persson, & Öhman, 1969) and result in abnormal patterns of speech movement coordination, measures of stiffness for the orofacial system are woefully needed in order to produce a more complete picture of the effects of stiffness in PD speech. Therefore, this study primarily focused on the hypokinetic aspect of parkinsonian dysarthria.

Kinematic Analyses of Speech Production in PD

Kinematic studies demonstrate that individuals with PD manifest reduced movement amplitude (hypokinesia) and velocity (bradykinesia) during speech production. Such limitations on range and velocity of movement have been identified as common features of PD limb movements and speech articulator movements. Using the x-ray microbeam, Hirose and colleagues (1981) suggested that the limb and speech motor control deficits in PD may have a common substrate. When asked to produce syllables, the pattern of hypokinetic movements of the lower lip of PD subjects was similar to the hypokinesia and festination of the legs during walking. One study documented articulatory movements of the jaw, lower lip, tongue blade, and tongue dorsum during the production of vowels in PD and amyotrophic lateral sclerosis (ALS)

patients using an x-ray microbeam and demonstrated that tongue movements in PD and ALS speakers differed from normal controls, particularly along the dimension of increased movement duration (Yunusova, Weismer, Westbury, & Lindstrom, 2008). More specifically, PD groups tended to take a much longer time to move their tongues the same distance as to the normal controls. However, these authors caution that the results might not be generalized to speech movements of other sounds in different phonetic contexts or populations due to limited speech samples.

Changes in the function of the lips and jaw have been observed in studies of individuals with PD. Lower lip movements of individuals with PD were reduced in amplitude and velocity (Caligiuri, 1987; Forrest & Weismer, 1995; Forrest, Weismer, & Turner, 1989). Similar to the lip movement, jaw movement during speech also demonstrated reduced amplitude and velocity in individuals with PD when compared to healthy controls (Connor, Abbs, Cole, & Gracco, 1989; Forrest, et al., 1989). Upon analysis of each articulator, the greatest difference between individuals with PD and healthy controls was observed in the jaw, with PD speakers using a relatively "fixed" jaw position during speech production (Forrest, et al., 1989).

Other studies reported that PD speakers showed decreased labial amplitude displacement (Hunker, et al., 1982), decreased labial velocities (Hirose, et al., 1981), and incomplete labial closures during diadochokinetics (DDK) tasks (Ackermann, Hertrich, & Hehr, 1995). These findings contradict the clinical observation of an abnormally fast speech rate in PD. They also demonstrate that the reduction in range of movement may be attributed to rigidity and hypokinesia of the articulatory muscles. If articulator-movement limitations exist in the PD speakers due to increased rigidity, are the kinematic variables associated with its production different for PD and neurologically normal speakers? Studies of limb movement show such

kinematic deviations for PD subjects when they accurately produced gestures. PD subjects could hit a target position, but did so in irregular steps toward the required position (Flowers, 1976). In other investigations, PD speakers were able to maintain an appropriate scaling between movement amplitude and velocity during syllable (Connor, et al., 1989; Forrest & Weismer, 1995) and sentence (Forrest, et al., 1989) productions.

Deficits in the timing, coordination, and mobility of articulators may affect intelligibility in speech production. Even though the characteristics of speech impairment in individuals with PD have been described previously, the kinematic bases for these changes have been rarely investigated. More comprehensive kinematic studies are needed to better understand the relations between muscle rigidity and speech characteristics in individuals with PD. In the present investigation, discrete movement parameters (peak amplitudes and velocity) associated with upper lip (UL) and lower lip+jaw (LL+J) movement during alternating speech rates for the syllable "pa" were evaluated.

The "scaling of movement" hypothesis

Neurophysiological (Turner & Anderson, 1997) and brain imaging studies (Turner, Desmurget, Grethe, Crutcher, & Grafton, 2003; Turner, Grafton, Votaw, Delong, & Hoffman, 1998) provide evidence that basal ganglia play an important role in the control of amplitude and velocity of voluntary movements. Several hypotheses have been proposed concerning the role of basal ganglia in motor control. One such theory, "scaling of movement" proposed by DeLong (1990) posits that interactions in the direct/indirect pathway determine the output of movement (i.e., increased or decreased in amplitude or velocity). Wichmann & DeLong (1996) further explored the theory and showed that scaling of movement can be achieved by a combination of inhibition of the GPi/SNr neurons via the direct pathway and excitation of these output cells via

the indirect pathway in the basal ganglia circuit. Increased activity in the direct pathway (or decreased activity in the indirect pathway) causes decreased inhibition from Gpi/SNr projection to the motor thalamus, resulting in active movement. In contrast, increased activity in the indirect pathway (or decreased activity in the direct pathway) increased inhibition to the motor thalamus, resulting in active movement that is decreased. The balance between these two pathways would modulate the amount of disinhibition of thalamocortical neurons, providing a mechanism by which the movement (in amplitude and velocity) can be scaled. In the event of PD, it is still debated, whether the motor control problem is because of under-scaling of the central motor commands (Berardelli, Rothwell, Thompson, & Hallett, 2001), the inability of the neuromuscular system to adapt quickly to the required force level (Weiss, et al., 1997), or the inability of the muscular system to react due to high stiffness (Ostry, Keller, & Parush, 1983).

Because of the critical role of BG in movement control, it is reasonable to suspect that BG dysfunction associated with PD may have a significant impact on speech kinematic parameters. When examining velocity patterns of the lower limb in a reaching task, neuronal activity in the BG increases as reaching speed increase, indicating a parallel relation between increases in velocity and BG activation (Desmurget, Grafton, Vindras, Grea, & Turner, 2003; Turner, et al., 1998). Scaling of velocity for specific movement amplitude is a problem for individuals with PD which resulted in bradykinesia, a generalized slowness of movement (Marsden, 1990). The BG motor circuit may be preferentially involved in controlling and/or scaling the dynamics of arm movements (Turner, et al., 1998). Because of dopamine's role in the modulation of limb movements, it is also believed that similar planning properties may exist in both limb and speech movements.

Electrophysiological studies have shown reduced pre-movement or readiness potentials in the SMA of PD patients when performing automatic movements, thus resulting in deficient scaling of amplitude over the entire movement sequence. This idea of insufficiency in generating appropriate extent has been demonstrated in PD gait and hand writing (McLennan, Nakano, Tyler, & Schwab, 1972). Because speech and limbs are highly reliant on fronto-striatal mechanisms and are highly practiced complex motor skills, one would expect articulator motor control would show similar hypokinesia patterns as in PD gait and hand writing.

Because of physiological differences associated with the disease, PD speakers may aim to control different parameters of movement from those controlled by the normal speaker. In this experiment, changes in amplitude displacement and velocity were monitored as a function of speech rates in a sequence of consonant-vowel (CV) syllables. The focus of this study was to examine how the PD speakers alter kinematic parameters, particularly amplitude and velocity movements associated with UL and LL+J. If neurological impairments, such as PD, affect the control of kinematic variables critical to a movement sequence, we would expect that such a disruption should be evidenced in LL+J movement since this is the primary articulator involved in the production of an utterance.

Motor Equivalence of Speech Production in PD

Motor equivalence is conceptualized as the ability of the speech production mechanism to make a variety of different vocal configurations while achieving the same acoustic output (Ladefoged, 1983). Hughes and Abbs (1976) defined motor equivalence as a coordination strategy by which the speech production mechanism achieved the "same end-product with considerable variation in the individual components [upper lip, lower lip, and jaw] that contribute to that output" (p.199). In another study, Perkell and colleagues (1993) reported that

normal speakers varied their lip and tongue movements in order to achieve an acoustic equivalent for the vowel [u].

A reduction of articulatory movement coordination in PD speakers has been reported (Weismer, Yunusova, & Westbury, 2003). Specifically, PD speakers showed a reduced measure of F2 extent (index of articulatory change across the vowel) in the vowel [u], indicating a reduction in vocal tract change across the vowel. Another study found that PD speakers showed significantly reduced measures of F1 and F2 transition rates (ΔHz/duration), indicating that PD speakers have a reduced ability to coordinate articulatory movement for syllable production. Since PD speakers appear to have a reduced capacity for motor equivalence, one may hypothesize that increases in speech rate will exacerbate end point accuracy for lips, jaw, and tongue. Forrest, et al. (1989) suggested that PD speakers adopted a control strategy to limit their jaw movements during speech production with increases in speaking rate. Another study has shown that PD speakers can increase lower lip movement as a means to compensate for reductions in movement by other articulators (Connor, et al., 1989).

Speech hastening, or a rapid shift from one rate to another rate, is an articulatory compensatory mechanism associated with PD (Ackermann, et al., 1997). Speech hastening is contradicted by what is expected in slowed motor movements associated with bradykinesia in PD. For example, in a syllable repetition task, a PD subject exhibited a rapid shift in repetition rate from 4 to 8 Hz when cued to produce at a 5 Hz rate. However, this was at the expense of hypokinesia or incomplete lower lip movements, reduced velocity, and general articulatory undershoot as speech rate increased (Ackermann, et al., 1997). To produce speech, the neural system must generate signals to control muscle activity. There is no muscular insufficiency preventing individuals with PD from speaking with larger lip and jaw movements and/or at a

louder volume when cued to increase vocal intensity (Sadagopan & Huber, 2007). However, no study has addressed the speech motor control compensatory strategy by manipulating speech rates in individuals with PD. In this present investigation, it was hypothesized that individuals with PD will show significant reduction in displacement and velocity in the UL and LL+J as speech rates change.

Speaking Rate in PD

The ability to adaptively generate equivalent motor actions that produce the same outcomes (motor equivalence) is important for preserving speech intelligibility and speaking rates (Hertrich & Ackermann, 2000; Hughes & Abbs, 1976). Intelligible speech is produced through the precise control over articulatory displacement, velocity, and movement duration. Speaking rates have been shown to be an important variable influencing amplitude, velocity and duration of the labial movement (Caligiuri & Abbs, 1985). Changes in speech rates involve marked changes in relative timing, muscle recruitment patterns, and orofacial muscle stiffness (Müller & MacLeod, 1982; Ostry & Munhall, 1985).

Because the basal ganglia is responsible for regulating temporospatial parameter at the motor cortex, the rate of speech in PD patients is often perceived differently from those of healthy speakers (Brown & Marsden, 1998; Goberman, 2005). Perceptual studies have found mixed findings in which some perceived speakers with PD to have a normal rate of speech while others were perceived as having slower or faster than normal speech rates. For example, individuals with PD have demonstrated a faster articulatory rate when producing phrases or reading passages at a habitual and/or fast rate (McRae, Tjaden, & Schoonings, 2002). In another study, Skodda and Schlegal (2008) found that PD patients demonstrated an accelerated rate with a significant reduction in the total number of pauses resulting in an impairment of timing

organization and speech rhythm. However, Caligiuri (1989) reported that PD patients were able to produce normal syllabic rates and found a reduction of the range of movements with faster rates of diadochokinetics (DDK). In general, individuals with PD are perceptually determined to have a slower rate of speech resulting from the associated bradykinesia. PD patients showed abnormal pause deficits with shorter speech duration and a greater time-per-pause, mainly due to the patient's inability to initiate articulatory movements efficiently (Hammen & Yorkston, 1996).

Due to inherent biomechanical limitations, articulators must reorganize their coordination patterns in order to achieve adequate system output for an increased rate of speech. In order to maintain speech intelligibility, the speaking rate can be modulated through changes in movement displacement and speed. The speaking rate will increase with either decreases in displacement or increases in speed. If speech intelligibility decreases during faster speaking rates, then speaking rate reductions may be implemented as a compensatory strategy to maintain speech intelligibility. In other words, individuals with PD may slow down their speaking rates in order for articulators to reach the speech targets. Kinematic studies may provide evidence to reveal the underlying mechanisms that affect the speaking rate in individuals with PD.

Kinematic studies have shown that healthy controls manipulate their speaking rates by altering movement speeds and the displacements of articulators (Smith & Kleinow, 2000). In most cases, speakers reduce their articulators' displacements and increase velocity in order to speak faster, indicating that in addition to timing reorganization for faster speech, muscle commands are reorganized to increase force of movements. In patients with PD, however, lip movements become more hypokinetic as speech rates increase providing evidence that reduced articulatory movements play a significant role in the perception of HKD (Caligiuri, 1989). The reduction of articulatory movement amplitude observed in PD may reflect a compensatory

mechanism to maintain normal syllabic rates. Rapid shifting from one rate to another rate is another compensatory mechanisms associated with PD speech (Ackermann, et al., 1997), which contradicts what is expected in slowed motor movements associated with bradykinesia. These articulatory abnormalities critically impose a negative effect on speech intelligibility. Therefore, it is important to learn how combinations of movements contribute to the overall outcome of modified speech rates and to learn which control variables lead to the most predictable performance in PD, so that intervention can be planned on the basis of how the speech mechanism typically responds to rate changes.

It is unclear which kinematic variables differ for PD compared to neurologically normal speakers during the production of different speech rate, and how these variables change with medication states. Investigating how articulation changes is an important area of study for clinical reasons because it is possible that one type of cue may result in articulatory patterns more similar to that of normal speakers. In this experiment, presenting different metronome rates to monitor speech production in PD and control groups provided us with information to examine at which speech rates PD group breakdown occurred during speech production. In addition, information about compensatory strategies used by the PD group during speech production was derived. Knowing the speech rates at which PD group breakdown and the possible compensatory skills they utilize during speech production could assist clinicians to plan for speech intervention.

Variability of Speech Production in PD

The variability of speech movements has been used as an indicator of speech skills in children and an indicator of neuromotor control in individuals with speech motor disorders. In the current study, the spatiotemporal index (STI), a composite measure of spatial and temporal

variability in articulatory movement sequence was employed to assess the stability of speech movements across multiple repetitions of syllables and sentences during rate manipulations. A high STI reflects a more variable pattern of movements, while a lower STI reflects a more stable pattern of movements (Smith, Goffman, Zelaznik, Ying, & McGillem, 1995). Variability in adults and motor speech disorder populations are often attributed to the loss of motor control and the breakdown of the articulatory system (Smith, 2006; Walsh, 2007; Wohlert & Smith, 1998). For example, previous work on speakers with dysarthria secondary to traumatic brain injury (TBI) has shown that STI values increase with speech severity and speaking rate decline (McHenry, 2003).

Using STI measurements, individuals with PD demonstrated less stable trial-to-trial articulatory movement patterns compared to young healthy adults (Kleinow, Smith, & Ramig, 2001). Specifically, speech production at a slow rate was associated with the most variability and the normalized movement pattern for the loud condition resembled that of habitual speech. This showed that changes in speech motor performance resulting from rate and intensity manipulations may document neuromotor correlates of behavioral management for motor speech disorders. Individuals with PD are able to recruit an existing coordinative organization that is highly stable despite the increase in amplitude of movement associated with loud productions. Given that current findings reported that healthy young adults increased variability and decreased articulatory stability with sentences varying in complexity and length (Kleinow & Smith, 2006; Maner, Smith, & Grayson, 2000), it is possible that individuals with articulatory impairment, like PD, may be affected to an even greater degree. Individuals with PD may need an adaptable system in order to compensate for progressive motor control declines associated with PD.

Previous studies of speech movements in PD have demonstrated mixed results in speech kinematic parameters such as displacement amplitude and velocity. These studies generally utilized non-words, syllables, or word-level production tasks. Based on perceptual assessments, individuals with PD are often able to produce accurate speech at the single-word level and breakdowns in articulatory precision are more likely to occur on longer words and phrases (Weismer, Jeng, Laures, Kent, & Kent, 2001). Given that breakdowns in speech production are likely to occur in longer utterances (Yorkston & Beukelman, 1980), it is important to examine the kinematics of speech movements using more natural, phrase-sentence level utterances. Therefore, this study included both syllables and sentences to further examine the changes of speech movements in PD. Specifically, this study focused on the stability of repeated speech movements.

Electrophysiological Analyses of Speech Production in PD

Damage to the basal ganglia circuit results in hypoactivation of the motor structures within the circuit and hyperactivation of additional motor cortical areas. Abnormal activation of cortex was observed in PD patients during paragraph reading, with overactivation in the orofacial motor cortex, the inferior lateral premotor cortex, and the supplementary motor area (SMA) (Liotti et al., 2003). Similar results were also reported in an fMRI study, in which mild-moderate PD subjects exhibited increased activation of the orofacial motor cortex while reading full sentences (Rektorova, Barrett, Mikl, Rektor, & Paus, 2007). An increased activation in the lateral cortical motor areas during speech and nonspeech tasks in PD patients may represent an attempt at compensation for inadequate involvement of motor areas due to decreased input from the basal ganglia (Brown & Marsden, 1998; Caviness, Liss, Adler, & Evidente, 2006). Taken together, this additional recruitment of the cortical areas has been hypothesized as a

compensatory mechanism for improving motor movement or may reflect the pathophysiology of PD.

Investigation of the perioral muscle activity comparing the amplitude of EMG signals in older and younger healthy subjects found that older subjects exhibited increased EMG amplitudes compared to those of younger women, reflecting that more motor units may be active to compensate for less effective contraction of muscle fibers (Wohlert, 1996). Increased amplitude of EMG signals in healthy controls correlated strongly with the rates of speech, suggesting a continuum of neuromotor drive from slow to fast speech (Wohlert & Hammen, 2000). In the event of BG dysfunction associated with PD, the inability of the motor cortex to receive accurate information may result in erroneous scaling, selection and sequencing of muscle synergists required for movement. Such abnormal levels of synergist muscle activity have been reported in the perioral system (Hunker, et al., 1982; Leanderson, et al., 1972).

Hypokinetic patterns in PD can be related to deterioration in the reciprocal adjustment of the antagonistic muscles. Recordings of the EMG activities from several facial muscles in individuals with PD during labial sound production showed that there were persistent EMG discharges, indicating the loss of reciprocal patterns between the antagonistic muscle pairs (Leanderson, et al., 1972; Leanderson, et al., 1969). Due to the basal ganglia dysfunction, antagonistic muscle pairs appear to co-contract simultaneously in people with PD, leading to articulatory undershoot and the perception of increased speaking rate (Netsell, Daniel, & Celesia, 1975). This coactivation pattern of antagonistic muscle groups can be effectively reduced by administration of Levodopa (Leanderson, et al., 1971), and EMG visual feedback (Netsell & Cleeland, 1973).

Descending inputs that affect motoneuron discharge are of particular interest to understanding dysarthria, as this disorder is associated with anomalies in the central neural coding and motoneuron activity. Motor control processes of speech involve tonic and phasic inputs that converge on motoneurons (Humphrey & Reed, 1983; Moore, Smith, & Ringel, 1988) and interact with the biomechanical characteristics of speech structures (Gracco, 1994). These abnormal converging inputs to motoneurons innervating the orofacial muscles affect the efficient transition of the articulators' muscles for rapid and accurate speech production in PD patients. In the present investigation, we addressed the nature of how the central nervous system regulates muscle activation for speech as it is produced at varying rates through analysis of lip muscle activation and movement during repetition of CV syllables.

There are limited studies on the EMG correlates of speech kinematic (i.e., amplitude, duration, velocity) changes. At least three mechanisms may contribute to variations in movement velocity, including modulation of motor unit firing rates, motor unit recruitment, and regulation of muscle stiffness (McClean & Clay, 1995). The regulation of stiffness could change the mechanical properties of orofacial tissue and thereby alter the effects of phasic muscle activity (Müller & MacLeod, 1982). It is unknown how perioral phasic EMG activity changes as speech rates increase in PD.

The mechanism underlying speech rate changes must operate through the neural circuitry that controls the overall pattern of muscle activity for speech production. A study in cat locomotion suggests that a change in neural circuitry is selectively modulated, resulting in differences in functional linkages and activation patterns of different muscles (Smith, Chung, & Zernicke, 1993). This study indicates that the patterns and relative activation levels of different leg muscles vary in a relatively continuous manner until the gait changes from a walk to a trot, or

a trot to a gallop. During speech production, speech rate changes might involve marked changes in relative timing and muscle recruitment patterns.

As work on biomechanical modeling of the speech motor system progresses, we should make stronger inferences about muscle activation pattern underlying speech motor control from analysis of kinematic parameters. Inspection of the perioral movement and EMG is useful to understand the potential relation between rigidity, hypokinesia, and muscle activation patterns as the EMG signal reflects the recruitment and firing rate changes of motoneurons. Studies of EMG patterns in jaw muscles and perioral muscles during chewing (Steeve, Moore, Green, Reilly, & Ruark McMurtrey, 2008), nonspeech movement (Moore, et al., 1988), and speech production (Leanderson, et al., 1969) have shown a basic pattern of reciprocity among antagonistic muscles. HKD associated with PD can be related to deterioration in the reciprocity activity of the antagonistic muscles (Leanderson et al., 1972). Measures of perioral reciprocity EMG activities corresponding to speech tasks could provide a clearer picture of neuromotor dynamics and motor speech scaling patterns in PD patients.

Medical Treatment: Effects of Dopaminergic Treatments on PD Speech

Historically, pharmacological intervention using Levodopa represents the most efficacious treatment for alleviating motor symptoms in PD (Bertoni, Prendes, & Sprenkle, 2001; Suchowersky, 2002). While the responsiveness of limb motor systems to Levodopa has been widely studied, the corticobulbar speech system has received less attention. In general, the effect of dopaminergic stimulation on overall speech parameters and speech intelligibility in PD remains inconclusive. Some authors have reported improvements across the speech parameters following Levodopa administration while others found no effect of dopaminergic treatment on speech. Perceptual analyses of speech have documented improvements in articulation, pitch

variation, voice quality (Wolfe, Garvin, Bacon, & Waldrop, 1975), tongue strength and endurance (De Letter, Santens, & Van Borsel, 2003), and speech intelligibility (De Letter, Santens, De Bodt et al., 2007; De Letter, Santens, & Van Borsel, 2003; De Letter, Vantens, & Van Borsel, 2005) following Levodopa administration. Significant increases in muscle activation of the lips (De Letter, et al., 2003; Nakano, Zubick, & Tyler, 1973; Sandyk & Brennan, 1982) and mandible (Svensson, Henningson, & Karlsson, 1993) have been reported in kinematic studies utilizing electromyography (EMG) after Levodopa administration. In an EMG study of labial muscles, Leanderson et al. (1971) reported that tonic hyperactivity of labial muscles decreased after medication, suggesting that Levodopa normalized the neuromuscular system of labial muscle activity. This re-establishment of labial reciprocal inhibition muscle activity patterns may also contribute to the improvement of HKD in 6 out of 7 patients.

Conversely, Levodopa therapy has been documented to cause no improvement or a worsening of speech symptoms in patients with PD. In one study, De Letter et al. (2006) found no effects of Levodopa therapy on speech rate during a standardized reading task and an increased variability of speech rate during medication on state. This increased variability may be the consequence of respiratory deficits due to Levodopa-induced dyskinesia or an increase of dysfluencies. Perceptual analysis of speech performance in patients with PD has documented no significant improvement on articulation (Skodda, Visser, & Schlegel, 2010), fluency (Ackermann & Ziegler, 1991; Hughes, Daniel, Kilford, & Lees, 1992), and phonation (Plowman-Prine et al., 2009) after Levodopa administration.

Specific Aims

Hypokinetic dysarthria (HKD) is characterized by excessive rigidity of agonist and antagonist muscle groups, resulting in a decreased rate and range of movement of the articulator

structures (hypokinesia) (Yunusova, Weismer, Westbury, & Lindstrom, 2008). Despite the fact that more than 80% of PD patients exhibit HKD, the effects of orofacial rigidity (stiffness) and coordination of articulators are not well understood. Clearer understanding of the link between orofacial biomechanics-kinematics associated with PD and the underlying physiology is limited by the dearth of research on labial kinematics and the associated muscle rigidity in this population. Earlier studies of speech production in PD using perceptual, acoustic, and kinematic analyses have yielded mixed findings regarding the characteristics of articulatory movements underlying the speech disorder, whereby some studies reported reduced articulatory output and others revealed normal orofacial movement parameters for speech. Further difficulties include that limited studies measured the orofacial stiffness and the associated muscle activity when investigating labial kinematics. A systematic way of examining the relation between perioral stiffness and kinematics of PD speech production is needed to investigate if orofacial stiffness causes hypokinesia, in this population.

Inspection of perioral movement and electromyography activity levels (EMG) is useful in understanding the potential relation between rigidity and hypokinesia. Whenever there were abnormal levels in the stiffness of perioral system, there was also increased EMG activity at rest in PD speakers (Leanderson, et al., 1969). Increased background activity and disturbed reciprocal activation of the perioral muscles have been reported to alter normal coordination for speech in individuals with PD (Leanderson, et al., 1971, 1972). However, in these studies, rigidity was inferred from EMG, and observed movement patterns were not quantified. In a later study, Hunker and colleagues (1982) found that perioral stiffness was positively correlated with EMG in select muscles of the lower face and inversely related to the magnitude of lip movement during speech, thereby providing some evidence for a relationship between facial rigidity and

perioral hypokinesia. This finding suggests that antagonistic muscle groups were activated simultaneously, resulting in reduced movement of the lips. This reduced range of lip movement contributes to the hypokinesia observed in the PD orofacial system. To our knowledge, no study has attempted to replicate or validate this early work. By measuring the perioral stiffness, speech movements, and perioral EMG, it is possible to further examine a cause-effect relationship between the degree of perioral muscle stiffness and reductions in the range of movement.

The perioral muscles, because of their special role in speech movements, could provide some significant insights into the hypothesized causal relationship between muscle rigidity and hypokinesia. Therefore, this study examined the relation between perioral stiffness and coordination of articulators in individuals with PD using a combination of biomechanical, kinematic, and electrophysiological approaches.

The major objective of this study was to provide an integrative description of select kinematic parameters of speech and to determine the predictive relation between perioral stiffness on lip kinematics during speech, and associated perioral muscle activation (EMG) in individuals with PD as a function of anti-PD medication state. To achieve this goal, the specific aims of this study were threefold:

1) To assess the relation between non-participatory lip stiffness and the associated root mean square (RMS) of perioral EMG as a function of pharmacological states (i.e., ON vs. OFF) among individuals with PD, and a secondary comparison to healthy age- and sex-matched controls. It was hypothesized that an increase in perioral stiffness would be associated with increased RMS EMG among orbicularis oris superior (OOS*m*) and orbicularis oris inferior (OOI*m*) muscle recording sites, being proportionately greater in the OFF state.

2) To determine the relation between perioral stiffness and the properties of lip kinematics (amplitude, velocity) during speech produced at 3 speaking rates in individuals with PD during ON and OFF pharmacological states. These measures were compared to perioral stiffness functions, and a secondary comparison to healthy age- and sex-matched controls. It was hypothesized that labial kinematics (amplitude, velocity) will scale abnormally as speech rate is increased, presumably due to rigidity. Further dissolution in kinematic scale was expected between ON and OFF pharmacological states.
3) To examine the characteristics of perioral muscle reciprocity between an antagonistic muscle pair (orbicularis oris inferior and depressor labii inferioris) involved in lower lip closure/opening during bilabial syllable production at three rates. Muscle reciprocity, expressed as polar-phase notations, was examined in relation to perioral stiffness in PD during ON and OFF pharmacological states. These quantitative measures were compared to reciprocity functions obtained from healthy age- and sex-matched controls. It was hypothesized that the PD group will show decreased reciprocity EMG between OOS*m* and DLI*m*, and OOI*m* and DLI*m* muscle recording sites.

Salient Measures

Three measures were utilized to examine the relation between perioral stiffness and lip movements during speech in individuals with PD during ON and OFF pharmacological states. The perioral stiffness coefficients examined the orofacial biomechanics system and labial kinematics measurements provided an estimate of individual articulators' movement patterns as

a function of speech rates. In addition, electromyography reflects the muscle activation patterns as speaking rate changes.

Perioral Stiffness Coefficients ($\Delta F/\Delta X$) were derived by measuring the changes in force (ΔF) as a function of imposed interangle displacement (ΔX) in real-time providing a quantitative and sensitive measure that correlates with rigidity. To ensure the non-participation nature of the sampling, the RMS of the orbicularis oris superior (OOS*m*) and orbicularis oris inferior (OOI*m*) EMG signal were measured at each of the five perioral stretches.

Labial kinematics reflects the coordination between articulators, individual articulator movement patterns, and utilization of compensatory strategies for speech. Amplitude and velocity of the upper lip and lower lip (plus jaw) were examined to understand how speech rate affects articulator patterns. The speech rates were paced with an external metronome. During the speech tasks, an increase in velocity or a displacement reduction strategy could be used to shorten the movement durations to match the metronome paces. These are important parameters given that PD patients frequently manifest problems in scaling the dynamics for lips movement during speech production.

Electromyography (EMG) reflects the motor unit action potentials generated by alpha motoneurons within the facial nucleus. HKD associated with PD can be related to deterioration in the reciprocity activity of the antagonistic muscles (Leanderson et al., 1972). Inspection of the perioral movement and EMG is useful to understand the potential relation between rigidity, hypokinesia, and muscle activation patterns. Measures of perioral reciprocity EMG recording sites during speech production could provide information about the interarticulatory coordination between muscles and a clearer picture of neuromotor dynamics and motor speech scaling patterns in PD patients.

CHAPTER II: RESEARCH DESIGN AND METHODS

Participants

A total of twenty elderly adults were included in this study. Ten individuals with Parkinson's disease ($MEAN_{age}$ = 69 years (SD=10.38), $RANGE_{age}$ = 46 - 81 years, N female= 4, N male=6) and 10 neurologically normal adults ($MEAN_{age}$ = 70 years (SD=8.93), $RANGE_{age}$ = 57- 82 years) were tested. Table 1 shows the descriptive profiles for all participants. Both control and PD groups did not differ in terms of age, gender, level of education, weight, height, head-circumference, nasion-inion, and lip resting span. Profiles for the PD participants are given in Table 2.

Table 1. Descriptive profiles for all participants

Variable	All *N* (%) / *M* (*SD*)	Control *N* (%) / *M* (*SD*)	PD *N* (%) / *M* (*SD*)	χ^2 / *t*	*p*
	N = 20	*N* = 10	*N* = 10		
Age (year)	69.99 (9.43)	70.18 (8.93)	69.80 (10.38)	0.0897	0.93
Gender					
Male	12 (60%)	6 (60%)	6 (60%)	0.3501	1.00
Female	8 (40%)	4 (40%)	4 (40%)		
Education (year)	17.60 (3.5600)	18.90 (3.51)	16.30 (3.27)	1.7144	0.10
Weight (lb)	175.99 (33.58)	176.10 (28.63)	175.88 (39.50)	0.0143	0.99
Height (cm)	170.22 (11.22)	170.88 (10.89)	169.56 (12.08)	0.2566	0.80
Head circumference (cm)	56.90 (1.77)	57.02 (2.03)	56.77 (1.56)	0.3141	0.76
Naison-inion (cm)	38.10 (1.89)	37.47 (1.72)	38.7350 (1.92)	-1.5596	0.14
Lip resting (mm)	51.54 (4.36)	50.70 (4.74)	52.37 (4.00)	-0.8532	0.40
Post diagnosis (year)	N/A	N/A	6.40 (5.58)	N/A	N/A
Hoehn & Yahr score	N/A	N/A	2.30 (0.92)	N/A	N/A
UPDRS score	N/A	N/A	18.90 (3.51)	N/A	N/A

Table 2. Demographics of PD participants

Participant	Sex	Age	Years post Diagnosis	Hoehn & Yahr Stage	UPDRS	Medication	Dysarthria[1]
PD1	F	74	7	2.00	12	C-dopa/L-dopa	Normal
PD2	F	71	7	3.00	39	C-dopa/L-dopa	Normal
PD3	M	67	21	4.50	55	C-dopa/L-dopa Entacapone	Mild
PD4	F	75	6	1.00	19	C-dopa/L-dopa	Mild
PD5	M	65	3	2.00	28	C-dopa/L-dopa Pramipexole	Mild
PD6	M	81	2	2.00	44	C-dopa/L-dopa	Mild-Moderate
PD7	M	61	3	2.00	45	C-dopa/L-dopa Pramipexole	Mild-Moderate
PD8	M	72	5	2.50	69	C-dopa/L-dopa Selegiline	Mild
PD9	F	81	8	2.00	54	C-dopa/L-dopa	Normal
PD10	M	46	2	2.00	38	C-dopa/L-dopa Pramipexole	Normal

[1] Dysarthria severity was judged by 4 speech judges. Speech judges scored a speech survey (Appendix A) during the orthographic transcription of SIT speech recordings.

Participants with PD were recruited from a local PD support group and had been referred by a board-certified neurologist at the University of Kansas Medical Center Movement Disorder Clinic in the Department of Neurology. Inclusion in the present study was limited to individuals with PD defined clinically by the presence of two out of three cardinal motor symptoms (i.e., tremor, rigidity, bradykinesia) and positive response to Levodopa. Other inclusion criteria included: no known history of neurological disease other than PD, no known history of any neuropsychiatric disorder, no known history of speech disorder, and normal/corrected visual acuity. "OFF" medication recordings were conducted the morning after the patients were withdrawn from medications overnight (12+hours). "ON" mediation recordings were taken

approximately 60 minutes after administration of patients' standard Levodopa dose. All PD participants were under the Sinemet (Carbidopa-Levodopa) prescription at the point of the testing. Hoehn & Yahr (1967) scaling system was used to assess the severity of PD. The Hoehn and Yahr scale is a commonly used system for describing how the symptoms of PD progress. The scale allocates stages from 0 (mild) to 5 (severe) to indicate the relative level of disability.

In addition, 10 healthy age/sex matched adults were recruited with the assistance of the KU Biobehavioral Neurosciences in Communication Disorders (BNCD) subject recruitment database and by word of mouth. Inclusion in the control group was limited to individuals who were in general good health, had normal/corrected visual acuity, no history of speech disorder, neurological or psychiatric disease. The exclusion criteria for both PD and control groups included the presence of cerebellar signs, any history of stroke, transient ischemic attacks, and/or neurological diseases including brain tumors, dementia, and surgery of the head and/or neck. All participants were native speakers of American English. All participants were tested in one session at the Communication Neuroscience Laboratory located at the KU Wakarusa Research Facility, Lawrence. Each participant completed a written informed consent in compliance with the University of Kansas (KU) Human Subjects Internal Review Board (Protocol # 18368).

Protocol

Appendix B lists the pure-tone hearing screening threshold level for each participant at 500, 1000, 2000, and 4000 Hz. The hearing screening was measured to ensure that all participants were able to hear the external metronome pace presented through a headphone. All recruited participants completed the standardized Speech Intelligibility Test [CD] (Yorkston, Beukelman, & Hakel, 1996) to assess their speech intelligibility. Participants were instructed to read a series of 11-sentences (~5 minutes) while being recorded by a tape recorder. This

recorded speech allowed estimation of the subject's speech intelligibility level based on an orthographic transcription of perceived speech by four student listeners. The Speech Intelligibility Test (SIT) was completed to describe the speech intelligibility and speech rate of speakers with PD and controls during sentence productions. The perceptual scoring of the SIT and the calculated speech rate provide descriptive speech characteristics of these patients. Figure 1 illustrates the individual speech intelligibility scores of speakers with PD. The black solid line represents the mean of the control speakers and the dashed lines represent one standard deviation of the control group's mean.

Figure 2 displays the individual speaking rates of speakers with PD. The black solid line represents the mean of the control speakers and the dashed lines represent one standard deviation of the control group's mean. The performance patterns of speakers with PD and controls in speech intelligibility and speaking rate were similar.

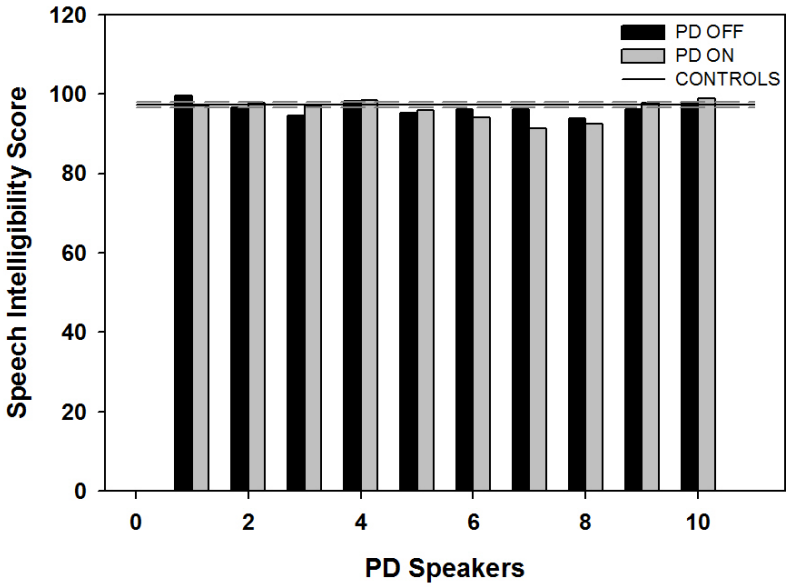

Figure 1. Speech intelligibility scores for speakers with PD and controls.

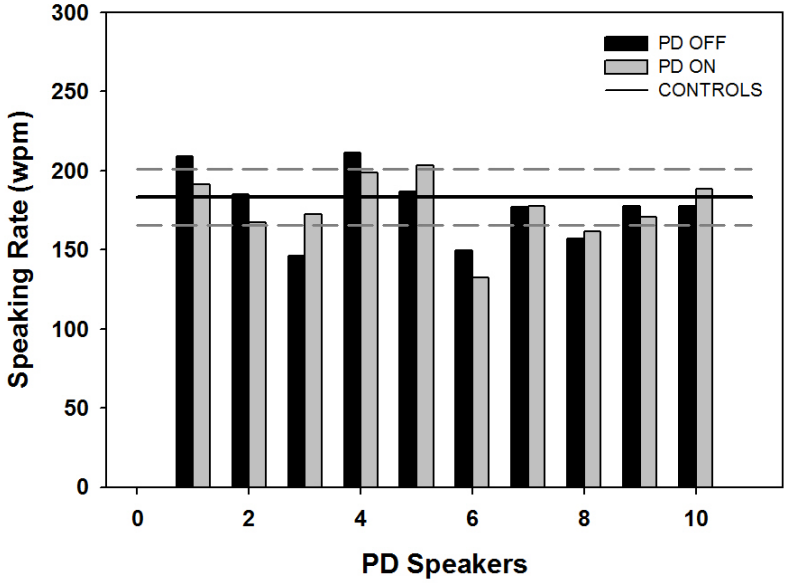

Figure 2. Speaking rates for speakers with PD and controls.

All testing was completed in one session (Figure 3). Subjects participated in two relatively brief, single session experiments. The first experiment (~15 minutes) involved the measurement of facial stiffness using a new instrument and software system which was designed in our laboratory. The second experimental procedure (~15 minutes) involved motion capture of orofacial movements using a 4-D infrared digital camera tracking system to map speech movements and electrophysiology (surface EMG) in real-time. PD subjects were tested under two conditions of their drug cycles: "Medication ON (MED ON)" and "Medication OFF (MED OFF)". Each PD subject arrived at the laboratory in the morning (8AM) after withholding their previous medication intake twelve hours prior to the testing. Once they finished the initial round of tests in the OFF condition (by 9AM), they took their prescribed medications with a drink, and we repeated the testing one hour later when they are ON. This testing procedure was recommended by the CAPSIT protocol for assessing the effect of intervention therapies in PD (Defer, Widner, Marie, Remy, & Levivier, 1999). Subsequently, this testing lasted for

approximately three hours for each PD subject. On the other hand, it took approximately one hour for the healthy control subjects to complete the study.

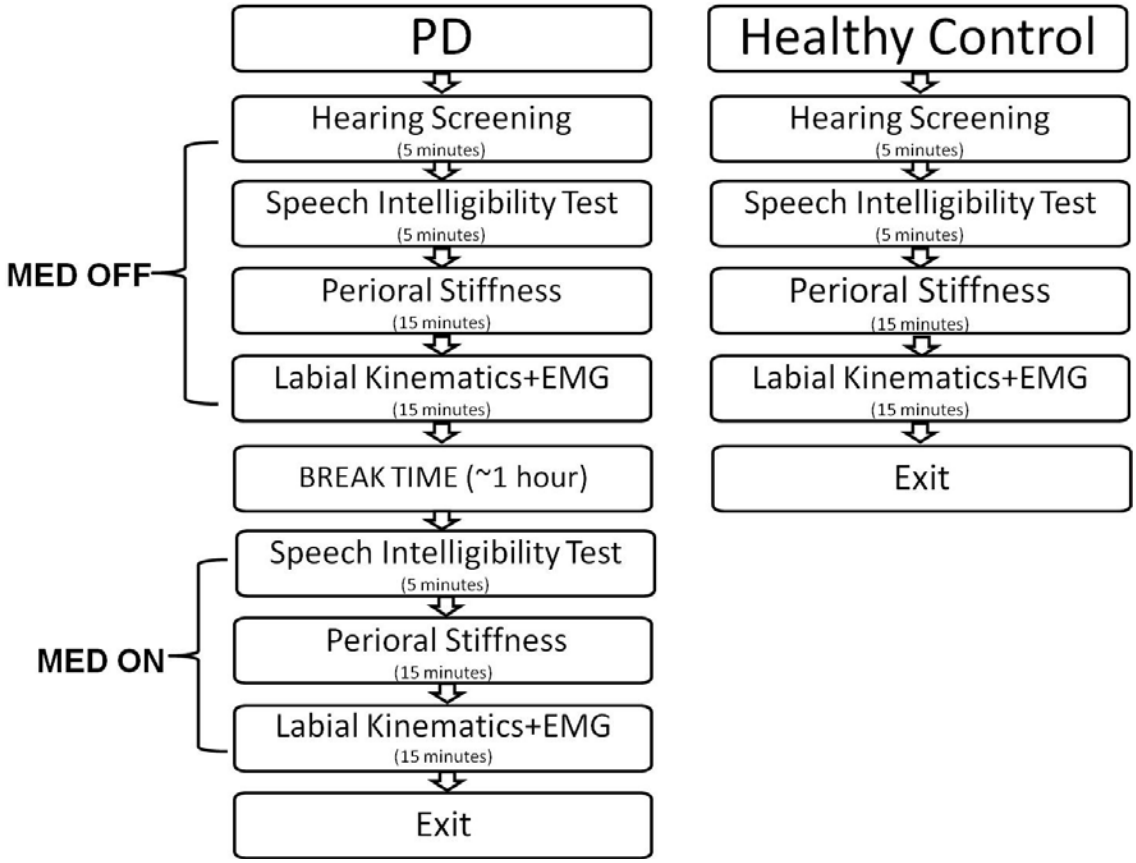

Figure 3. Participants' experimental procedures.

Equipment and Digital Signal Processing

1. Perioral Stiffness Sampling

1.1. Face-referenced OroSTIFF *device*

The perioral stiffness was quantified using a face-referenced OroSTIFF device that was developed at the Communication Neuroscience Laboratories (University of Kansas, Lawrence, KS). The face-referenced OroSTIFF device was built with thin wall tubular stainless steel (mass = 40.7gm) and was coupled bilaterally to the oral angles via lip saddles and supported on the

mental symphysis with a double-adhesive tape collar for vertical stabilization (Figure 4). This device incorporates a microminiature pneumatic glass-cylinder actuator instrumented for pressure (Honeywell #26PCCFAG +/- 15psi) and integrates in parallel with a subminiature differential variable reluctance transformer (S-DVRT, MicroStrain®, Inc) to encode lip aperture. A 30- gauge blunt cannula, vented to atmosphere, was coupled in parallel with the pneumatic system (Figure 5). This cannula provided a constant resistive load upon which the perioral recoil force would produce a measurable pressure drop as a function of displacement. The pneumatic actuator was manually pressurized with a 10-cc syringe, which in turn imposed an interangle stretch of 20 mm. The interangle oral aperture at rest provided an estimate of resting muscle length (L_0) and was measured with a digital caliper for each subject. The OroSTIFF interangle span was initialized to [L_0 + 15 mm] for all subjects. A series of 5 interangle stretch trials were completed while simultaneously sampling force, displacement, and electromyograms from bipolar electrodes placed on the OOS*m* and OOI*m* in real-time with custom software (OroSTIFF v.3.0.4) written in LabVIEW™ 8.0. Individual interangle stretch trials were completed within 10 seconds, and the entire stiffness protocol was completed within 5 minutes for each participant.

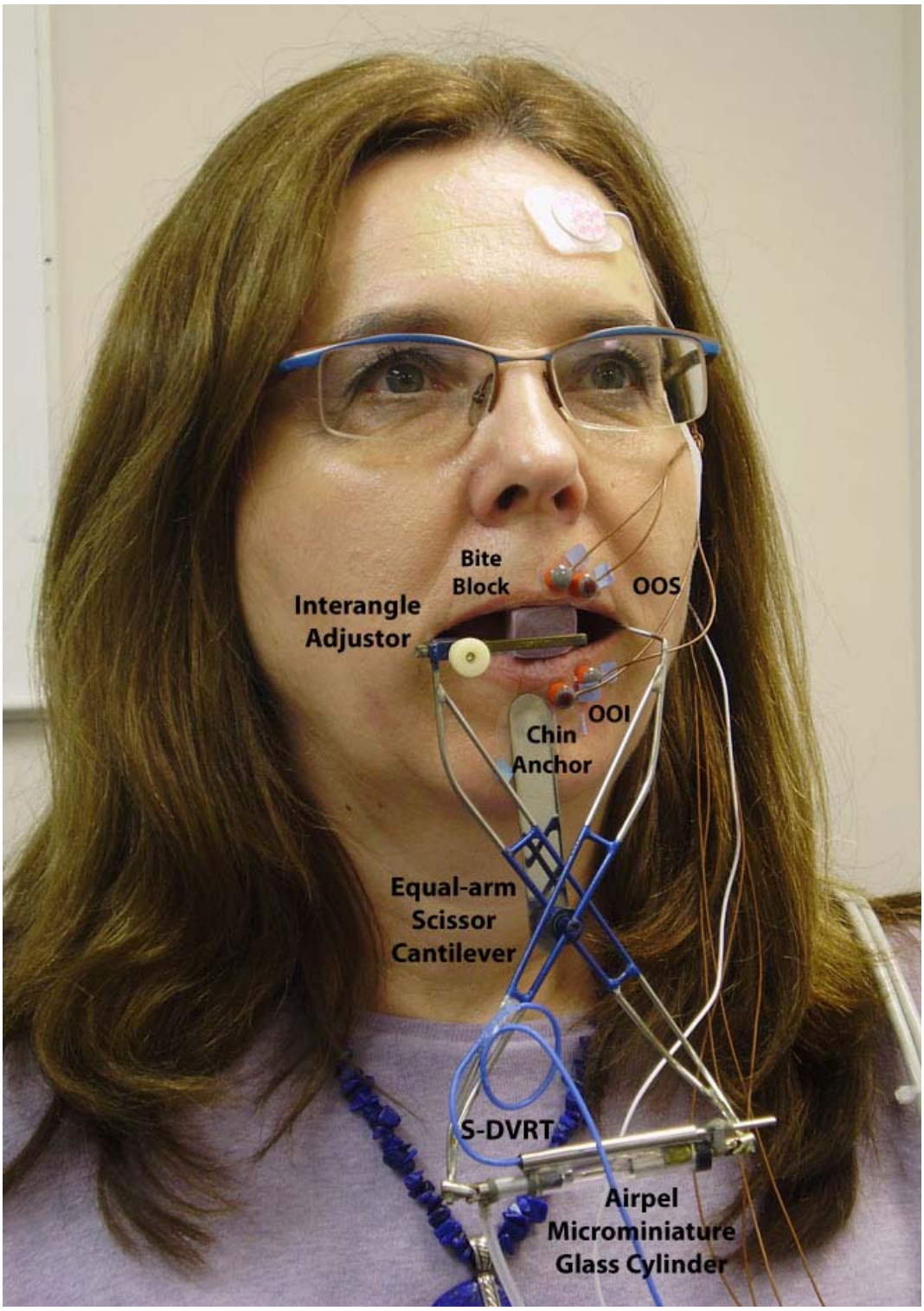

Figure 4. Face-referenced OroSTIFF testing setup.

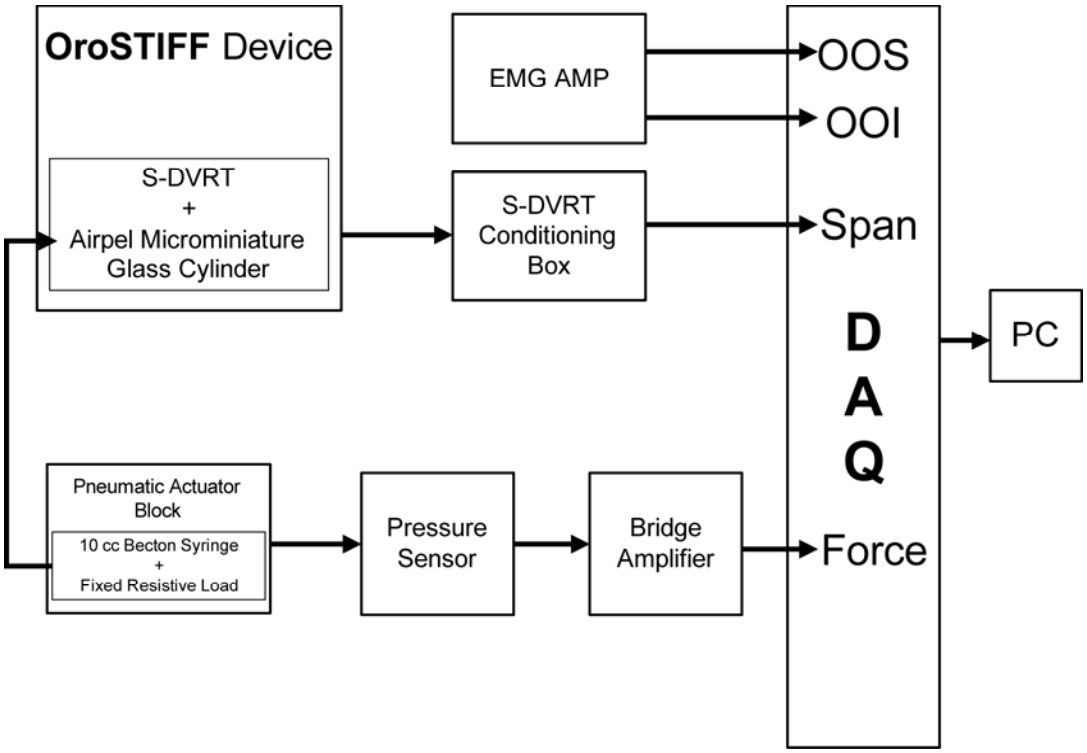

Figure 5. A schematic block diagram of the OroSTIFF system.
(Adapted from Chu, Barlow, Kieweg, & Lee, 2010, *J Biomechanics*)

Air pressure within the microminiature pneumatic glass-cylinder actuator and the displacement signal from the S-DVRT was digitized at 2000 samples/sec at 16-bits resolution (National Instruments PCI-6052E series multifunction I/O card). These waveforms were downsampled to yield 100 pressure and position samples which were digitally low-pass filtered (f_{lp} = 30 Hz, 2-pole Butterworth). These 100 samples were averaged in 10 bins of 10, yielding an effective sample rate of 200 Hz for real-time calculation and display of force, displacement, and derived stiffness.

1.2. Identifying nonlinear segment of force-displacement curve

Stiffness coefficients (N/mm) were automatically calculated during the phase of elastic recoil for each of 5 trials as the low-mass interangle yokes of the OroSTIFF device returned to the participant's interangle rest position in real-time with the OroSTIFF (v. 3.0.5) software. The

stiffness coefficient was calculated as the change in force over a 1 mm change in interangle span and is evaluated at 1 mm intervals. Real-time display of stiffness coefficient versus span begins when 3 conditions are met simultaneously: span > 0.5 mm, force decreasing, and a positive slope for a 10-point linear fit of force versus span. Graphic display continues until span < 0.5 mm (see Figure 6, points D to E). The absolute number of stiffness points along the recoil trajectory depends on the maximum interangle span achieved. To determine stiffness for a specific span a 100-point running cubic spline was evaluated at 0.5 mm above and below the desired span (for example, force was evaluated at 19.5 and 18.5 mm to calculate stiffness for a nominal span of 19 mm). The cubic spline allows force to be determined at regular displacement intervals.

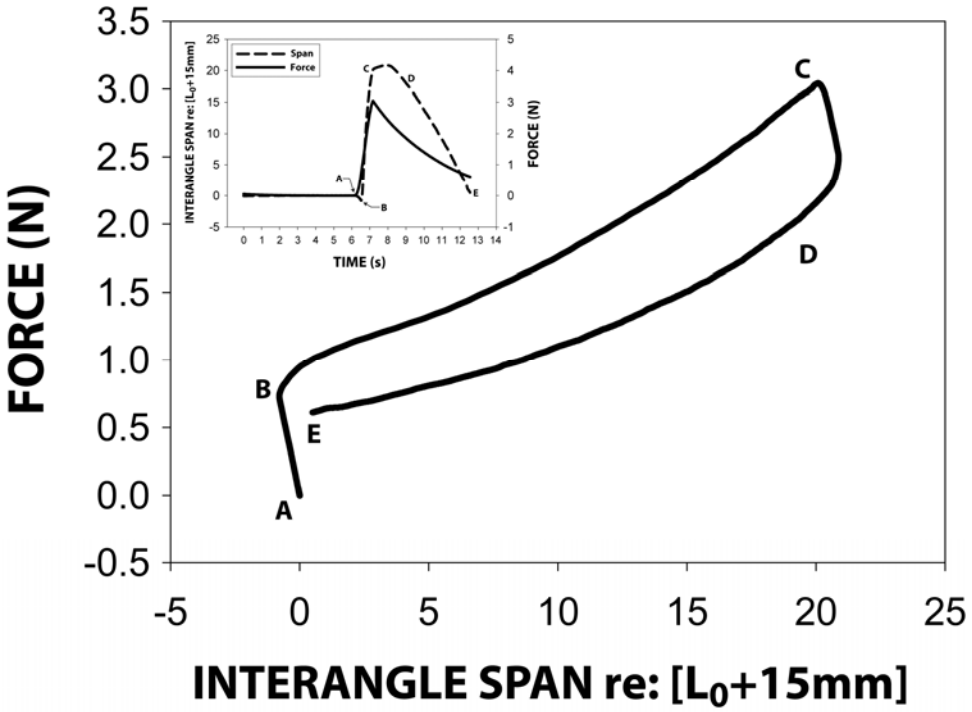

Figure 6. Force-span hysteresis curve from a normal adult subject.
The insert graphic shows the span-time (dashed line) and force-time (black line) of a typical force-span hysteresis curve sampled from a normal adult subject. Point A: preload condition of the OroSTIFF device on a subject's face; B: onset of the interangle stretch phase; C: peak interangle stretch; D-E: recoil of the perioral muscles during which stiffness is calculated (ΔForce/ΔSpan). (Adapted from Chu, Barlow, Kieweg, & Lee, 2010, *J. Biomechanics*).

1.3. Calibration of the OroSTIFF device

The DVRT factory calibration data and the digital caliper measurements were used to determine the ratio of DVRT position-to-interangle span. Force was calibrated with a load cell placed between the stainless steel interangle lip saddles of the OroSTIFF device. Device stiffness was determined by clamping the stainless steel interangle lip saddles and measuring position and force while modulating pressure with the 10-cc Becton syringe. After the OroSTIFF program initialization, voltage offsets were determined with pressure vented to atmosphere, position set to zero, and EMG disconnected. All four signals were scaled linearly using these offsets and previously determined calibration slopes to yield force (N), displacement (mm), and EMG (μV). The DVRT position signal was converted to interangle span by multiplying a constant to account for differences in the equal-arm scissor cantilever lengths on opposite sides of the central pivot needle bearing to correct for device stiffness. The negative slope seen in Figure 6 between points A and B, and C and D represent the effective device stiffness. Lastly, the measured force was divided by the effective device stiffness and subtracted from position to yield interangle span.

1.4. Perioral stiffness sampling procedure

Subjects were seated in a comfortable chair and instructed to remain speechless during the sampling. A 1-cm incisal bite block was molded (KERR Xtrude-XP) for each subject in order to stabilize the mandible during perioral stiffness sampling protocol (see Figure 4). To create the bite block, a small amount of soft bite block putty was placed between the jaws at the incisal plane. The subjects were instructed to bite down onto the 1-cm custom designed block that is positioned between the molars to create a 1-cm gap. The bite block was removed from the oral cavity after thirty seconds and placed on a clean surface to allow the putty to set. The bite

block was connected with a piece of string attached to the subjects' shirt collars to prevent the possibility of either choking or swallowing the bite block during the sampling.

Non-participatory stiffness coefficients under each condition were measured with a custom-designed device (OroSTIFF) by imposing a stretch at the interangle span of these individuals. Each participant underwent five interangle stretches while remaining speechless. The OroSTIFF device was positioned directly on the subject's interangle aperture and mental symphysis for stabilization. The perioral stiffness device was cold sterilized with MetriCide® prior to each use according to standard test procedures.

1.5. Determine muscle activity pattern during non-participatory stretch

To confirm the non-participatory nature of this sampling, silver/silver chloride Ag/AgC1 4mm-diameter bipolar electrodes were placed on the left quadrant of the upper lip (orbicularis oris superior [OOS*m*]) and lower lip (orbicularis oris inferior [OOI*m*]). The root-mean-square (RMS) of the OOS*m* and OOI*m* integrated EMG (IEMG) signals was computed during the phase of elastic recoil for each of 5 trials with an increment of 10 samples at 2000Hz (averaging time of 5 ms) to quantitatively assess non-participation of perioral muscles during sampling. After completing the perioral stiffness sampling, each subject was instructed to produce a series of speech tasks in order to measure their labial kinematics.

2. Labial Kinematics Sampling

2.1. Motion capture system

A 4-dimensional optical motion capture system (Motion Analysis Corporation, Santa Rosa, CA) was used to track the perioral movement during production of consonant-vowel syllables ("pa") and sentences from the rainbow passage as the speech rate is altered. The computerized tracking system consists of five infrared cameras that were strategically placed in

an arc within the recording suite to converge on the subject's face. This arrangement allows accurate capturing and tracking of the reflective markers on the lower face of the subject. Prior to recording, lens distortions were corrected and all cameras were calibrated according to manufacturer specifications. These cameras have a high resolution of 0.10 mm.

A diagram of each channel for the labial kinematics, acoustics signals, and EMG is shown in Figure 7. The movements were sampled at 119.88 Hz. A miniature microphone (SONY electret condenser microphone) was attached to the subject's shirt collar to record the audio signal. The speech acoustic signal was digitized at 4195.80 Hz sampling rate by an A/D unit (NI-USB 6218) within the Motion Analysis system, so that the acoustic signal was synchronized with the movement signals. The audio signal was amplified through a bridge amplifier (gain=2k). The audio signal was used offline to ensure that the target syllables and words were spoken correctly and that the kinematic data segmented for analysis corresponded to the appropriate speech sample. A digital video was recorded as a reference during the analysis of movement data.

Subjects were video recorded while producing these speech tasks. Full-face video recordings were captured directly onto the hard drive of the computer using a video camera (Panasonic MiniDV Model: AG-DVC 20P) coupled to the Cortex-64 (version 2.0.0.900) software program. During data collection, images from this camera were also displayed on a monitor to ensure that each marker retained its reflective properly throughout the data collection session.

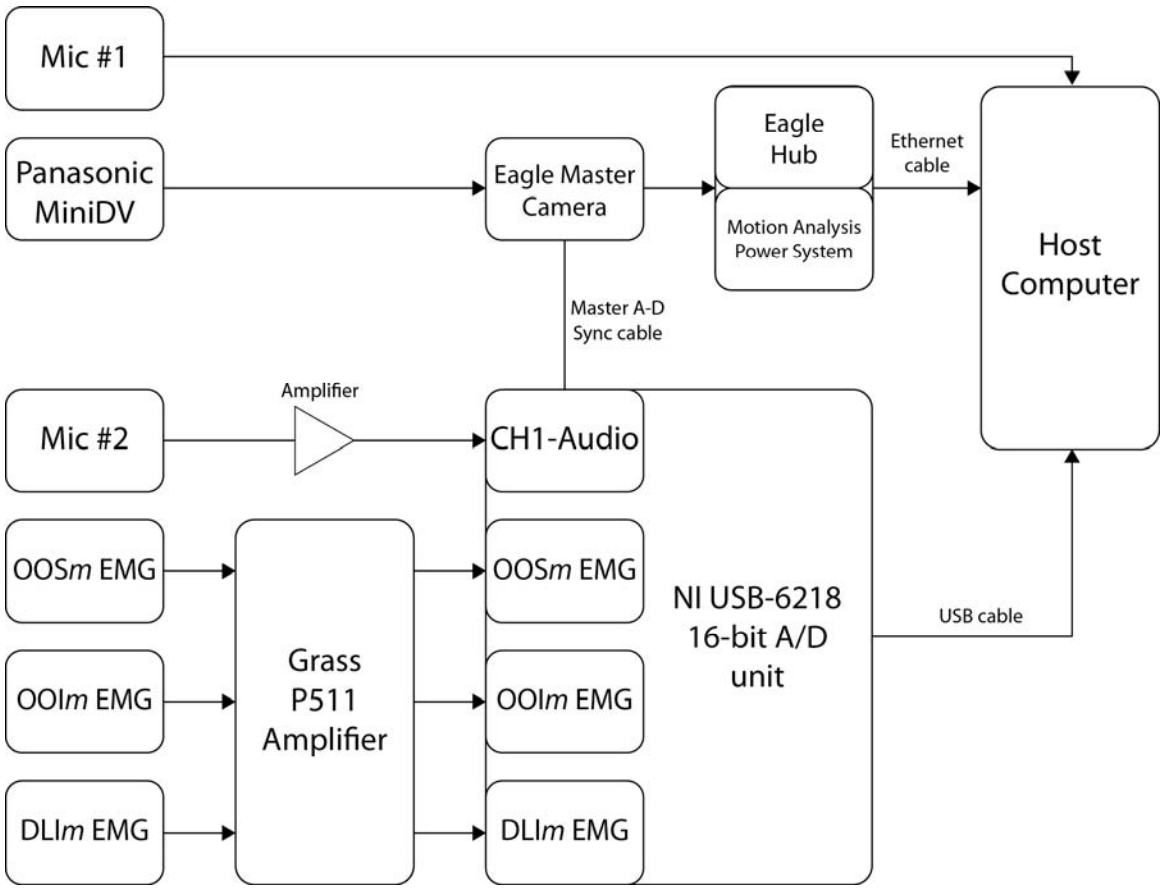

Figure 7. A schematic diagram of all signal channel inputs during speech task.

2.2. Reflective markers

Sixteen infrared reflective sphere markers (~6 mm in diameter) were placed on the subject's lower face with double-sided adhesive tape. Three markers were placed on the chin at the gnathion (JC) and approximately 3 cm to the right and left of the gnathion marker (JR and JL). One additional marker (Dummy) was positioned on the right lower corner of the mouth in order to create an asymmetrical dimension for the software to identify the right and left side of the face. This marker was not studied in this experiment. The reflective markers were illuminated with an infrared light source attached to the cameras. The placement of the reflective markers is shown in Figure 8.

2.3. Coordinate system

To obtain the movements of the facial markers that are independent of the head, the positions of the forehead coordinate system were used to re-express the positions of the targeted facial markers in a head-based coordinate system. The head motion was recorded with one reference marker array (consisting of four markers) centered at the forehead. The points on this marker marked the top right (RTH) and left side (LTH) and the bottom left (LBH) and right side (RBH) of the forehead (Figure 8). Data from these head markers were used to compute the three-dimensional axes (x-y-z) of the head. The head plate coordinate system was utilized to track the position of the head during speech trials. The motions of UL and LL+J were calculated relative to the head coordinate system after the correction for head motion. This step ensures that extraneous movements, due to dyskinesia for example, will not interfere with the collection of speech movements. The movement signals were digitally low-pass filtered (f_{lp} =10Hz) using a zero-phase shift forward-reverse digital filter (Butterworth, 8-pole) written in a custom MATLAB® program, *Speech Movements and Spatial Histograms*- SMASH (Green, 2008).

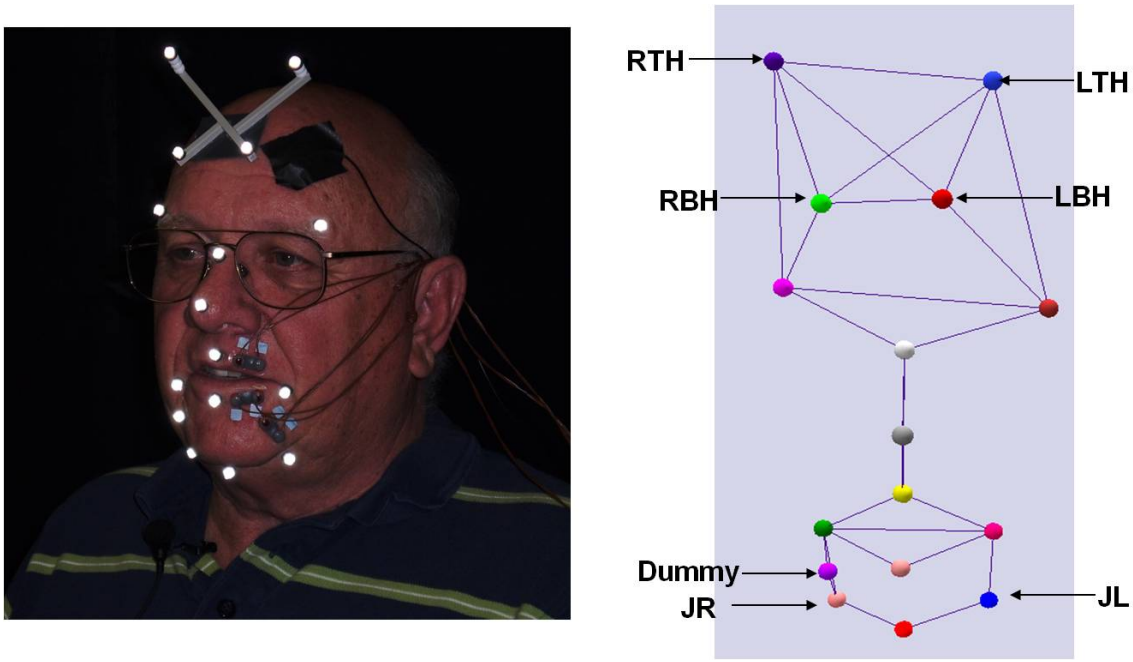

Figure 8. Markers placement.

2.4. Labial kinematics sampling procedure

All subjects participated in a speech practice session prior to testing. Subjects were asked to repeat the "pa" syllable and sentences from the rainbow passage in order to familiarize them with the experiment protocol. Stop plosive bilabial consonants (i.e., "pa") in this motor task have been studied extensively in young adult subjects and such consonants are among the most frequently disturbed in phonemic analysis of PD speech. Subjects were instructed to produce the "pa" syllable for 6 seconds at 2 syllable/sec (6 repetitions), 3.5 syllables/sec (3 repetitions), and 5 syllables/sec (2 repetitions) to ensure an adequate amount of data sampling for analysis (Table 3). Sentences from the rainbow passage were repeated six times at three different rates. The syllables and sentences were visually presented through a 40" Samsung LCD HD monitor placed approximately seven feet away from the subjects. The order of speech tasks were randomized for each subject.

Table 3. Speech tasks repetition.

Tasks/Repetitions	2 syllables/sec	3.5 syllables/sec	5 syllables/sec
"pa"	6	3	2
Rainbow passage	6	6	6

The metronome-paced repetition task was used to determine the strategies used by PD subjects to increase their speaking rate while maintaining speech intelligibility. A metronome program (Desktop Metronome, PA) was used to elicit the metronome pace oscillations at 2 syllables/sec (slow), 3.5 syllables/sec (habitual speech), and 5 syllables/sec (fast) at an RMS vocal intensity level of 70 dB SPL. These metronome paces were selected based on previous studies (Caligiuri, 1989; Hertrich & Ackermann, 2000). The metronome signal was played back via a headphone. Participants were instructed to produce speech tasks dependent on the metronome rate while simultaneously recording their speech acoustic signal, articulators' kinematics, and EMG signal.

3. Electromyography (EMG) Recording during Speech Production

3.1. EMG system

Biopotentials from each electrode pair were conditioned by a Grass P511 bioamplifier (gain=20K, bandpass filter =30Hz-1000Hz) prior to recording. All signals were digitized in real-time at 4195.80Hz. The EMG signals from the OOS*m*, OOI*m*, and DLI*m* were synchronized with the A/D unit within Motion Analysis tracking system while simultaneously recording the speech movements (see Figure 7).

3.2. EMG sampling procedure

A bipolar, electrophysiological sampling of perioral muscle activities was achieved by using microminiature Ag/AgC1 surface electrodes (4 mm diameter) placed over the right OOS*m*,

OOI*m*, and DLI*m* muscles unilaterally (Figure 9). These electrodes were custom designed fixed array electrodes with 5 mm interelectrode distance. A ground electrode was placed over the forehead. Application of the electrodes and verification of electrode placement were performed using the protocol described as follows: OOS*m*: The electrodes were placed on the left quadrant upper lip vermillion border with 5 mm inter-electrode distance. OOI*m*: The electrodes were placed on the left quadrant lower lip vermillion border with 5 mm inter-electrode distance. DLI*m*: The electrodes were placed on the left side of the face 1 ½ cm lateral to the midline and 1 cm inferior to the vermillion border with 3 mm between the electrodes. Verification of the electrodes placement was completed by asking the subjects to both pucker and pout their lips.

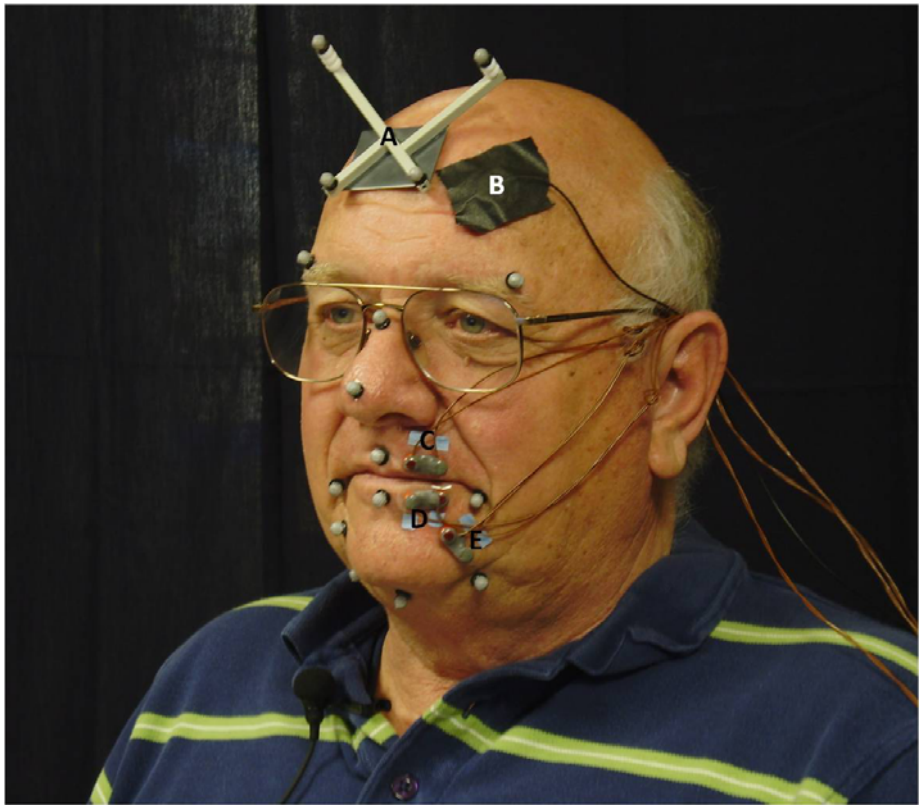

Figure 9. Labial kinematics and EMG testing setup.
Markers and electromyography (EMG) electrodes placements on a subject. A total of 16 markers and three sets of electromyography electrodes (unilaterally) were located on the subject's face. A- Headmount referenced. B- Electrodes ground. C- Electromyography electrodes on the OOS*m*. D- Electromyography electrodes on the OOI*m*. E- Electromyography electrodes on the DLI*m*.

Data Analysis

The research questions and each statistical analysis are presented in Table 4.

Table 4. Research questions and associated statistical analyses.

Research Question	Analysis	Method	Statistical Analysis	Specific Question
Orofacial Biomechanics Is there a causal relation between non-participatory lip stiffness and the associated root mean square (RMS) of perioral IEMG as a function of pharmacological states among individuals with PD, and secondary comparisons to healthy age-and sex-matched controls?	***Analysis 1.1:*** IEMG RMS changes as a function of interangle span	IEMG RMS	GLM-Multilevel Regression Analysis	a) Does the linear/quadratic function of perioral IEMG RMS change as interangle span changes across groups?
	Analysis 1.2: Group differences in IEMG RMS	IEMG RMS	GLM-Multilevel Regression Analysis	a) Does perioral IEMG RMS differ across groups?
	Analysis 1.3: Group changes in linear and quadratic components of the interangle stiffness	Linear and Quadratic components of the interangle stiffness	GLM-Multilevel Regression Analysis	a) Are there differences in linear and quadratic components of the interangle stiffness as a function of group?
	Analysis 1.4: *Modeling-* Group changes in IEMG RMS predicting stiffness	IEMG RMS, perioral stiffness	Multilevel Regression Analysis	a) Can IEMG RMS predict stiffness? If so, are they any interactions?
	Analysis 1.5: Correlation between stiffness and labial kinematic	Mean stiffness score	Correlation	a) Are there any correlations between perioral stiffness and labial kinematic?
Labial Kinematics Are there any differences in labial kinematics	***Analysis 2a:*** Group changes in amplitude and velocity of the closing and	Spatial Analysis: 1) Amplitude 2) Velocity	Paired-samples *t*-test, MANNOVA	a) Does LL+J and UL amplitude change as a function of

(amplitude, velocity, spatiotemporal stability) at 3 speaking rates across controls, PD ON, and PD OFF? If so, do these changes differ at 3 speaking rates?	opening gestures			group, gesture and speech rate? b) Does LL+J and UL velocity change as a function of group, gesture, and speech rate?
	Analysis 2b: Group changes in spatiotemporal stability	Spatiotemporal Analysis (STI)	MANOVA	c) How does spatiotemporal stability change as a function of group and speech rate?
EMG Are there any differences in reciprocal IEMG patterns at 3 speaking rates across controls, PD ON, and PD OFF?	***Analysis 3:*** Group changes in reciprocal muscle activities	Reciprocal activity of the following muscles: DLI*m* re: OOS*m* DLI*m* 2nd peak re: OOS*m* DLI*m* re: OOI*m* OOI*m* re: OOS*m*	MANOVA	a) How do reciprocal muscle activities change as a function of group and speech rate?

Analysis 1a: Orofacial Biomechanics: Tonic IEMG RMS during perioral stretch

1.1. The muscle activity pattern during non-participatory stretch

This analysis was used to consider the following question: Does the linear and quadratic function of perioral IEMG RMS change as interangle span changes across groups? To ensure subjects' non-participation (i.e., no reflex or voluntary EMG) during perioral stretches, silver/silver chloride (Ag/AgC1) 4mm-diameter bipolar electrodes were placed on the left quadrant of the upper lip (orbicularis oris superior [OOS*m*]) and lower lip (orbicularis oris inferior [OOI*m*]). The EMG data were processed offline resulting in an integrated EMG (IEMG) signal. The RMS of OOS*m* and OOI*m* IEMG signal were measured at each of the 5 stretches.

These data were subjected to regression analysis to test for a potential relation between IEMG activation and interangle span.

1.2. The tonic IEMG RMS differences across groups

This analysis provided a means to quantify changes in the RMS IEMG of the OOS*m* and OOI*m* muscles across groups. The RMS IEMG of the OOS*m* and OOI*m* muscles were extracted from each interangle span. This analysis was used to consider the following question: Does perioral IEMG RMS differ across groups?

Analysis 1b: Orofacial Biomechanics: Modeling of the perioral stiffness

1.3. Linear and quadratic function of the interangle perioral stiffness

This analysis was used to consider the following question: Are there any differences in linear and quadratic components of the interangle stiffness as a function of group (Control, PD ON, PD OFF)? Perioral interangle stiffness of the controls, PD ON, and PD OFF groups during passive interangle stretches were extracted to determine the group difference across interangle span. The interangle stiffness was fitted with multilevel regression model to determine linear and quadratic components for interangle stiffness as a function of span.

1.4. Modeling of the perioral stiffness using IEMG RMS levels

The purpose of this analysis was to create a statistical model to predict perioral stiffness using tonic IEMG RMS levels. This analysis was used to consider the following question: Can IEMG RMS predict stiffness? If so, are they any interactions? The tonic IEMG during perioral stretch was used to estimate the perioral stiffness across three groups (Control, PD ON, PD OFF).

1.5. The relation between perioral stiffness and labial kinematics

This analysis was used to consider the following question: Are there any correlations between perioral stiffness and labial kinematic? All of the UL and LL movement amplitude and velocity were used to correlate with the stiffness scores derived from the perioral stiffness function curve at 12 mm interangle span.

Analysis 2a: Labial Kinematics

This analysis was used to consider the following question:

a) Does UL and LL+J amplitude change as a function of group, gestures, and speech rate?

b) Does UL and LL+J velocity change as a function of group, gestures and speech rate?

All kinematic analysis was focused on plosive bilabial consonants (i.e., /p/ in "pa") for the syllable repetition task. Movements were analyzed in the anterior-posterior (x), inferior-superior (y), and medial-lateral (z) dimensions for the UL and LL+J. Since the kinematics of opening versus closing gestures differ in normal speakers (Kuehn & Moll, 1976), separate analysis was completed for each gesture type.

2.1. Quantitative analyses of the kinematic traces: "pa" syllable task

Both opening and closing gestures of amplitude and velocity of the movement from UL and LL+J were analyzed to characterize how these kinematic parameters change as speech rates increase. The amplitude displacement and velocity of each articulator marker was calculated to understand 1) how these kinematic variables' magnitude change as pharmacological states change, and 2) how these variables scale as speech rates increase. As the metronome pace increases, a speed strategy or a displacement reduction strategy could be used to shorten the movement durations in order to match the metronome pace. These analyses, all stages of which

were completed using custom MATLAB® (version 7.9, MathWorks Inc., 2004) algorithms, are described in the following sections.

A total of 30 consecutive syllable repetitions at three different rates were selected for analysis. For each subject, amplitude and velocity of the UL and LL+J were calculated and averaged across the thirty selected movement cycles for the same metronome pace. To systematically select 30 productions of the "pa" syllable for the kinematic analysis, these rules were followed. The first and the last peaks of the syllable trains were disregarded (Figure 10). The next five consecutive repetitions at 2 Hz productions (5x6 repetitions=30), ten repetitions for 3.5 Hz (10x3 repetitions=30), and fifteen repetitions for 5 Hz (15x2 repetitions=30) were selected for analysis. To ensure that all starting and ending points of "pa" syllable trains were accurately selected, the $[LL+J]_y$ zero-crossing points of the velocity signal (superior-inferior dimension, y-axis) were used to define the beginning (positive slope) and ending (negative slope) points of syllable trains (Figure 10). Several important parameters were obtained from the amplitude (first panel) and velocity functions (second panel). The zero crossing points in the velocity function define the starting (positive slope in velocity function) and the ending (negative slope in velocity function) points of the lower lip closing gesture. A more detailed process of parsing rules for "pa" syllable analysis is described in Appendix C.

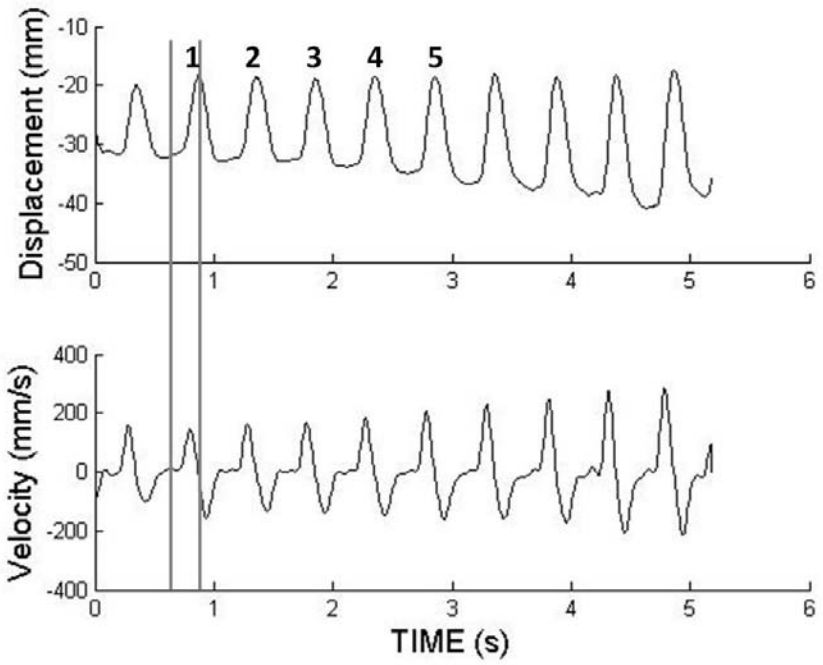

Figure 10. Parsing rules of "pa" syllable task. All parsing were based upon the $[LL+J]_y$ movement.
These plots show original kinematic data from a control participant during production of the "pa" syllable at 2 Hz. The $[LL+J]_y$ velocity signal is plotted below the displacement trajectory. The velocity signal is used to segment the data for all utterances produced by each speaker. In this figure, the vertical lines pass through the zero-crossing velocity of the bilabial closing movement, the /p/ in "pa".

The difference between minimum and maximum displacement distance for the "pa" movement was defined as the amplitude of the opening/closing gesture. Mean velocity was defined as the slope (ΔDisplacement/ΔTime) calculated from the 10% to 90% intercepts of either the closing or opening displacement trajectory (Figure 11). On the basis of these temporal landmarks, the following parameters were determined:

1) Amplitude and velocity of the opening gesture (i.e., the difference between the minimum LL+J distance during the production of the first /p/ of the target word and maximum LL+J distance during production of the target vowel);

2) Amplitude and velocity of the closing gesture (i.e., the difference between the minimum LL+J distance during the production of the second /p/ of the target word and maximum LL+J distance during production of the target vowel);

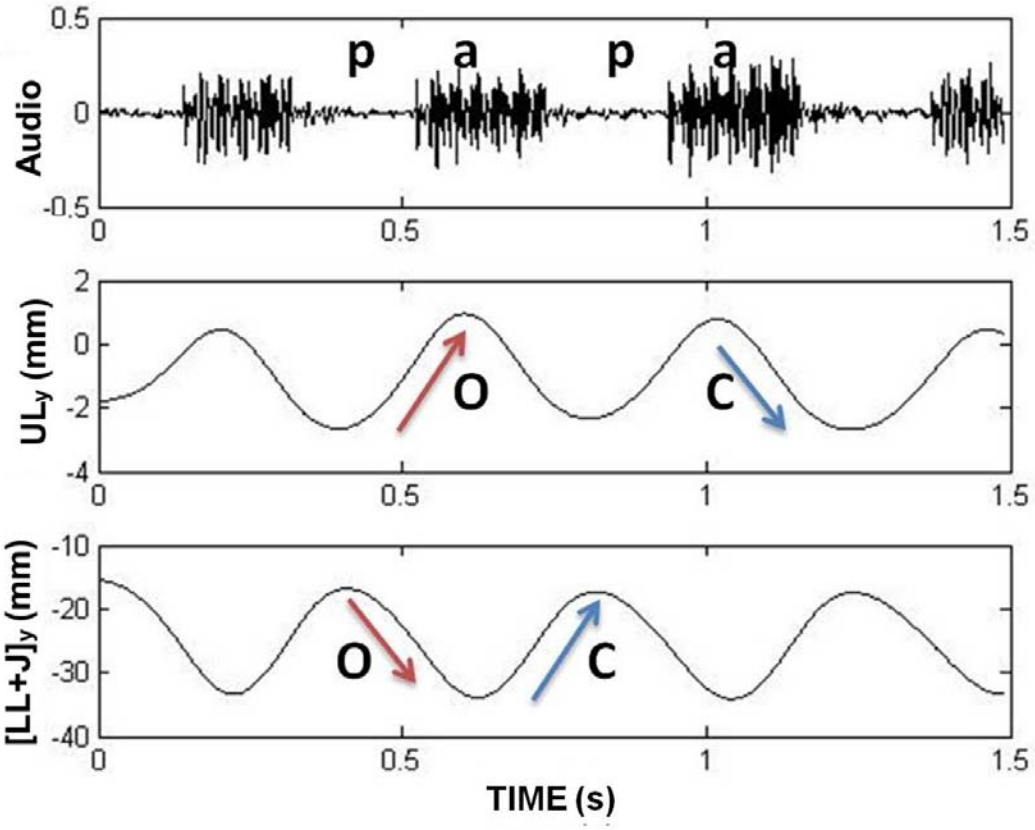

Figure 11. Description of opening (O) and closing (C) gestures for UL and LL+J.

Using a peak-detection alogorithm written in LabVIEW™ v8.5, all detected amplitudes and mean velocity were calculated along the x-, y-, and z-dimensions to examine if different kinematic strategies were used across groups to maintain different speech rates (Figure 12). The peak-detection alogorithm was based on the quadratic fit alogorithm to index peaks in either velocity or amplitude. For y-dimension, both closing and opening gestures were confirmed based upon acoustic signal. For x- and z- dimensional analyses, gestures greater than the specified 0.2 mm threshold were selected for statistical analysis. The threshold of 0.2 mm was

chosen based upon the measured infrared camera residuals (resolution = 0.10 mm) to ensure that all desired movements were captured and analyzed.

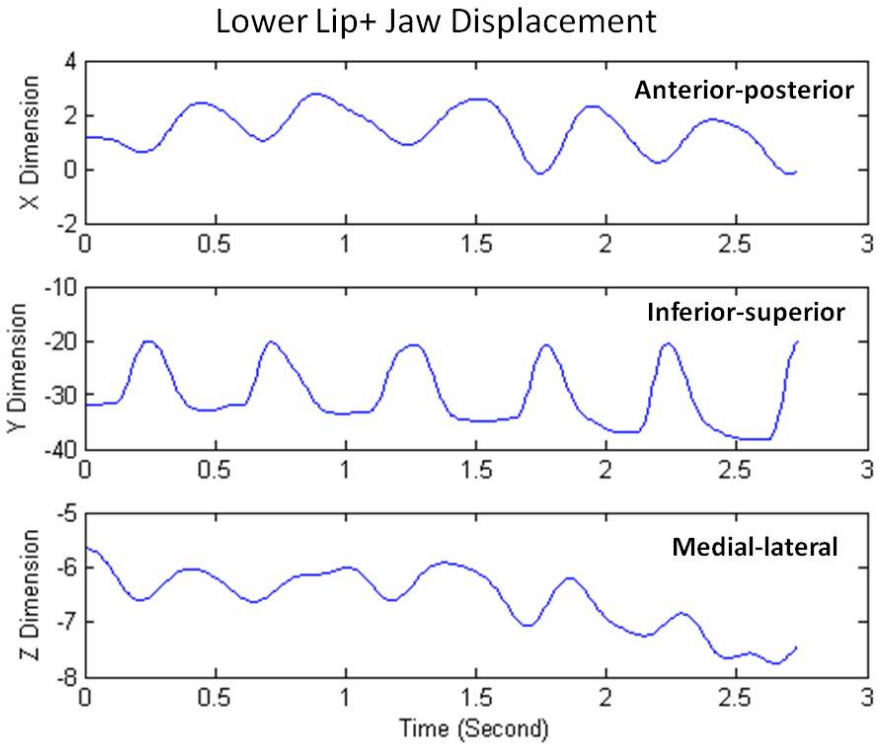

Figure 12. $[LL+J]_y$ kinematic data from a control subject during production of "pa" syllable.

Analysis 2b: Spatiotemporal Stability (STI)

This analysis was used to address the following question: How does spatiotemporal stability change as a function of group and speech rate?

2.2. Quantitative analyses of the kinematic traces-normalization of "pa" syllable task

A second analysis was to calculate the spatiotemporal index (STI) for the "pa" syllable. Only the inferior-superior UL_y and $[LL+J]_y$ data was analyzed using STI measurements. Segmentation rules for the UL_y and $[LL+J]_y$ for STI calculation were similar as described in previous section (see Appendix D). All movement traces were amplitude- and time-normalized using SMASH software (Green, 2008). Amplitude normalization was achieved by dividing each

movement trace by its standard deviation. Subsequently, the linear temporal normalization was achieved by interpolating each signal to 1000 points using a commercially available cubic spline fit algorithm (MATLAB®). Spatiotemporal normalization of the signals provided a means to examine changes in relative time while minimizing variation from rate and absolute movement across and within speakers. Figure 13 displays the raw and normalized traces for the $[LL+J]_y$ from five repetitions of "papa" produced by a healthy adult subjects.

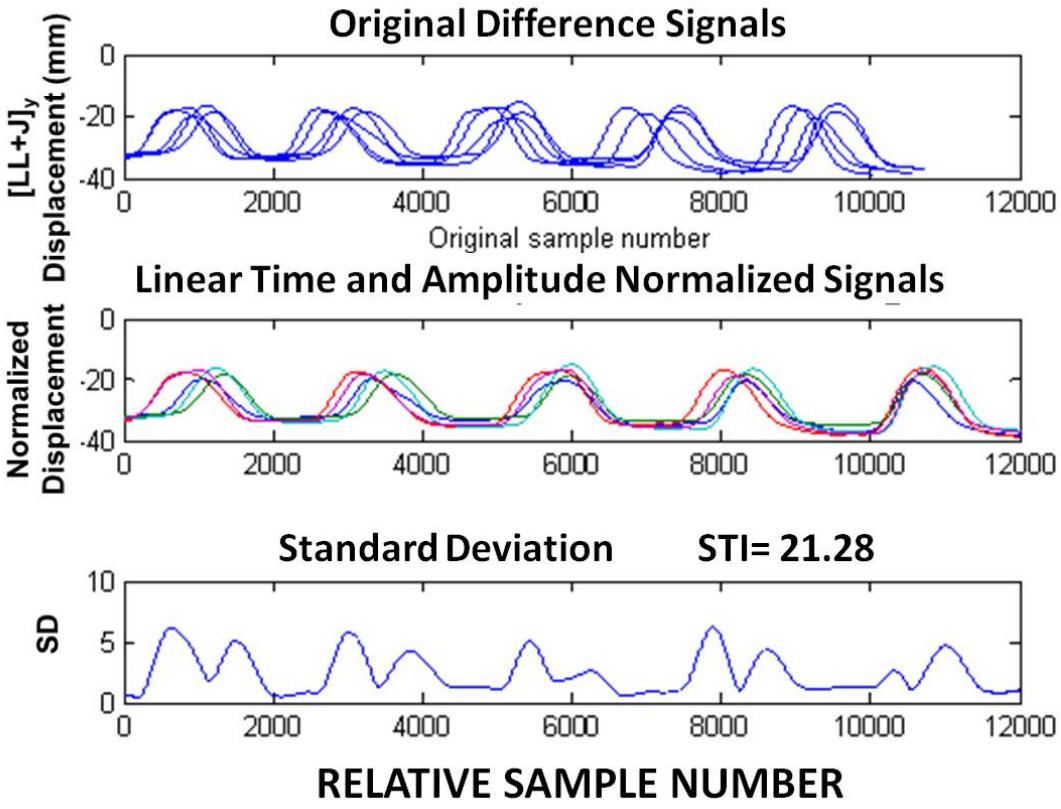

Figure 13. Steps for STI calculation for one control participant.
The top panel shows five original $[LL+J]_y$ displacement trajectories of the "pa" syllable. In the middle panel, the trajectories have been time- and amplitude-normalized. The bottom panel shows the standard deviations of the five normalized $[LL+J]_y$ amplitude trajectories. High STI values result from large standard deviations between lip displacement waveforms, and thus reveal increased variability in the underlying movement pattern. Low STI values result from small standard deviations between lip displacement waveforms, and thus reveals stability or invariance in the underlying movement pattern.

2.3. Quantitative analyses of the kinematic traces-normalization of sentence repetition task

The sentence, "When the sunlight strikes raindrops in the air, they act like a prism and form a rainbow" was used for analysis. The first phrase ["when the …air"] and the second phrase ["they act…rainbow"] of the sentence were compared (Figure 14) to determine if movement trajectories stability change between phrases. To systematically select the sentences for the STI analysis, the following rules were followed (for more detailed process, see Appendix E):

1. All data collected from each subject using Cortex-64 (version 2.0.0.900) were exported into *.c3d format. For the first phrase, the parsing begins at the starting acoustic signal of /wh/ ["when"] and ends at the vowel /ae/ ["air"]. The second phrase begins at the /th/ ["they"] and ends at /o/ ["rainbow"].
2. Using the SMASH program, extraneous head movement of all markers was corrected.
3. The raw data of the UL_y and $[LL+J]_y$ were exported for STI analysis.
4. A total of five repetitions of the rainbow passage at three different rates were selected for analysis.

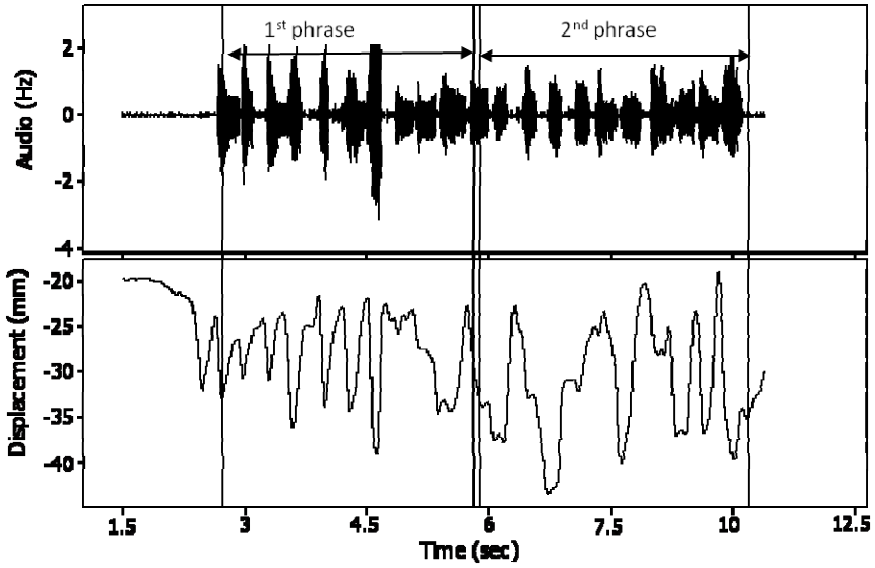

Figure 14. Parsing rules of rainbow sentences task.

Analysis 3: EMGs

This analysis was conducted to address the following question: How does reciprocal muscle activity change as a function of group and speech rate? Two techniques (post-processing of raw EMG signals followed by amplitude ratio/phase polar plot) were implemented to quantify the coordinative organization exhibited by these EMG signals using custom routines written in MATLAB®. Selected periods of activity for the bilabial consonants were obtained relative to the lower lip amplitude signal during the production of bilabial consonants. In other words, all selected periods of EMG data correspond to the selected "pa" kinematic analysis described in the previous section. Using the SMASH program, the raw data of the OOS*m*, OOI*m*, and DLI*m* EMG signals were demeaned, full-waved rectified, and low-pass filter (5-pole Butterworth filter, low-pass cut off = 0.18 Hz for 2 Hz speech rate), low-pass cut off = 0.4 Hz for 3.5 Hz speech rate, low pass cut off = 0.55Hz for 5 Hz speech rate (Figure 15). Using the SMASH program, 30

samples of the "pa" syllable at each speech rate were used for analysis. A detailed description of EMG analysis is shown in Appendix F.

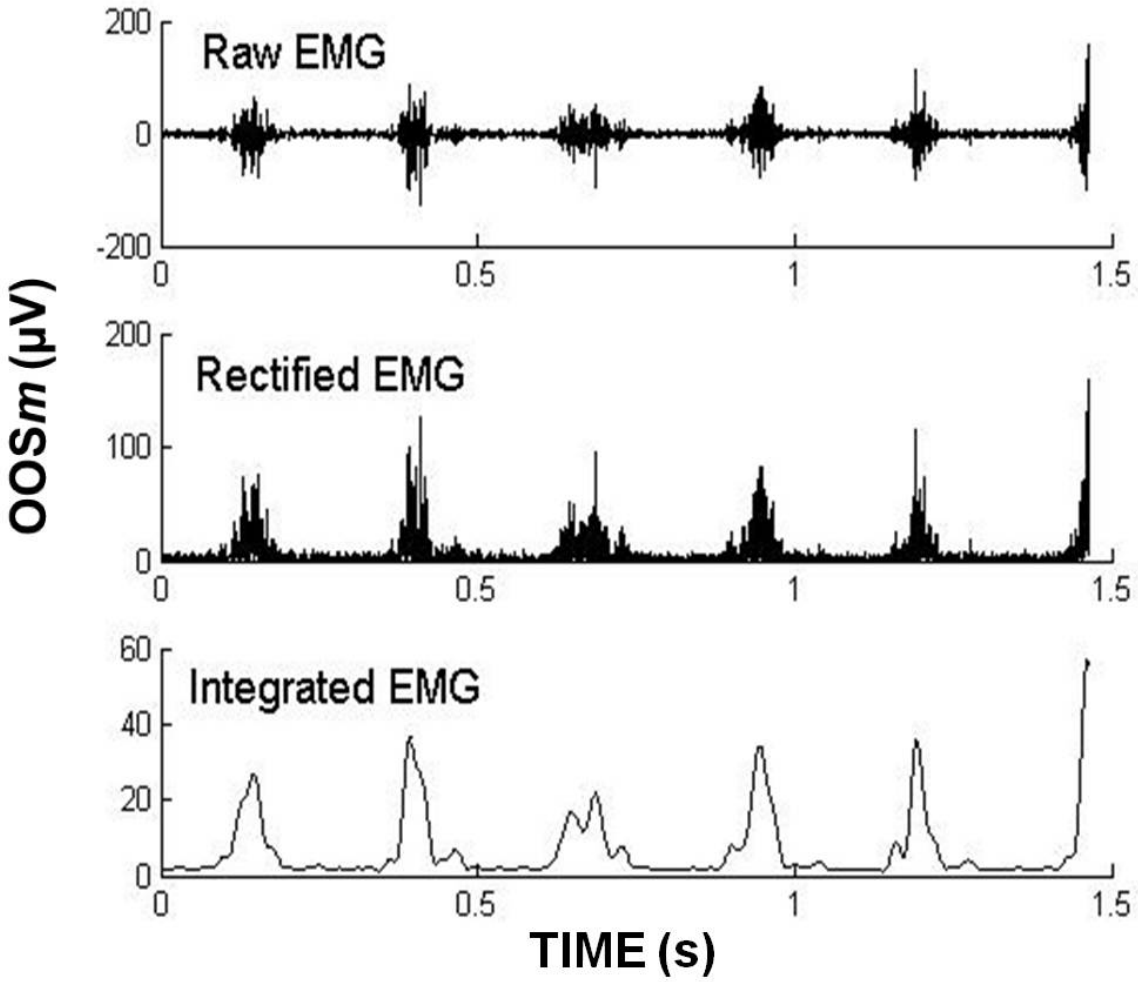

Figure 15. An example of raw EMG (OOS*m*) post-processing steps.

To examine the characteristics of the perioral EMG activities during the speech task, the integrated EMG [IEMG] of the OOS*m*, OOI*m*, and DLI*m* signals were calculated. Figure 16 illustrates an example of reciprocity of OOS*m* and DLI*m* signals. When OOS*m* is activated, DLI*m* is deactivated during the production of "pa" by a healthy control. This simultaneous activation of OOS*m* and deactivation of DLI*m* represents a high reciprocal activity between these two muscles.

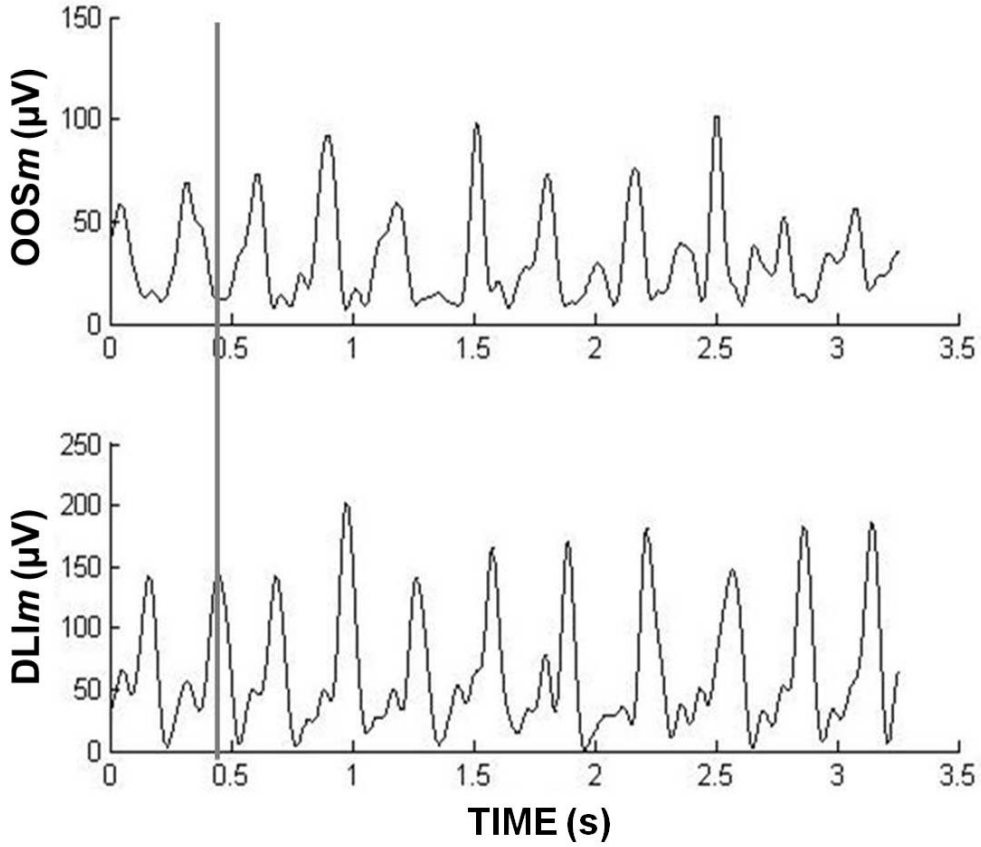

Figure 16. An example of reciprocity of IEMG signals.
The gray line in the figure shows that OOS*m* activates prior to DLI*m* activation. This is an example of muscle reciprocity between upper lip closer (OOS*m*) and lower lip opener (DLI*m*). Coactivation of OOS*m* and OOI*m* shows the finite lag of cross-correlation between these muscles.

First, peak amplitude was automatically detected using a peak-detection algorithm written in LabVIEW™. Then, an amplitude ratio was calculated for each muscle cycle consisting of the muscle peak amplitude (A_{21}) divided by the peak amplitude of the reference muscle (A_{11}) (Figure 17). Angular phase (polar plot azimuth) was defined as the time difference between the peaks of two muscles ($P_{c21\text{-}c11}$) divided by the period of the reference muscle (P_{12}) and converted into degrees. In these polar plots, the amplitude ratio corresponded to the radius and angular phase represents azimuth (circumference). A high coactivation phase (1:1 relation

between two muscles) was evidenced by a grouping of the data points near the 100% amplitude ratio radius and a restricted phase angle range. This analysis provided information regarding the amplitude ratio and lag of muscles activations between two muscles.

Amplitude ratio = (A_{21}/A_{11}), (A_{211}/A_{11}), (A_{212}/A_{11})

Angular phase= ($P_{c21\text{-}c11}/P_{12}$), ($P_{c211\text{-}c11}/P_{12}$)

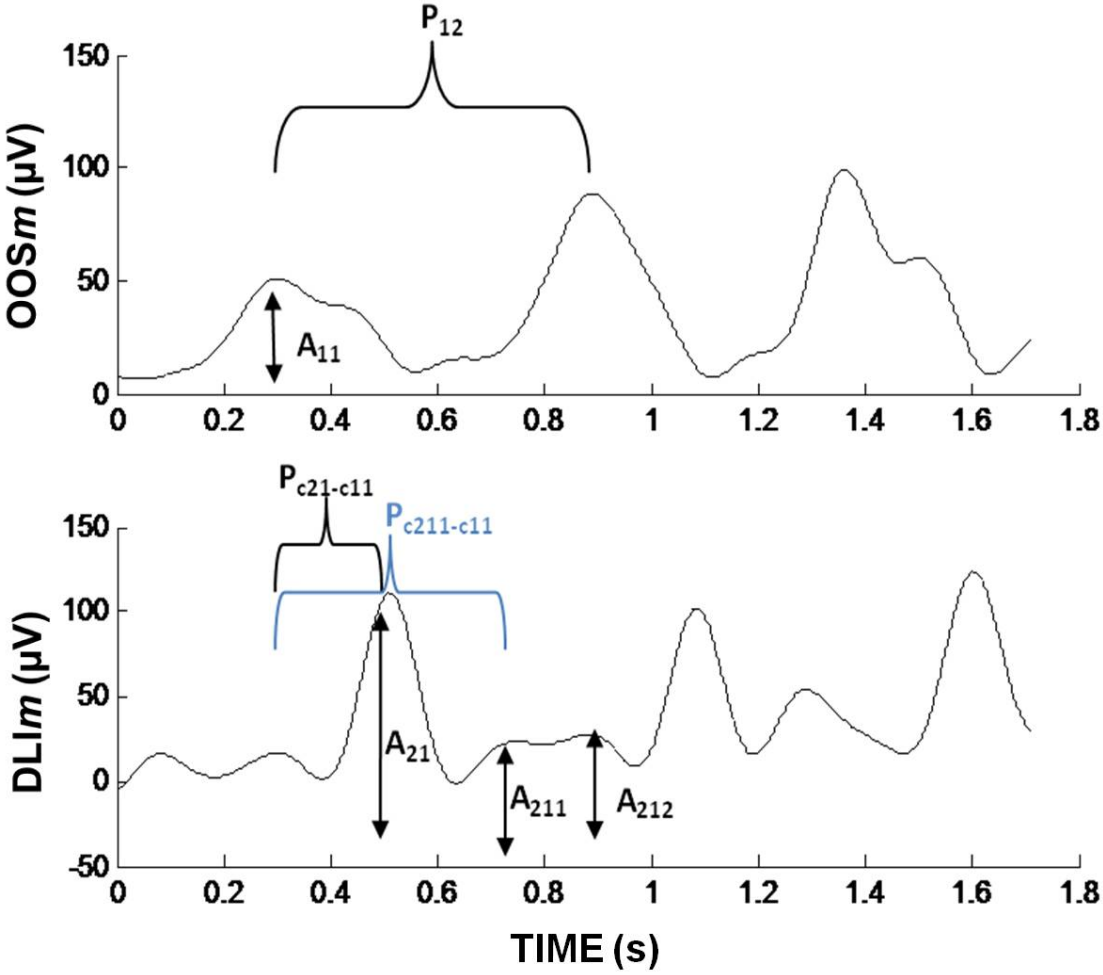

Figure 17. Calculation of perioral IEMG reciprocity.

An example of the polar plot expression from a single control subject is shown in Figure 18. Each of the red asterisks demonstrates the peak of muscle activation compared to the reference muscle. A total of 30 peaks are presented based upon the speech tasks, which consists

of 30 “pa” syllables. In this example, OOS*m* serves as the reference muscle for comparison, hence denoted as OOI*m* re: OOS*m*. Panel A shows the coactivation of muscles OOS*m* and OOI*m*, whereby the data points locate nearby the 0° angular phase. Panel B demonstrates the reciprocity of two muscles (DLI*m* re: OOI*m*), whereby the data points shift to approximately 180° out of phase.

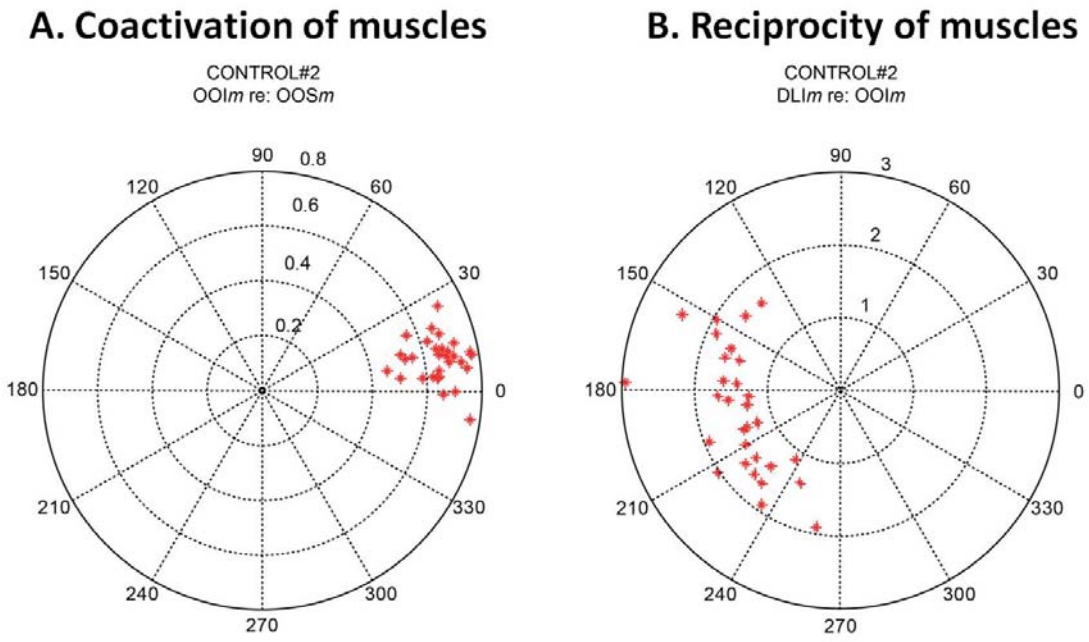

Figure 18. An example of perioral muscle coactivation (OOI*m* and OOS*m*) and reciprocity (DLI*m* and OOI*m*).

An example of a perioral IEMG polar plot from a control subject and a PD subject is shown in Figure 19. This particular PD subject demonstrated a coactivation pattern between the DLI*m* re: OOI*m*, indicating a lack of reciprocity between muscles when compared to a control subject. Moreover, this PD subject demonstrated a lower amplitude ratio (i.e, lower radius, range- 0.1-0.5) compared to the control subject (range 1-3).

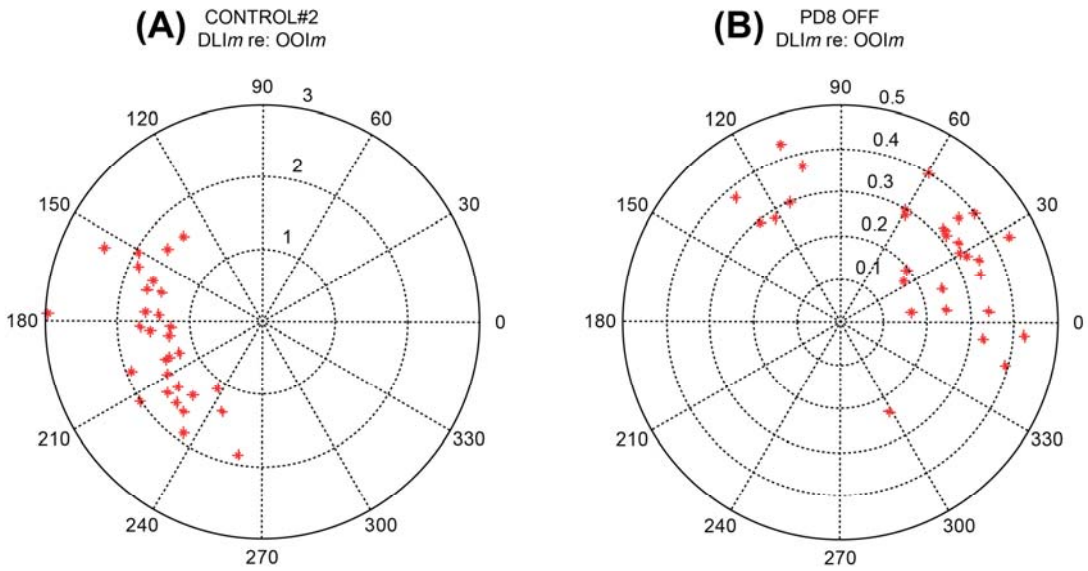

Figure 19. An example of the DLI*m* re: OOI*m* from a matched healthy control and a PD subject.

The following muscle pairs were compared:

1. OOI*m* re: OOS*m*
2. DLI*m* re: OOS*m*
3. DLI*m* re: OOI*m*
4. DLI*m* 2nd peak re: OOS*m*

Power Calculations and Statistical Treatment

To determine adequacy of the experimental design, power calculation were derived based on a portion of the preliminary data. The SAS power procedures were conducted for the general linear models of this study. A sample size of seven subjects per group was sufficient to provide power greater than .80 to detect the (linear) associations of the RMS of perioral IEMG with perioral stiffness (.89 – .97) and group (.81 – .85) (Aim #1). A sample size of nine participants per each group, with an alpha level of .05, was adequate to provide power greater than .80 to detect group, speech rate, and articulator differences (Aim #2). Results indicated that 10 participants per group were adequate to achieve power close to .80 to detect a medium effect size

(Glass's $\Delta = 0.750$) for group differences in the reciprocal IEMG (Aim #3). Taken together, a sample size of ten participants per group (ten PD, ten controls) were sufficient to provide power to detect moderate differences or effects among the outcome variables examined in this study.

Statistical Analyses

Analysis 1a: Orofacial Biomechanics: Tonic IEMG RMS during perioral stretch

1.1. The muscle activity pattern during non-participatory stretch

The main purpose of this analysis was to confirm the non-participatory nature of the muscle activity pattern during non-participatory stretch. The root mean square (RMS) of the OOS*m* and OOI*m* IEMG was used to examine the patterns (e.g., linear, quadratic) of IEMG change over the interangle span [L_0+15mm]. Because of the nested nature of the data in which the IEMG RMS muscle activity were measured through a series of interangle stretch trials (level-1) in each subject (level-2), the general linear mixed modeling (e.g., multilevel regression analysis) was used to evaluate the significance at different levels. Multilevel regression analysis accounts for the correlation between observations of the same individuals at multiple time points. Using the residual (restricted) maximum likelihood method, group differences, span effects, group difference in the span effect (interaction effects) were estimated at .05 alpha level. All analyses were conducted using SAS version 9.2 (SAS Institute Inc., 2002-2008).

1.2. The tonic IEMG RMS differences across groups

A separate multilevel regression analysis was conducted to compare the IEMG RMS level between groups. Group differences were estimated at .05 alpha level, using residual (restricted) maximum likelihood method. When group differences or interaction effects were significant, estimated IEMG RMS means were pair-wise compared using the SIMULATE adjustment test. The SIMULATE adjustment computes adjusted *p*-values and confidence limits

from the simulated distribution of the maximum or maximum absolute value of a multivariate random vector (Edwards & Berry, 1987). All analyses were conducted using SAS version 9.2 (SAS Institute Inc., 2002-2008).

Analysis 1b: Orofacial Biomechanics: Modeling of the perioral stiffness

1.3. Linear and quadratic function of interangle perioral stiffness

The purpose of this analysis was to examine the patterns of perioral stiffness (e.g., linear, quadratic) change over the interangle span. Because of the nested nature of the data in which the perioral stiffness was measured through a series of interangle stretch trials (level-1) in each subject (level-2), the general linear mixed modeling (e.g., multilevel regression analysis) was used to evaluate the patterns (e.g., linear, quadratic) of perioral stiffness change over the interangle span. A second goal was to determine if these patterns differ between groups. Multilevel regression analysis allowed us to estimate random effects as well as fixed effects that occur at more than one level. The level-1 (trial; i.e., span, span^2) and level-2 (subject; i.e., PD OFF vs. control, PD ON vs. control) effects and cross-level interaction effects were introduced into a null model, with their significant random variance components. The trial-level effects represent the linear and quadratic changes of the perioral stiffness within the range of interangle spans. The cross-level interaction effect was utilized to contrast the control and pre-/post-treatment conditions (PD OFF vs. control, PD ON vs. control) in terms of the linear and quadratic changes of the perioral stiffness. Control group data was used as reference in this analysis. Finally, the shape of these perioral stiffness changes was contrasted with that estimated from the control group. Group differences, span effects, and group differences in span effects (interaction effect) were estimated at .05 alpha level, using the residual (restricted) maximum likelihood method. All analyses were conducted using SAS 9.2 (SAS Institute Inc., 2002-2008).

The fitted null model is given by the expression,
$Stiffness_{ij} = \gamma_{00} + u_{oj} + r_{ij}$, where $u_{oj} \sim N(0, \tau_{00})$ and $r_{ij} \sim N(0, \sigma^2)$ for trial *i* and participant *j*.

This model can be viewed as a one-way random effects ANOVA model. This model expresses the stiffness scores as the sum of an overall mean (γ_{00}), a series of random deviations from that mean (u_{oj}), and a random error (r_{ij}) associated with the *i*th trial in the *j*th participant.

The final multilevel regression model included two trial-level predictors (linear and quadratic increases in span) and cross-level interaction terms. The cross-level interaction terms were included to test whether the regression slope differed between groups. This model can be written as

$$Y_{ij} = \gamma_{00} + \gamma_{10}OFF_{ij} + \gamma_{10}ON_{ij} + \gamma_{10}Span_{ij} + \gamma_{20}Span_{ij}^2 + \gamma_{10}\left(OFF_{ij} \times Span_{ij}\right) + \gamma_{10}\left(ON_{ij} \times Span_{ij}\right) + \gamma_{21}\left(OFF_{ij} \times Span_{ij}^2\right) + \gamma_{21}\left(ON_{ij} \times Span_{ij}^2\right)$$

,where $\begin{pmatrix} u_{oj} \\ u_{1j} \end{pmatrix} \sim N\left[\begin{pmatrix} 0 \\ 0 \end{pmatrix}, \begin{pmatrix} \tau_{00} & 0 \\ 0 & \tau_{11} \end{pmatrix}\right]$ and $r_{ij} \sim N(0, \sigma^2)$ for trial *i* and participant *j*.

1.4. Modeling of the perioral stiffness using IEMG RMS levels

A separate multilevel regression analysis was conducted to compare the perioral stiffness between groups using IEMG RMS. The first hypothesis was that group significantly differed in perioral stiffness. The second hypothesis was the tonic IEMG RMS significantly predicts perioral stiffness and that there were significant interactions between group and IEMG RMS in predicting stiffness. Group differences, IEMG RMS effects and group differences in the IEMG RMS effects (interaction effects) were estimated at .05 alpha level, using residual (restricted) maximum likelihood method. When group differences or interaction effects were significant, estimated IEMG RMS means were pair-wise compared using the SIMULATE test. All analyses were conducted using SAS version 9.2 (SAS Institute Inc., 2002-2008).

1.5. The relation between perioral stiffness and labial kinematics

Pearson's correlation analyses were conducted to examine the relationship between perioral stiffness and hypokinesia. Stiffness scores at 12 mm interangle span derived from each subject were correlated to the opening and closing gestures of the UL_y and $[LL+J]_y$ movement displacement amplitude. Stiffness score at 12 mm span was chosen because this was the maximum span from a PD subject that we could derive. The UL_y and $[LL+J]_y$ were used because this is the primary dimension during speech movement. Stiffness scores were correlated across groups (Control, PD ON, PD OFF), gestures (opening, closing), and speech rates (2 Hz, 3.5 Hz, 5 Hz). All analyses were conducted using SAS 9.2 (SAS Institute Inc., 2002-2008).

Analysis 2a: Labial Kinematics

2.1. Compare UL vs. LL+J movement variables

A paired-samples *t*-test was conducted to examine the UL and LL+J differences in amplitude and velocity for all groups (Control, PD ON, PD OFF) and speech rates (2 Hz, 3.5 Hz, 5 Hz). The dependent variables (DVs) were: UL_x, UL_y,UL_z, $[LL+J]_x$, $[LL+J]_y$, and $[LL+J]_z$. All analyses were conducted using the SAS version 9.2 (SAS Institute, 2002-2008).

2.2. Does UL and LL+J amplitude differ between groups, gestures, and speech rates?

The purpose of this analysis was to determine if labial movement displacement differed between groups, gestures, and speech rates. A multivariate analysis of variance (MANOVA) was performed on six DVs: UL_x, UL_y,UL_z, $[LL+J]_x$, $[LL+J]_y$, and $[LL+J]_z$. Independent variables (IVs) were groups (Control, PD ON, PD OFF), gestures (closing and opening), and speech rates (2 Hz, 3.5 Hz, 5 Hz). When significant main effects (groups, gestures, or speech rates) were found, post-hoc comparisons were conducted using a Tukey's HSD criterion of

significance. All analyses were conducted using the SAS version 9.2 (SAS Institute, 2002-2008).

2.3. Does UL and LL+J velocity differ between groups, gestures, and speech rates?

The purpose of this analysis was to determine if labial movement velocity differed between groups and gestures as speech rates change. A MANOVA was performed on six dependent variables: UL_x, UL_y,UL_z, $[LL+J]_x$, $[LL+J]_y$, and $[LL+J]_z$. Independent variables were groups (Control, PD ON, PD OFF), gestures (closing and opening), and speech rates (2 Hz, 3.5 Hz, 5 Hz). When significant main effects (groups, gestures, or speech rates) were found, post-hoc comparisons were conducted using a Tukey's HSD criterion of significance. All analyses were conducted using the SAS version 9.2 (SAS Institute, 2002-2008).

Analysis 2b: Spatiotemporal Stability (STI)

2.4. Does "pa" STI differ between group and speech rates?

A MANOVA was conducted between groups and speech rates to determine the group related changes in the spatiotemporal stability of speech production. The DVs were UL_y and $[LL+J]_y$. Tukey's HSD post-hoc comparison was conducted when any of the group, speech rate, or interaction between group and speech rate effects was significant. All analyses were conducted using the SAS version 9.2 (SAS Institute, 2002-2008).

2.5. Does Rainbow STI differ between group and speech rates?

The purpose of this analysis was to determine if the Rainbow passage STI differed between phrases, groups, and speech rates. A MANOVA was conducted between the group and speech rate to determine the group related changes in the temporal stability of speech production. Tukey's HSD post-hoc comparisons were conducted when any of the group, speech rate, or

interaction between group and speech rate was significant. All analyses were conducted using the SAS version 9.2 (SAS Institute, 2002-2008).

Analysis 3: EMGs

A MANOVA was conducted to compare the group differences and speech rate effects on the IEMG variables. The IEMG DVs were: OOI*m* re: OOS*m*, DLI*m* re: OOS*m*, DLI re: OOI*m*, and DLI*m* 2nd peak re: OOS*m*. Due to the nature of the data, two sets of analyses were conducted: Theta and Rho. The theta represented the time delay between two comparison muscles while the rho represented the amplitude magnitude of the muscle. Tukey's HSD post-hoc comparisons were conducted if the group, speech rate, or interaction between group and speech rate effects were significant. All analyses were conducted using SAS version 9.2 (SAS Institute, 2002-2008).

CHAPTER III: RESULTS

In this section, we discuss the orofacial biomechanics, labial kinematics, and electromyography findings separately, and then discuss the general implication of the three levels of analysis taken together.

Analysis 1a: Orofacial Biomechanics: Tonic IEMG RMS during perioral stretch

1.1. The muscle activity pattern during non-participatory stretch

The estimated distribution of the IEMG RMS values for the OOS*m* and OOI*m* muscle recording sites pooled among subjects is shown in Figure 20. The parameter estimates from the fitted final model are shown in Table 5 (OOS*m*) and Table 6 (OOI*m*). No significant main effect was found on the OOI*m* IEMG (*SE*= .02, *t* [2792] = .69, *p* = .49) as the interangle span increased, indicating that tonic drive to the perioral muscles remained constant during interangle stretch. For the OOS*m* IEMG, PD ON group showed a steeper increase than the control group as the interangle span increased, while the PD OFF group showed no change in slope when compared to control group (*SE*= .01, *t* [2790] = 1.43, *p* = .15). Although all groups showed a slight increase in the linear pattern of the OOS*m* IEMG during perioral stretches, this increase was less than 1μV as interangle span increased from zero to approximately 25mm. Therefore, there was no evidence of reflex and/or voluntary activity during perioral stretches. Overall, these findings suggested that the perioral muscle activity remained constant as interangle span increased confirming the non-participatory nature of the experiment task. The fact that IEMG RMS remains constant across trials imply that the growth in stiffness coefficient as interangle span increase is presumable due to a combination of elastic forces generated by muscle and connective tissue. The final model of the IEMG RMS as a function of interangle span is expressed in Equation 1 (OOS*m*) and Equation 2 (OOI*m*).

Equation 1. OOS*m* IEMG RMS expression during non-participatory perioral stretch

$$\hat{Y}_{ij} = 6.5268 - 0.6806 \times OFF_j - 0.5268 \times ON_j + 0.0194 \times SPAN_i + 0.0149 \times (OFF_j \times SPAN_i) + 0.0248 \times (ON_j \times SPAN_i)$$

Equation 2. OOI*m* IEMG RMS expression during non- participatory perioral stretch

$$\hat{Y}_{ij} = 7.8251 + 1.3112 \times OFF_j + 15.7337 \times ON_j + 0.0316 \times SPAN_i$$

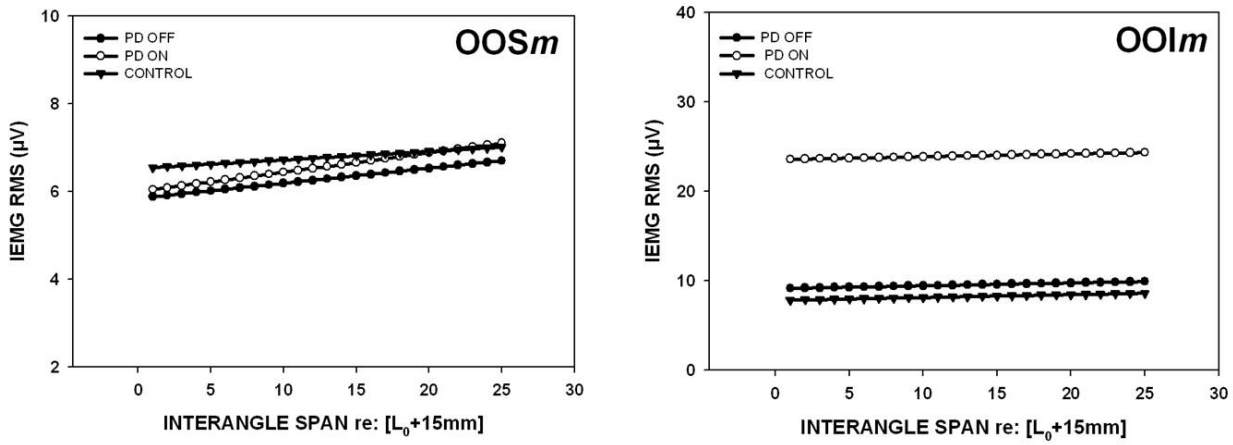

Figure 20. The distribution of the mean IEMG RMS values for upper lip (OOS*m*) and lower lip (OOI*m*) during "face-relaxed" non-participatory conditions.

Table 5. Estimate parameters for the OOS*m* IEMG RMS

Effect	Estimate	*SE*	*p*
Intercept	6.5268	1.984	0.0000
Group			
PD OFF	-0.6806	1.5539	0.6730
PD ON	-0.5268	1.5538	0.7433
CONTROL (Reference)	–	–	–
Span	0.0194	0.0064	0.0024
Group × Span			
PD OFF	0.0149	0.0104	0.1520
PD ON	0.0248	0.0102	0.0156
CONTROL (Reference)	–	–	–

Table 6. Estimate parameters for the OOI*m* IEMG RMS

Effect	Estimate	*SE*	*p*
Intercept	7.8251	3.9248	0.0607
Span	0.0316	0.0460	0.4925
Group			
PD OFF	1.3112	5.5066	0.8178
PD ON	15.7337	5.5062	0.0212
CONTROL (Reference)	–	–	–

1.2. The tonic IEMG RMS differences across groups

A significant group effect was found in the PD ON vs. control groups (t [8] = 2.84, p < 0.05) at the OOI*m* IEMG RMS level (Table 7 and Table 8). Post-hoc comparison revealed significant mean differences between PD ON and PD OFF groups (SIMULATE, p < .05) for both OOS*m* and OOI*m* IEMG levels (Figure 21). There was a significant difference between OOS*m* and OOI*m* RMS level, t (2814) = -19.25, p < .001. Specifically, the PD ON group showed a greater OOI*m* IEMG mean ($\overline{X}$ = 23.86 μV) than OOS*m* IEMG ($\overline{X}$ = 6.42 μV), mainly due to antigravity function. Overall, PD participants showed a greater IEMG RMS compared to control, and this elevated IEMG RMS became greater after the consumption of Levodopa. The final model expression for OOS*m* and OOI*m* RMS IEMG comparison to group are given in Equation 3 and 4.

Equation 3. Expression for OOS*m* IEMG RMS for group comparison

$$\hat{Y}_{ij} = 6.7454 - 0.5804 \times OFF_j - 0.3261 \times ON_j$$

Equation 4. Expression for OOI*m* IEMG RMS for group comparison

$$\hat{Y}_{ij} = 8.1814 + 1.2504 \times OFF_j + 15.6762 \times ON_j$$

Table 7. Summary of OOS*m* IEMG RMS across three groups

Effect	Estimate	*SE*	*p*
Intercept	6.7454	1.0938	0.0000
Group			
PD off	-0.5804	1.5470	0.7173
PD on	-0.3261	1.5470	0.8383
Control (Reference)	–	–	–

Table 8. Summary of OOI*m* IEMG RMS across three groups

Effect	Estimate	*SE*	*p*
Intercept	8.1814	3.8980	0.0494
Group			
PD off	1.2504	5.5168	0.8264
PD on	15.6762	5.5165	0.0218
Control (Reference)	–	–	–

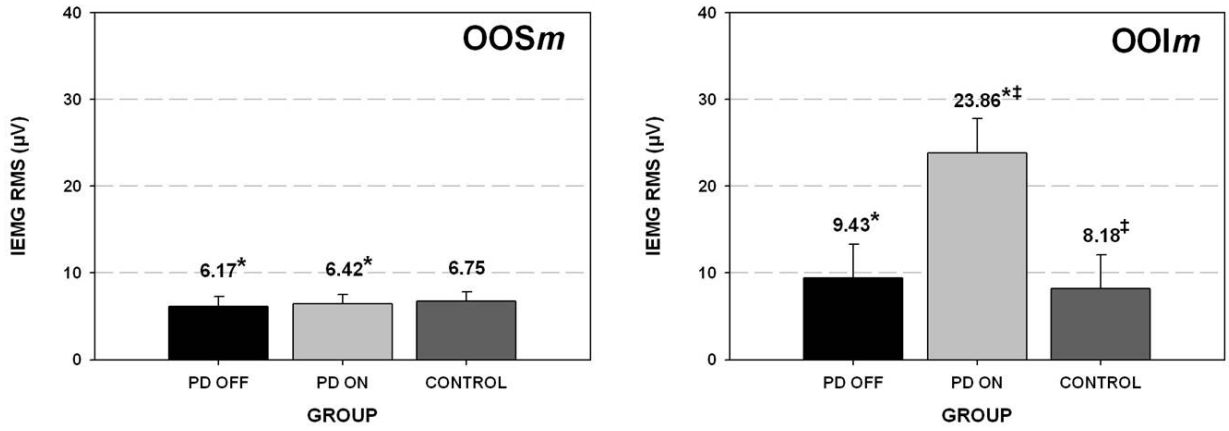

Figure 21. Estimated IEMG RMS means for each group.

Analysis 1b: Orofacial Biomechanics: Modeling of the perioral stiffness

1.3. Linear and quadratic function of interangle perioral stiffness

Perioral stiffness ($\Delta F/\Delta X$) was modeled with multilevel regression techniques. The parameter estimates from the fitted final model are shown in Table 9. The perioral stiffness function demonstrated a significant quadratic relation between imposed interangle stretch and

resultant perioral force for each of the three groups, $\hat{\gamma}_{20}$ = .0003, t (2787) = 26.52, p < .001. More importantly, PD ON group showed a significantly greater quadratic increase than those in the control group, $\hat{\gamma}_{21}$ = .0001, t (2787) = 3.82, p < .001. The quadratic increase did not differ between PD OFF and control groups, $\hat{\gamma}_{10}$ = -.000, t (2787) = -.06, p = .95. For the PD ON group, the stiffness score increased by .0004 points with each one-unit increase in the interangle span. For the PD OFF group, the stiffness score increased by .0003 points with each one-unit increase in the displacement. A supplemental analysis showed that quadratic increases of perioral stiffness significantly differed between PD ON and PD OFF groups, whereby PD ON group had more rapid stiffness increase than PD OFF group. This is consistent with the presence of high OOI*m* IEMG RMS in the PD ON group, as detailed in previous section (see *1.2*). Although the linear function of the interangle span was also significant, there was no significant difference between PD ON and control groups in the linear slope, $\hat{\gamma}_{10}$ = -.0002, t (2787) = -.43, p = .66.

Table 9. Multilevel regression parameter estimates of between- and within-level components

Effect	Estimate	*SE*	*p*
Intercept	0.0329	0.0053	0.0000
Group			
PD OFF	0.0006	0.0076	0.9343
PD ON	0.0046	0.0076	0.5559
CONTROL (Reference)	–	–	–
Span	-0.0044	0.0003	0.0000
$Span^2$	0.0003	0.0000	0.0000
Group × Span			
PD OFF	0.0014	0.0005	0.0019
PD ON	-0.0002	0.0005	0.6647
CONTROL (Reference)	–	–	–
Group × $Span^2$			
PD OFF	-0.0000	0.0000	0.9508
PD ON	0.0001	0.0000	0.0001
CONTROL (Reference)	–	–	–

Figure 22 illustrates the estimated perioral stiffness function derived from the multilevel regression model. For all groups, the stiffness score is expected to show slow decrease until the 7^{th} interangle span and steep increase after then. While there were 15 observations at the 25mm interangle span for the control group, only 1 observation was noted for the PD OFF group at 25mm span. None of the PD ON subjects reached the 25mm stretch. This implies that the PD group had stiffer faces compared to the control group. This finding is in direct support of the idea that non-participatory stiffness of the perioral tissue-muscle complex increase as a function of imposed displacements between the oral angles. Overall, the PD participants showed a higher stiffness quadratic function than the control group, indicating the presence of stiffer facial muscles. The final model is expressed in Equation 5.

Equation 5. Perioral stiffness linear and quadratic function

$$\hat{Y}_{ij} = 0.0329 + 0.0006 \times OFF_j + 0.0046 \times ON_j - 0.0044 \times SPAN_i - 0.0003 \times SPAN_i^2 + 0.0014 \times (OFF_j \times SPAN_i) - 0.0002 \times (ON_j \times SPAN_i) - 0.0000 \times (OFF_j \times SPAN_i^2) + 0.0001 \times (ON_j \times SPAN_i^2)$$

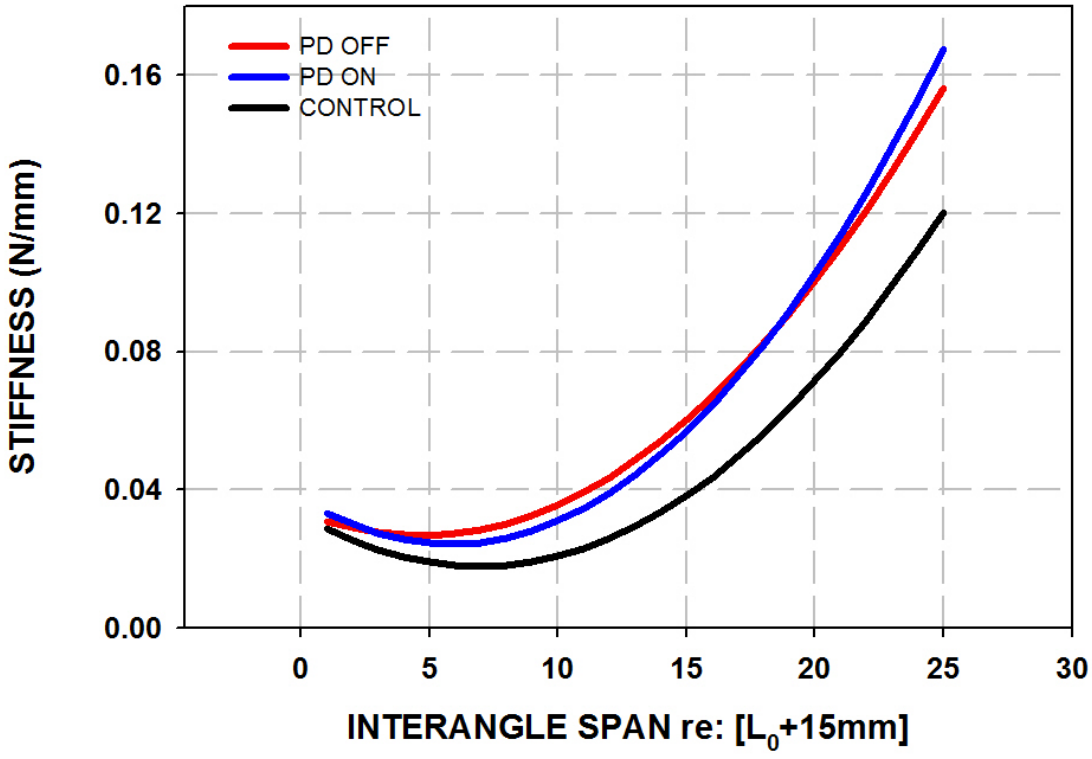

Figure 22. Estimated regression model for PD OFF (red line), PD ON (blue line) and Control (black line).

1.4. Modeling of the perioral stiffness using IEMG RMS levels

The parameter estimates of the perioral stiffness using the adjusted mean OOS*m* and OOI*m* IEMG RMS levels derived from the multilevel regression analysis is shown in Table 10. Perioral stiffness was significantly different between groups. More importantly, there were significant interactions between PD OFF and control groups (*SE*= .001, *t* [2787] = 2.29, $p < 0.05$), and between PD ON and control groups (*SE*= -0.0006, *t* [2787] = -2.00, $p < 0.05$) on the

OOI*m* IEMG RMS level. Because there was significant interaction between groups and IEMG RMS in predicting interangle stiffness, we completed further analysis to determine the three groups' stiffness coefficients at three different IEMG RMS points (lower 95% CI, Mean, and upper 95% CI).

Table 10. Multilevel regression parameter estimates of the OOS*m* and OOI*m* IEMG RMS values on perioral stiffness

Effect	Estimate	*SE*	*p*
Intercept	0.0121	0.0056	0.0438
Group			
PD OFF	0.0104	0.0076	0.2050
PD ON	0.0177	0.0076	0.0485
CONTROL (Reference)	–	–	–
IEMG RMS			
OOS*m* (UL)	0.0030	0.0006	0.0000
OOI*m* (LL)	0.0006	0.0003	0.0677
Group × OOS*m*			
PD OFF	-0.0022	0.0008	0.0072
PD ON	-0.0010	0.0008	0.2446
CONTROL (Reference)	–	–	–
Group × OOI*m*			
PD OFF	0.0010	0.0004	0.0219
PD ON	-0.0006	0.0003	0.0458
CONTROL (Reference)	–	–	–

Figure 23 depicts the adjusted perioral stiffness mean as a function of the OOS*m* IEMG RMS and OOI*m* IEMG RMS. The IEMG RMS 95% confidence intervals are also presented. Overall, the PD OFF and PD ON groups showed greater OOS*m* and OOI*m* IEMG RMS compared to the control group. Pair-wise comparison test showed a significant mean differences between PD OFF and PD ON groups (SIMULATE, $p < .05$) when estimating the perioral stiffness from the OOS*m* and OOI*m* IEMG RMS. Specifically, medication OFF condition

yielded a higher stiffness coefficients compared to ON medication state, at the selected mean of 6.51 uV OOS*m* IEMG RMS level and selected mean of 12.45uV OOI*m* IEMG RMS level. At the upper 95% CI, PD ON group showed approximately normal range of perioral stiffness for both the OOS*m* and OOI*m*. This model indicates a causal relationship between perioral stiffness and IEMG RMS level. This final model is written in Equation 6.

Equation 6. IEMG RMS modeling in predicting perioral stiffness

$$\hat{Y}_{ij} = 0.0121 + 0.0104 \times OFF_j + 0.0177 \times ON_j + 0.0030 \times UL_i + 0.0006 \times LL_i$$
$$- 0.0022 \times (OFF_j \times UL_i) - 0.0010 \times (ON_j \times UL_i) + 0.0010 \times (OFF_j \times LL_i) - 0.006 \times (ON_j \times LL_i)$$

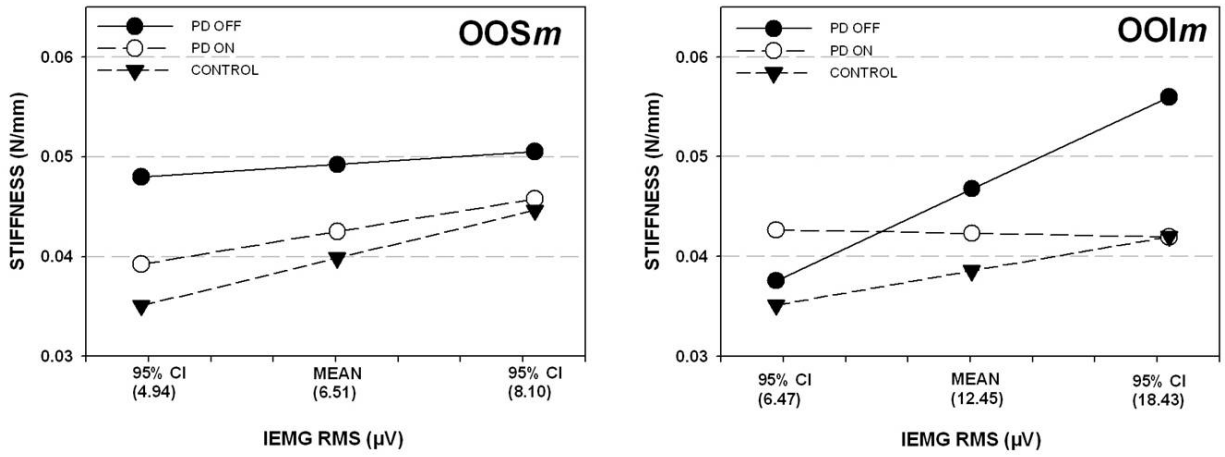

Figure 23. Modeling of the perioral stiffness as a function of the OOS*m* and OOI*m* IEMG RMS levels derived from the multilevel regression equation.
In this figure, a mean value of 12.45μV of the OOI*m* was used to estimate the perioral stiffness. This selected mean value was pooled across 3 groups. The perioral stiffness score is subject to change depending on the mean value of IEMG RMS level selected for this model. The 95% CI was estimated from the multilevel regression to predict stiffness.

Model of the IEMG RMS levels in predicting perioral stiffness: a case study

Figure 24 shows examples of background IEMG RMS values from an elderly control subject (black line) and a PD subject ON (blue line) and OFF(red line) during a series of 5 perioral stiffness stretches. High tonic activity and spiking of the IEMG was a common feature

in all PD subjects but was not seen in the elderly control subjects. Because of this high level of tonic muscle activity, the imposed displacement generated by the OroSTIFF device was approximately 30% less than the control subject (inserted figure). Administration of the anti-PD medications had a significant effect on reducing the tonic IEMGs levels for this particular subject, especially the OOI*m* muscle. This, in turn, reduced the perioral stiffness as the tonic IEMG reduced. As mentioned previously, OOI*m* IEMG RMS consistently shows a higher muscle activity compared to the OOS*m*, consistent with its underlying muscle anatomy and function. We have successfully demonstrated that IEMG RMS affects perioral stiffness.

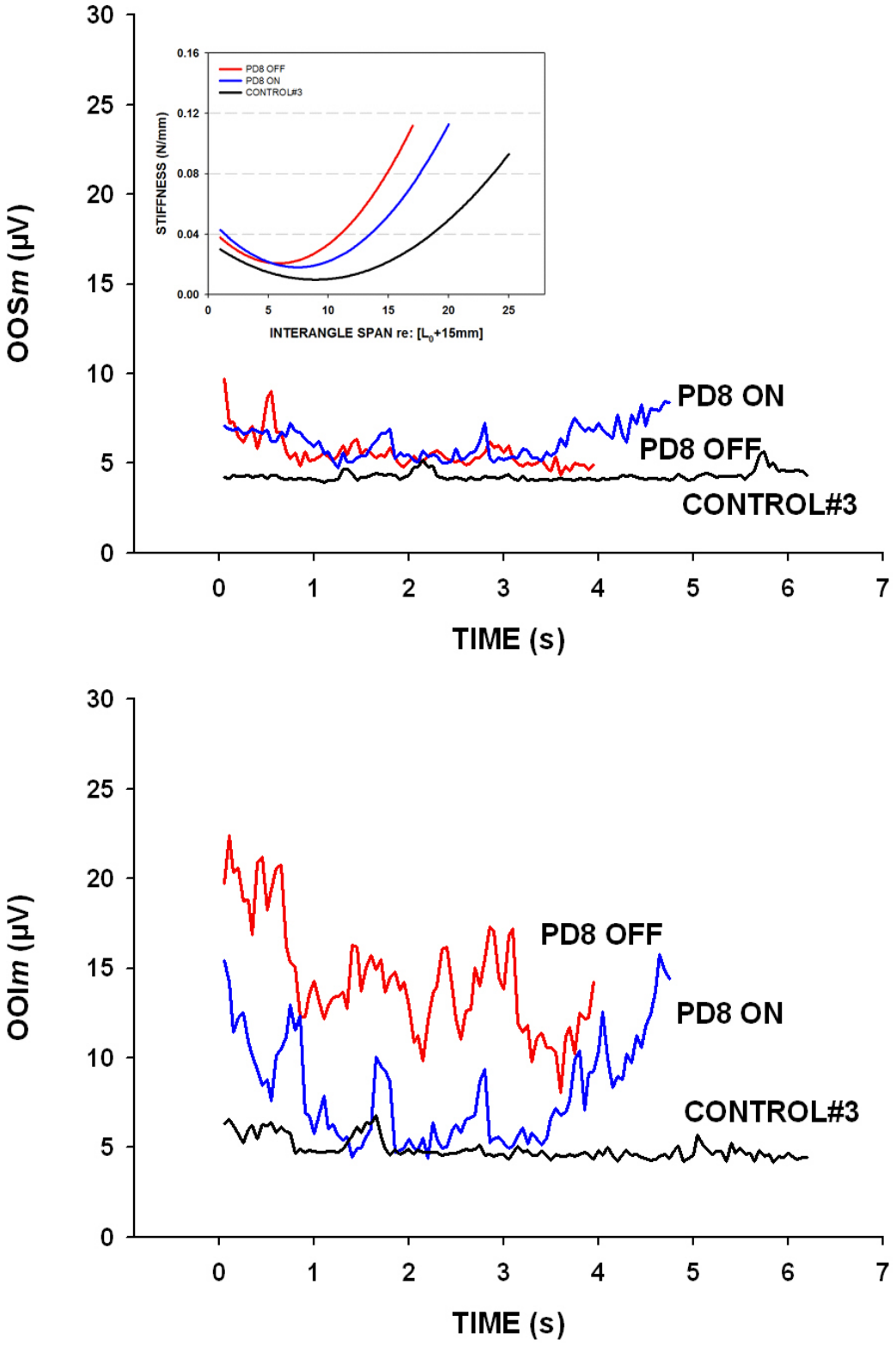

Figure 24. An example from a PD subject to demonstrate the relation between perioral stiffness and IEMG RMS level.

1.5. The relation between perioral stiffness and labial kinematics

Table 11 lists the individual and group means and standard deviations for perioral stiffness score at 12 mm interangle span for normal control and PD subjects. Stiffness scores were correlated with labial amplitudes and velocities across all groups (Control, PD ON, PD OFF), gestures (opening/closing), and speech rates (2Hz, 3.5 Hz, 5 Hz). For control and PD OFF groups, no statistically significant correlations were found between perioral stiffness and any of the DVs (Table 12,Table 13). However, a significant correlation was found in the PD ON group for two DVs. Specifically, there was a significant correlation between perioral stiffness and UL_y opening amplitude, r (8) = .64, p <.05; UL_y closing amplitude, r (8) = .69, p <.05; and UL_y opening velocity, r (8) = .73, p <.05, at 5 Hz speech rate. These findings confirm a relationship (*Pearson's r*, large effect) exist between the perioral stiffness and UL_y movement displacement at high speech rate.

Table 11. Individual and group means and standard deviations for perioral stiffness score at 12 mm interangle span for normal control and PD subjects.

CONTROL	Stiffness @12mm	PD ON	Stiffness @12mm	PD OFF	Stiffness @12mm
1	0.04	1	0.09	1	0.02
2	0.01	2	0.09	2	0.08
3	0.02	3	0.02	3	0.01
4	0.09	4	0.04	4	0.03
5	0.02	5	0.08	5	0.08
6	0.01	6	0.02	6	0.01
7	0.03	7	0.07	7	0.05
8	0.02	8	0.03	8	0.05
9	0.01	9	0.03	9	0.10
10	0.00	10	0.11	10	0.09
MEAN	0.03		0.06		0.05
SD	0.03		0.03		0.03

Table 12. Correlation between perioral stiffness and movement amplitude

Amplitude Variable	Articulator	CONTROL *r*	PD ON *r*	PD OFF *r*
2 Hz opening	UL_y	-0.13	0.18	-0.20
2 Hz opening	$[LL+J]_y$	0.25	-0.25	-0.44
2 Hz closing	UL_y	-0.11	0.32	-0.45
2 Hz closing	$[LL+J]_y$	0.26	-0.27	-0.43
3.5 Hz opening	UL_y	-0.04	0.20	-0.06
3.5 Hz opening	$[LL+J]_y$	0.30	-0.21	-0.19
3.5 Hz closing	UL_y	-0.06	0.26	-0.07
3.5 Hz closing	$[LL+J]_y$	0.29	-0.22	-0.19
5 Hz opening	UL_y	-0.33	0.64*	0.26
5 Hz opening	$[LL+J]_y$	0.11	-0.01	-0.14
5 Hz closing	UL_y	-0.32	0.69*	0.22
5 Hz closing	$[LL+J]_y$	0.12	-0.02	-0.15

* denotes significance, $p < .05$

Table 13. Correlation between perioral stiffness and movement velocity

Velocity Variable	Articulator	CONTROL *r*	PD ON *r*	PD OFF *r*
2 Hz opening	UL_y	-0.39	0.34	-0.14
2 Hz opening	$[LL+J]_y$	0.45	-0.27	-0.36
2 Hz closing	UL_y	0.21	0.25	-0.61
2 Hz closing	$[LL+J]_y$	-0.11	-0.03	-0.28
3.5 Hz opening	UL_y	0.01	0.31	0.06
3.5 Hz opening	$[LL+J]_y$	0.36	-0.27	-0.18
3.5 Hz closing	UL_y	0.07	0.30	-0.18
3.5 Hz closing	$[LL+J]_y$	0.19	-0.12	-0.18
5 Hz opening	UL_y	-0.27	0.73*	0.14
5 Hz opening	$[LL+J]_y$	0.23	-0.18	-0.23
5 Hz closing	UL_y	-0.38	0.57	-0.14
5 Hz closing	$[LL+J]_y$	0.20	-0.09	-0.22

* denotes significance, $p < .05$

Analysis 2a: Labial Kinematics

2.1. Compare UL vs. LL+J movement variables

Means and standard deviations of the movement amplitude and velocity variables are shown in Appendix G (Control), Appendix H (PD ON), and Appendix I (PD OFF). Significant

differences were found between the UL and LL+J for all x-y-z dimensions for all groups, $p <$ 0.001, implying that UL and LL+J were independent structures. The paired samples *t*-test for the UL and LL+J at x-y-z dimensions for all groups is listed in Appendix J.

2.2. Does UL and LL+J amplitude differ between groups, gestures, and speech rates?

With the use of Wilks' criterion, the combined DVs were significantly affected by both groups, F (12, 314) = 14.57, $p < .001$, and speech rate, F (12, 314) = 3.15, $p < .001$, but not by their interactions, F (24, 548.92) = 1.11, $p = .33$. Gestures (opening vs. closing) did not affect the combined DVs, F (6, 157) = .16, $p = .99$. A summary of the Wilks' lambda test is listed in Appendix K. Overall, no significant interaction was found between all IVs (groups, gestures, speech rates).

Follow-up univariate analyses of variances found significant group effects on each of the DVs, $p < .001$ (Appendix L). However, neither opening nor closing gestures had a significant effect on any of the DVs. Significant effects of speech rates were found in the UL_z [F (2, 314) = 6.79, $p < .05$, $\eta_p^2 = .08$]; $[LL+J]_y$ [F (2, 314) = 12.76, $p < .001$, $\eta_p^2 = .14$]; and $[LL+J]_z$ [F (2, 314) = 3.32, $p < .05$, $\eta_p^2 = .04$]. No significant interactions between groups, gestures, and speech rates were observed. The 3D opening/closing gestures for the UL and LL+J movement displacements are represented in Appendix M and Appendix N.

Group effect

Post-hoc comparison across groups showed significant difference on each of the DVs when comparing the mean amplitude of PD ON vs. control, and PD OFF vs. control (Figure 25). However, only the $[LL+J]_y$ differed significantly between the PD ON and PD OFF groups (Tukey's HSD, $p < .05$). Overall, the inferior-superior (y) dimension appeared to be the dominant dimension for speech production. PD participants showed a significantly lower

movement compared to those in the control group, indicating the presence of hypokinesia in the labial structure.

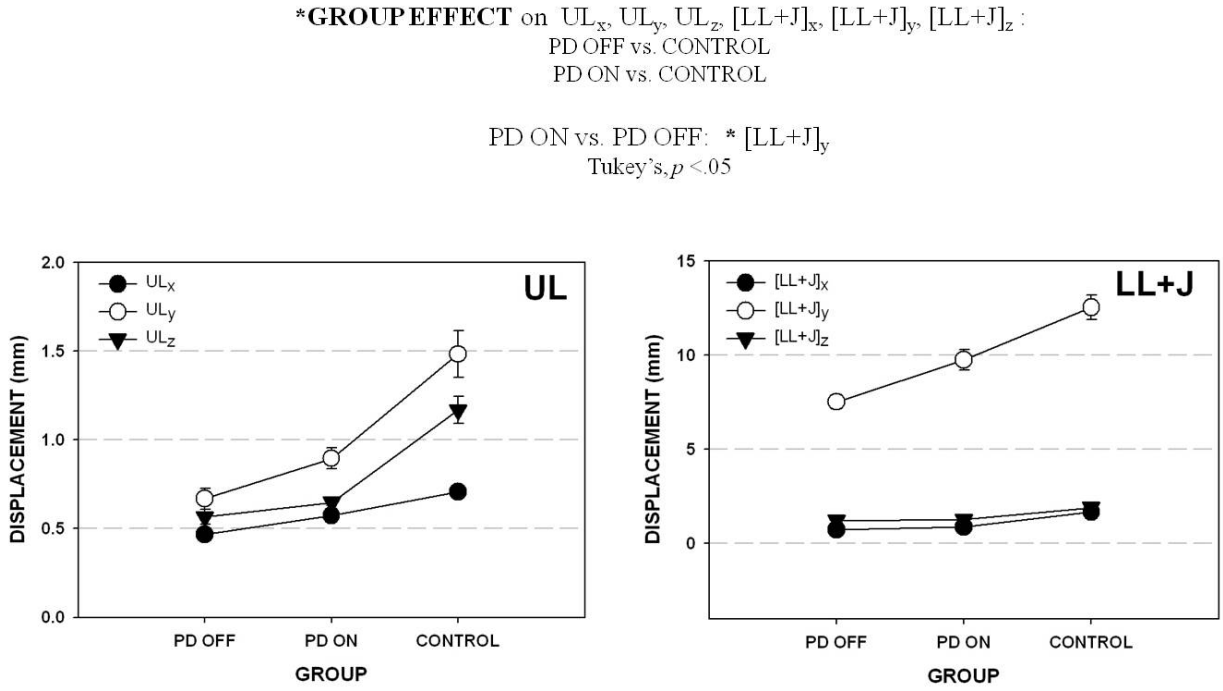

Figure 25. The UL and [LL+J] movement displacement as a function of group.

Speech rate effect

Post-hoc comparison across speech rates showed significant differences between 2 Hz and 5 Hz, and between 3.5 Hz and 5 Hz in the UL_z and $[LL+J]_y$ structures (Tukey's HSD, $p < .05$). As seen in Figure 26, the movement displacement decreased as speech rates increased, especially in the $[LL+J]_y$. Again, the $[LL+J]_y$ (inferior-superior) showed a greater main effect compared to the anterior-posterior (x) and medial-lateral (z) dimensions, indicating a better option to differentiate main effect within and between groups.

These findings indicate that as speaking rate increased to 5 syllables/sec, PD subjects produced syllable trains with labial movements having significantly lower displacement amplitudes. That is, their lip movements became more hypokinetic. At a slower speaking rate

(i.e., 3.5 Hz), however, PD OFF $[LL+J]_y$ displacement showed the greatest reduction (42%) when compared to control.

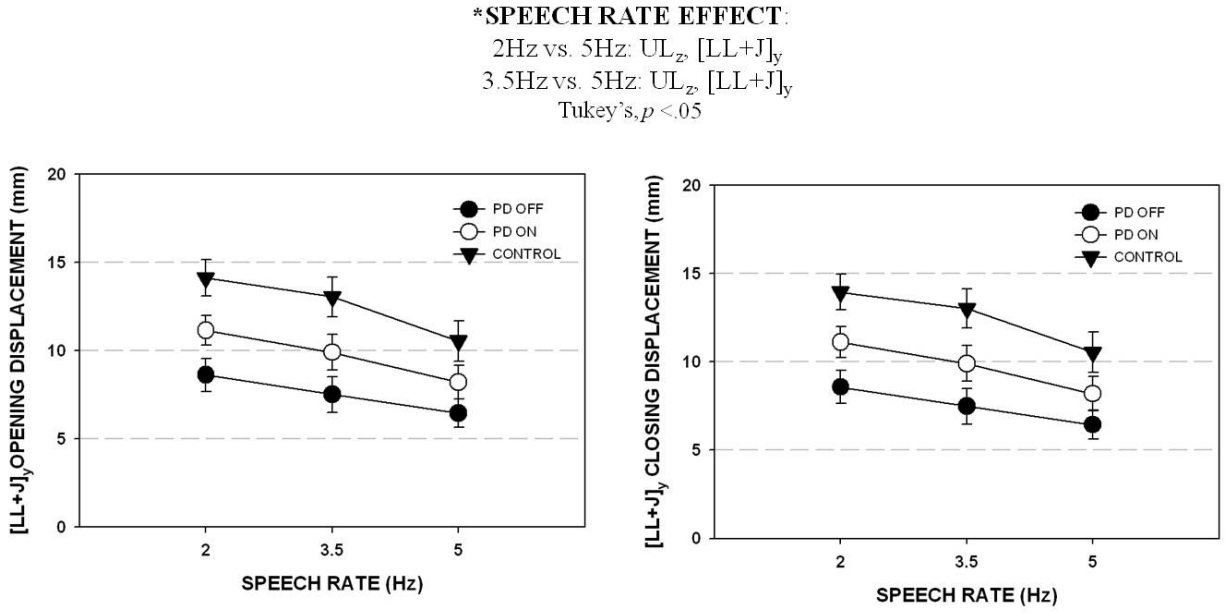

Figure 26. $[LL+J]_y$ movement displacement as a function of speech rate.

2.3. Does UL and LL+J velocity differ between groups, gestures, and speech rates?

With the use of Wilks' criterion, the combined DVs were significantly affected by both groups, F (12, 314) = 11.03, $p < .001$, and speech rates, F (12, 314) = 2.14, $p < .05$, but not by their interactions, F (24, 548.92) = 1.22, $p > .05$. Similar to the amplitude findings, neither opening nor closing gestures had any effect on these six DVs, F (6, 157) = 1.29, $p = .27$. A summary of the Wilks' lambda test is listed in Appendix O. Overall, no significant interaction was found between all IVs (groups, gestures, speech rates).

Univariate analyses of variances found significant group effects on all of the DVs, $p < .001$ (Appendix P). Significant effects of speech rate were found in the UL_y [F (2, 314) = 4.36, $p < .05$, $\eta_p^2 = .05$]; UL_z [F (2, 314) = 4.59, $p < .05$, $\eta_p^2 = .05$]; $[LL+J]_x$ [F (2, 314) = 3.17, $p < .05$,

$\eta_p^2 = .04$], and $[LL+J]_y$ [F (2, 314) = 7.97, $p < .05$, $\eta_p^2 = .09$]. The 3D opening/closing gestures for the UL and LL+J movement velocities are represented in Appendix Q and Appendix R.

Group effect

Post-hoc comparison across groups showed significant difference of all DVs when comparing the mean velocity of PD ON vs. control, and PD OFF vs. control (Figure 27). However, only the $[LL+J]_y$ differed significantly between the PD ON and PD OFF groups (Tukey's HSD, $p < .05$). PD OFF group consistently showed a reduction of 30%-48% velocities movement for both opening and closing gesture when compared to control. This trend was similar with the movement displacement data set, indicating that $[LL+J]_y$ excursion not only served as the primary articulator during speech, but also appeared to be a better variable to distinguish the group differences, even within the same subject.

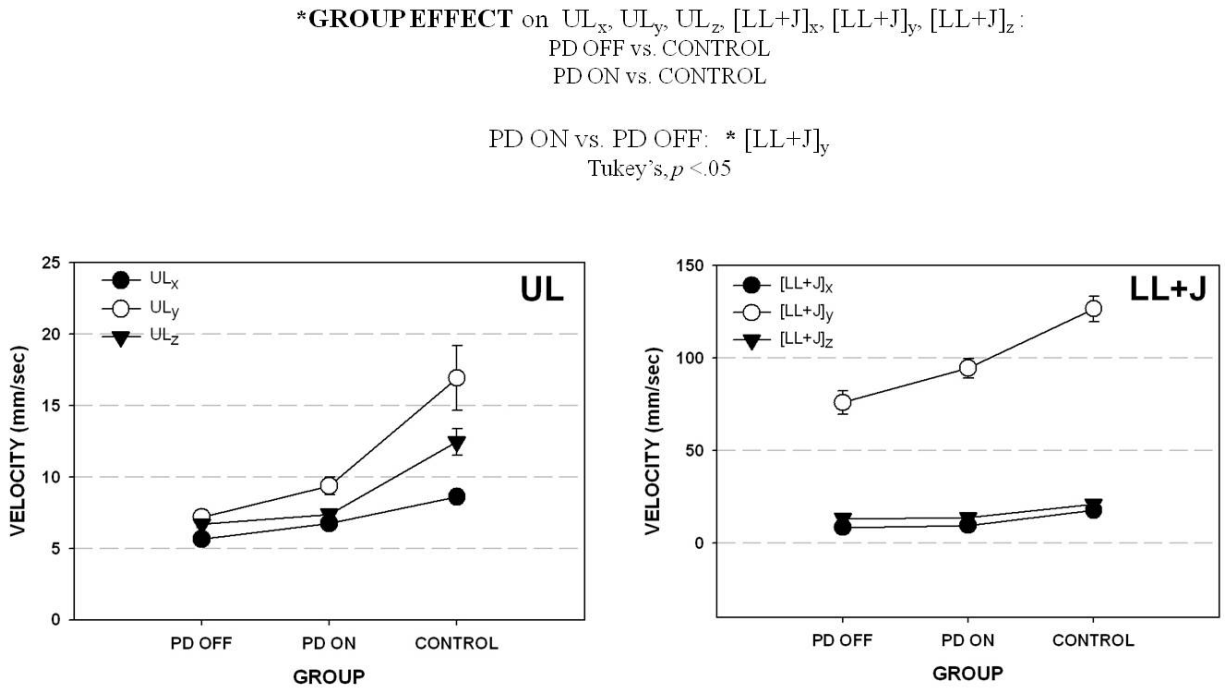

Figure 27. The UL and $[LL+J]_y$ movement velocity as a function of group.

Speech rate effect

Post-hoc comparison across speech rates showed significant differences between 2 Hz and 3.5 Hz in the UL_y and UL_z. Significant differences were also found in the UL_y, UL_z, $[LL+J]_x$, and $[LL+J]_y$ structures at 2 Hz and 5 Hz (Tukey's HSD, $p < .05$) (Figure 28). In fact, this trend was found in the movement displacement, when comparing 2 Hz and 5 Hz rate, confirming that velocity increased with increased speech rates while amplitude decreased as speech rates increased.

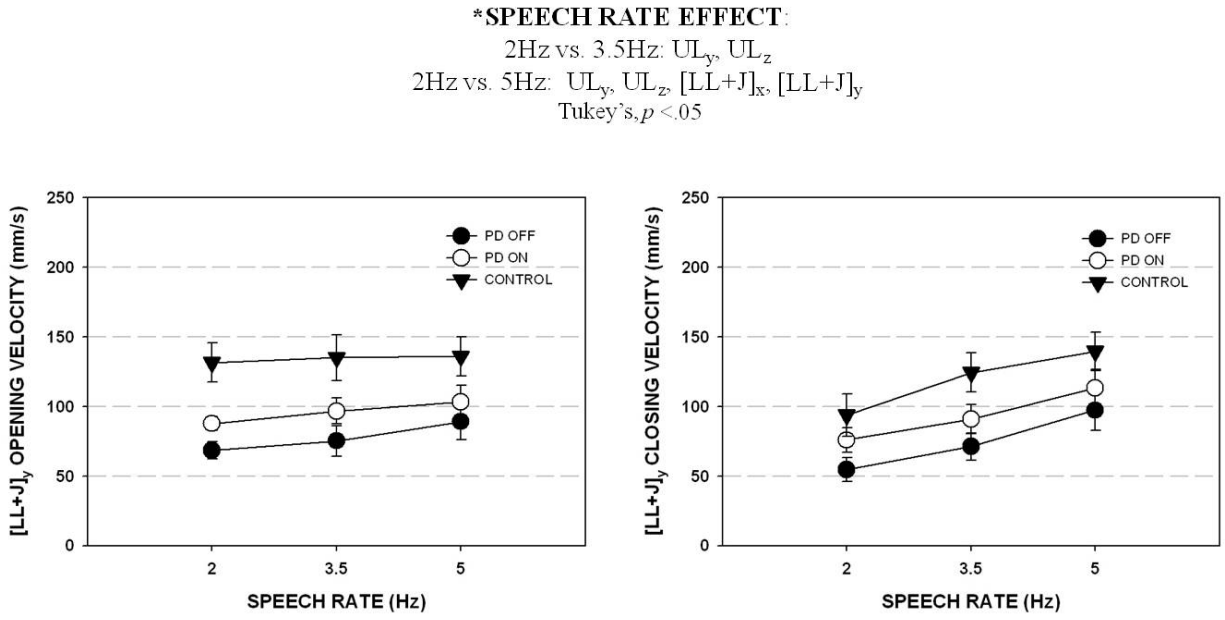

Figure 28. $[LL+J]_y$ movement velocity as a function of speech rate.

2.4. Relation between movement amplitude and velocity

Although peak velocities were lower for the PD than the control subjects, velocity changes were consistent with reduced movement amplitude. In Figure 29, the individual data points for opening/closing UL_y and $[LL+J]_y$ displacement and velocity are plotted (x-axis, displacement; y-axis, velocity). Each data point in these figures represents a lip movement to produce the syllable "pa" averaged across 30 repetitions for each participant. As these figures

suggest, the majority of the individuals with PD (ON-open circles, OFF-filled circles) are clustered in the bottom left quadrant of the graph denoting lower velocity and smaller displacements compared to the control participants (filled triangles). The tight clustering of data points for the PD subjects reflects the limited amount of lips displacement and velocity kinematics for PD compared to control. Comparison of these graphs shows a reduced range of movement for the PD group, particularly during OFF state. These results confirmed that after Levodopa consumption, PD participants increased their movement space toward normal range, but they were still not able to meet the normal range of movement.

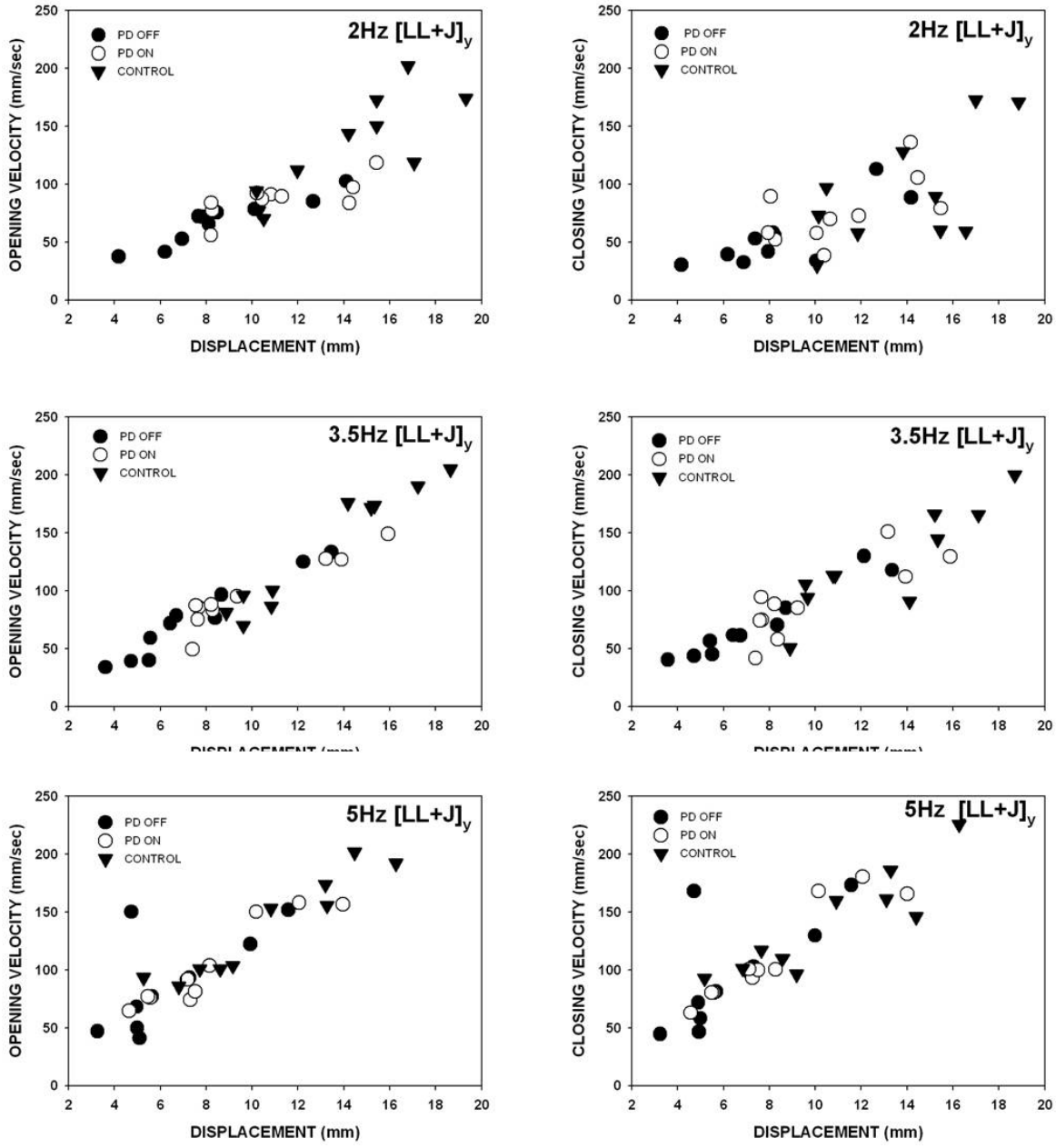

Figure 29. Individual data points for opening/closing UL_y and $[LL+J]_y$ displacement as a function of velocity at 3 speaking rates.

Analysis 2b: Spatiotemporal Stability (STI)

2.5. Does "pa" STI differ between group and speech rates?

The means and standard error bars for the "pa" syllable STI of the UL_y and $[LL+J]_y$ are presented in Figure 30 (see Appendix S for STI means (+*SD*) table). Using the Wilks' Lambda

criterion, the group effect for STI was not significant, F (4, 160) = .73, p = .58. Although significant main effect was found in the speech rate, F (4, 160) = 10.63, p < .001, there was no significant interaction between groups and speech rates, F (8, 160) = .50, p = .86. The main effect of speech rates was found in the $[LL+J]_y$ structure, F (2, 160) = 13.83, p < .001, η_p^2= .25. These findings indicate that both PD and control groups showed a linear trend of increased movement variability as speech rates increased (i.e., PD OFF, 2 Hz= 24.68, 5 Hz = 32.07; Control, 2 Hz= 24.23, 5 Hz=30.84). As shown in Figure 31, the majority of the PD participants had variability indexes similar to those in the control group, denoting similar spatiotemporal motor stability patterns among groups. This result is consistent with the perceptual speech intelligibility test that the majority of the PD subjects demonstrated normal-mild dysarthria.

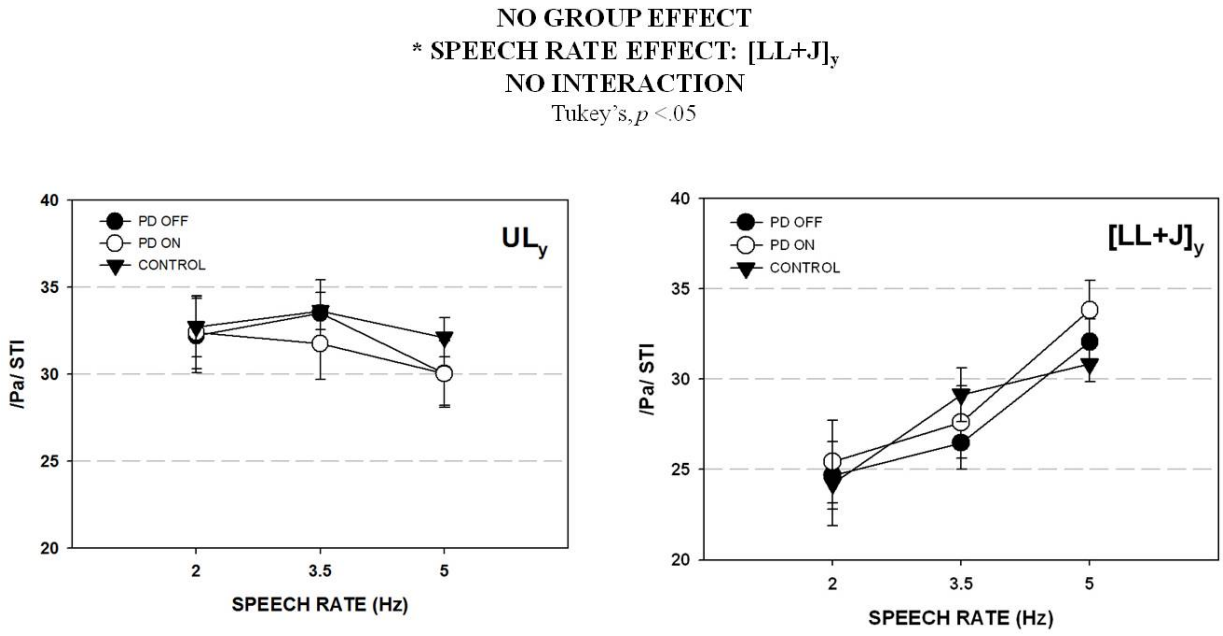

Figure 30. Means and standard error bars for the UL_y and $[LL+J]_y$.

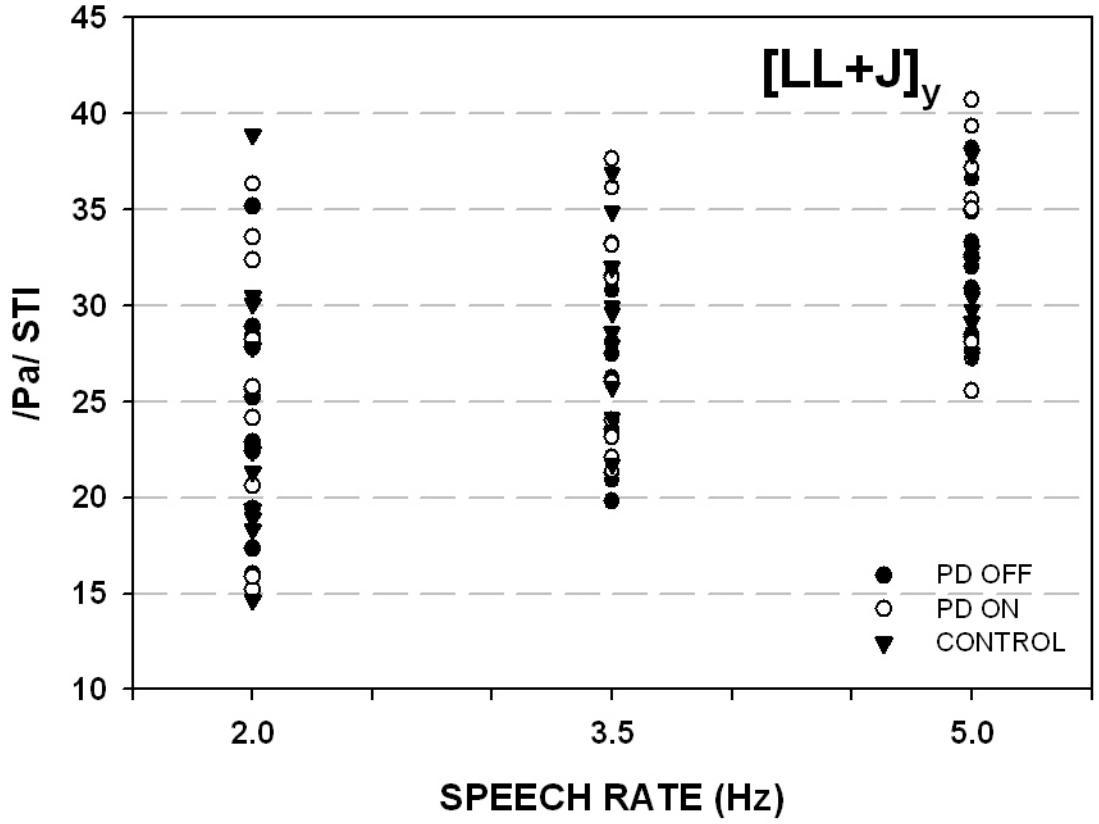

Figure 31. Individual STI value for the $[LL+J]_y$ as a function of speech rate.

2.6. Does Rainbow STI differ between groups and speech rates?

The STI means and standard deviations of the PD participants and control at each speech rate are represented in Appendix T. Using the Wilks' lambda test, there was no significant group effect, F (4, 160) = 2.28, p = .06, or speech rate effect, F (4, 160) = 1.41, p = .023, on either the first or second phrases of the rainbow passage (Figure 32). Although the control group tended to show a higher STI value on the second phrase as speech rates increased, this observation was not significant, UL_y, F (2, 160) = 1.53, p = .22, η_p^2= .04, $[LL+J]_y$, F (2, 160) = 2.60, p = .008, η_p^2= .06. These results are consistent with the "pa" STI findings that PD participants showed motor

control speech stability that was similar to the control group, regardless if they produced the first or second phrase of the rainbow passage.

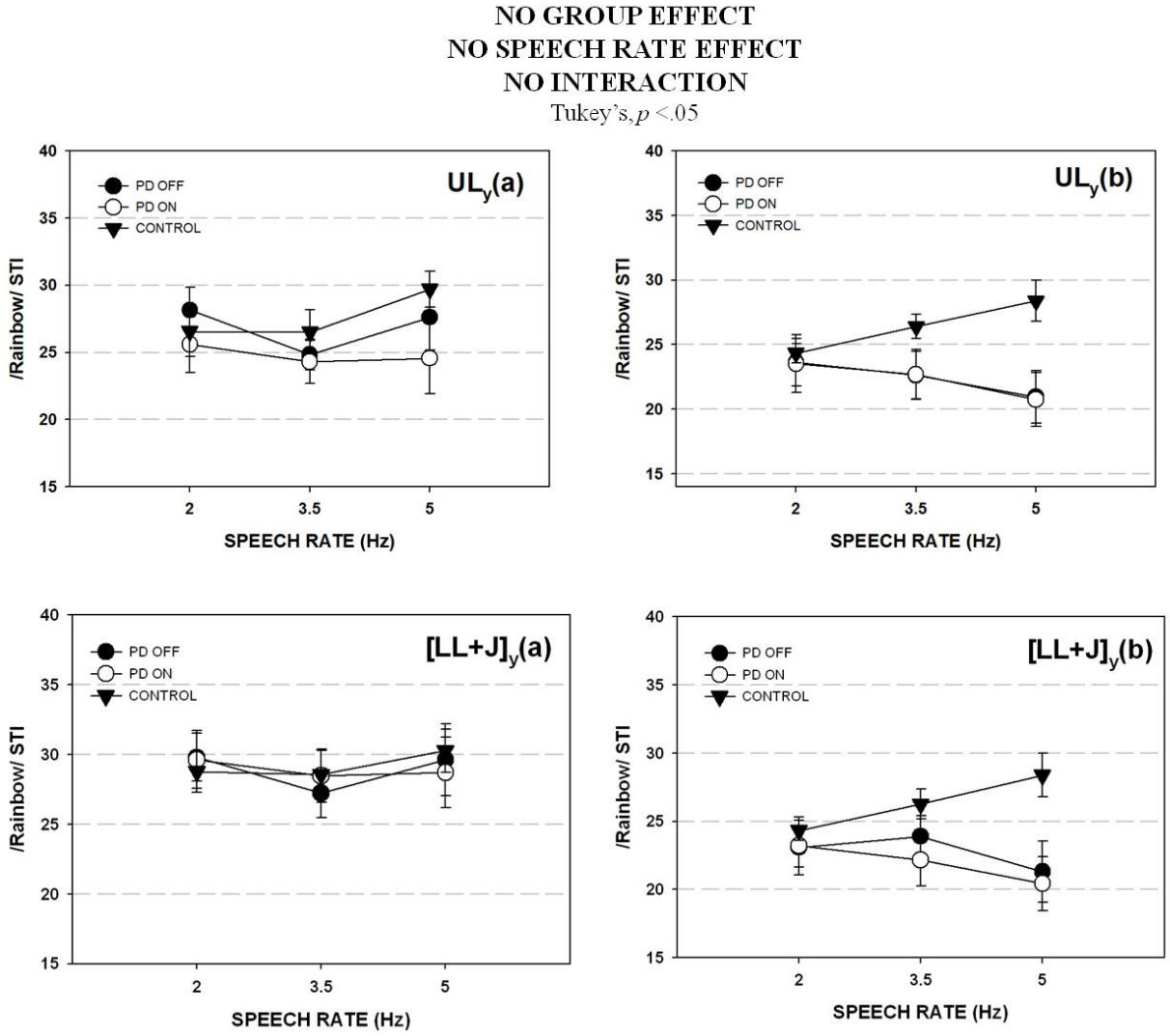

Figure 32. Mean and standard error bars for the UL_y and $[LL+J]_y$ for the first phrase of rainbow passage [UL_y(a), $[LL+J]_y$ (a)] and second phrase of the rainbow passage [UL_y(b), [LL+J $_y$ (b)].

Analysis 3: EMGs

3.1. Reciprocity of muscles (Theta)

Using the Wilks' lambda test, the combined DVs were not significantly affected by the group (Control, PD ON, PD OFF), F (8, 156) = .88, p = 0.54, or speech rate, F (8, 156) = 1.46, p = .17. In addition, no interaction was found between the group and speech rate, F (16, 238.93) =

.52, $p = .94$. Table 14 lists the summary of the IEMG DVs results. These findings indicated that there were no significant differences on the temporal aspect of the IEMG muscle activation level between groups or speech rates.

Table 14. Summary of the Univariate Analyses of Variance: Reciprocity of muscles (Theta)

Source	*df*	*F*	*p*	*Partial* η^2
DV=OOI*m* re: OOS*m*				
Group	2	1.15	0.3213	0.0276
Speech Rate	2	1.22	0.3006	0.0292
Group × Speech Rate	4	0.34	0.8508	0.0165
DV=DLI*m* re: OOS*m*				
Group	2	0.45	0.6381	0.0110
Speech Rate	2	0.54	0.5834	0.0132
Group × Speech Rate	4	0.18	0.9465	0.0090
DV=DLI*m* re: OOI*m*				
Group	2	0.73	0.4850	0.0177
Speech Rate	2	0.22	0.8070	0.0053
Group × Speech Rate	4	0.06	0.9935	0.0029
DV=DLI*m* 2nd peak re: OOS*m*				
Group	2	0.14	0.8677	0.0035
Speech Rate	2	1.21	0.3043	0.0289
Group × Speech Rate	4	0.13	0.9728	0.0062

3.2. Amplitude magnitude of muscles (Rho)

Using Wilks' lambda test, the combined DVs were not significantly affected by the group (Control, PD ON, PD OFF), F (8, 156) = 1.46, $p = 0.17$, and speech rate, F (8, 156) = .71, p = .68, on the IEMG Rho. No interaction between groups and speech rates were found, F (16, 238.93) = .42, $p = .98$.

Univariate analysis of variance showed the DLI*m* re: OOI*m* was significantly affected by group, F (2, 156) = 3.60, $p < .05$, $\eta_p^2 = .08$ (Table 15). However, there was no speech rate effect, F (2, 156) = .48, $p = .62$, $\eta_p^2 = .01$, or interaction between group and speech rate, F (4, 238.93) =

.21, p = .93, η_p^2= .01 when comparing the DLI*m* re: OOI*m* Rho. Post-hoc comparison showed the amplitude of DLI*m* re: OOI*m* was significantly different in the PD ON vs. control group (Tukey's HSD, $p < .05$), whereby the control group showed higher IEMG amplitude compared to those in the PD ON group. Overall, the PD group showed similar reciprocity patterns compared to those of control subjects in the following muscle pairs: DLI*m* re: OOS*m*, DLI*m* 2nd peak re: OOS*m*. In addition, PD group showed similar coactivation of the OOS*m* and OOI*m* as those of the control subjects. The only significant difference between the PD and normal groups was observed in the DLI*m* re: OOI*m*, whereby PD group showed a significant reduction in the amplitude magnitude of these muscles.

Table 15. Summary of the Univariate Analyses of Variance: Amplitude magnitude of muscles (Rho)

Source	*df*	*F*	*p*	*Partial* η^2
DV=OOI*m* re: OOS*m*				
Group	2	1.18	0.3136	0.0282
Speech Rate	2	0.40	0.6719	0.0098
Group × Speech Rate	4	0.06	0.9940	0.0028
DV=DLI*m* re: OOS*m*				
Group	2	0.70	0.4995	0.0170
Speech Rate	2	0.03	0.9676	0.0008
Group × Speech Rate	4	0.19	0.9448	0.0091
DV=DLI*m* re: OOI*m*				
Group	2	3.60	0.0317*	0.0817
Speech Rate	2	0.48	0.6198	0.0117
Group × Speech Rate	4	0.21	0.9334	0.0102
DV=DLI*m* 2nd peak re: OOS*m*				
Group	2	0.14	0.8677	0.0035
Speech Rate	2	1.21	0.3043	0.0289
Group × Speech Rate	4	0.13	0.9728	0.0062

Figure 33 illustrates an example of integrated DLI*m* muscle activity from a PD subject during OFF state and a control subject during "pa" syllables production. Note that this particular PD subject demonstrated a significant reduction in the DLI*m* amplitude (approximately 4 times lower) when compared to the control's muscle activation level. More than 50% of the participants in this current study showed this muscle activation pattern.

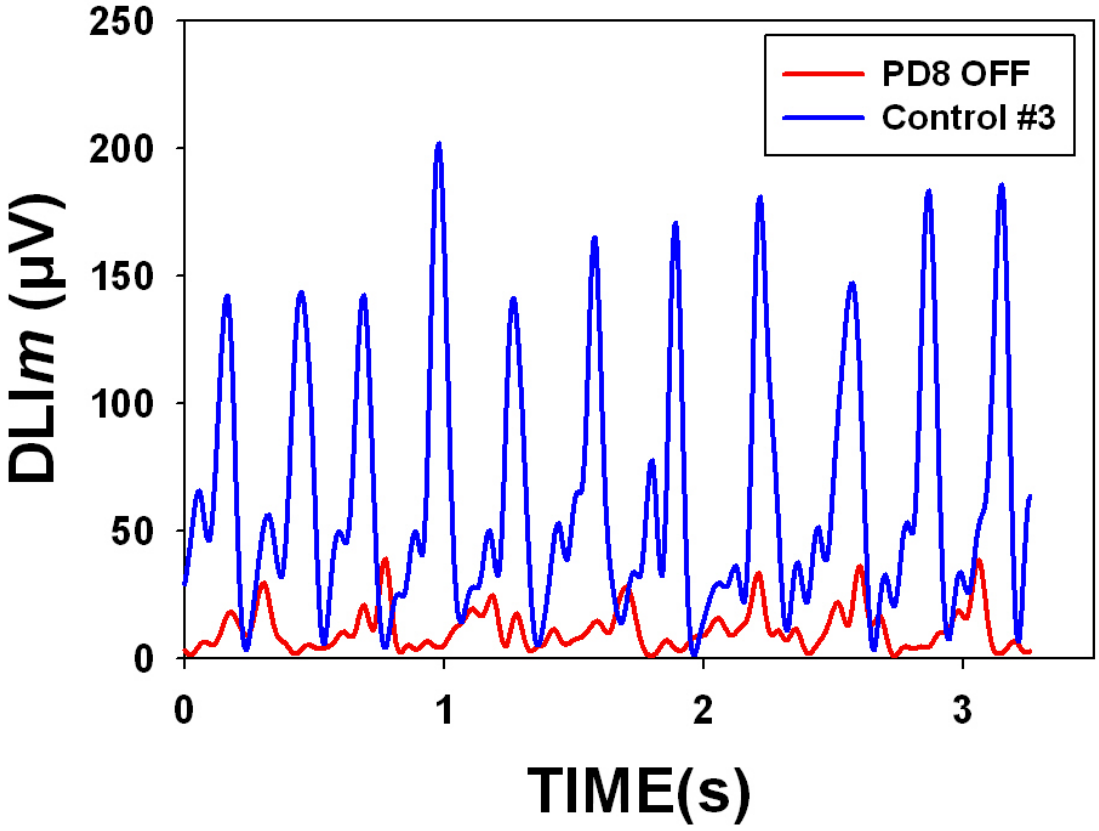

Figure 33. An example of integrated DLI*m* muscle activity from a PD subject and a control subject.

The overall DLI*m* re: OOI*m* from each group were averaged and presented in polar plot format (Figure 34). As seen in Figure 34, PD subjects showed at least 50% of reduction in the amplitude magnitude (blue asterisk vs. red asterisk, green asterisk vs. red asterisk), whereby the

mean amplitude of muscle consistently range between 0-1.5 radian (versus 1.5-2 radian for control).

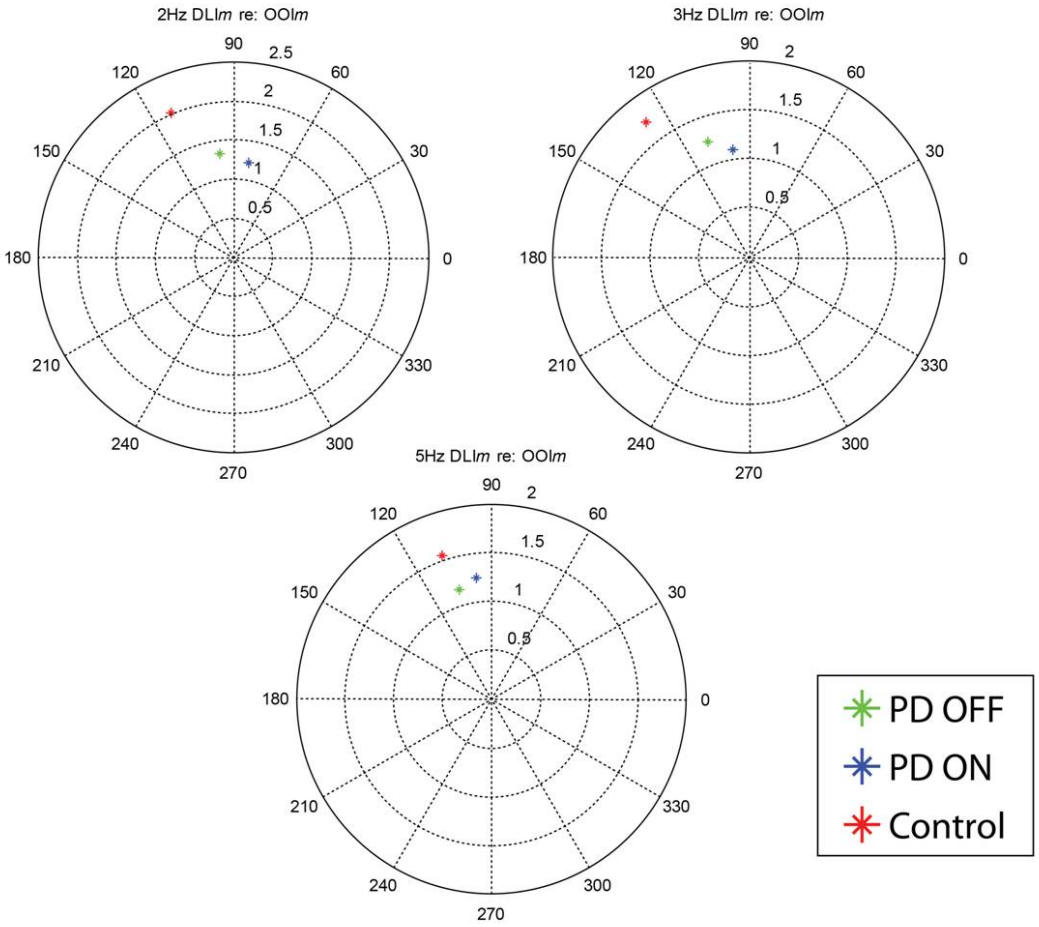

Figure 34. Polar plots for DLI*m* re: OOI*m* for 3 speaking rates.

3.3. Characterization of perioral IEMG muscles activity patterns

Figure 35 shows the IEMG recordings from a healthy control (Panel A) and a patient with PD (Panel B and C) producing "pa" syllables at 3.5 Hz. There are three main differences in the IEMG patterns produced by PD speakers compared to the elderly healthy group. First, the temporal patterns of the muscle activity were similar in both PD and control groups, indicating that PD speakers were able to select the appropriate muscle groups and activation patterns to perform simple "pa" syllables production. The IEMG patterns in the muscles of the patient with

PD, however, differed from those of the healthy control in that the magnitude of IEMG amplitude was significantly reduced (compare Panel A-DLI*m* with Panel C- DLI*m*, pointed with red arrows). Specifically, this control shows elevated DLI*m* amplitude, approximately 3 times greater than PD ON subjects. Administration of anti-PD medications increases the DLI*m* amplitude in this patient; however, the amplitude is still 50% below the normal levels. This pattern of reduced amplitude magnitude was seen in 2 Hz, 3.5 Hz and 5 Hz speech rates. Our findings showed a significant difference in the DLI*m* re: OOI*m* muscles between PD ON vs. control group.

Second, the IEMG activation pattern for the DLI*m* during "pa" production is accompanied by a primary peak followed by a secondary peak in the elderly control group. However, the speakers with PD tend to produce a primary peak follows by secondary and tertiary peaks, with extent reduction magnitude in amplitude (as shown in panel B-C, pointed with black arrows). This pattern shows that the IEMG pattern that occurred once in the control group was repeated several times in the patients with PD. Although multiple peaks characteristics were observed in the group, statistical analyses showed non-significant differences between groups and muscles.

Another observation from this experiment depicted in Figure 35, shows the patterns of co-activation of the agonists and antagonists muscles in PD patient. The OOS*m* and OOI*m* are known to assist during lip closing gestures, while the DLI*m* activate during lip opening gestures. During speech production of "pa", the OOS*m,* OOI*m* and DLI*m* should activate reciprocally. This reciprocity pattern is illustrated clearly in Figure 35 (black line, Panel A). In contrast, the OOS*m,* OOI*m* and DLI*m* in PD subjects were activated simultaneously (Figure 35, Panel B-C). In PD patients, less synchronized activity of both agonists and antagonists muscles in simple

ballistic movements were observed (Wiesendanger & Ruegg, 1978). However, we found no significant differences between the DLI*m* re: OOS*m*, DLI*m* re: OOI*m*, DLI*m* 2nd peak re: OOI*m*, indicating that temporal reciprocity between these muscles were preserved in these patients.

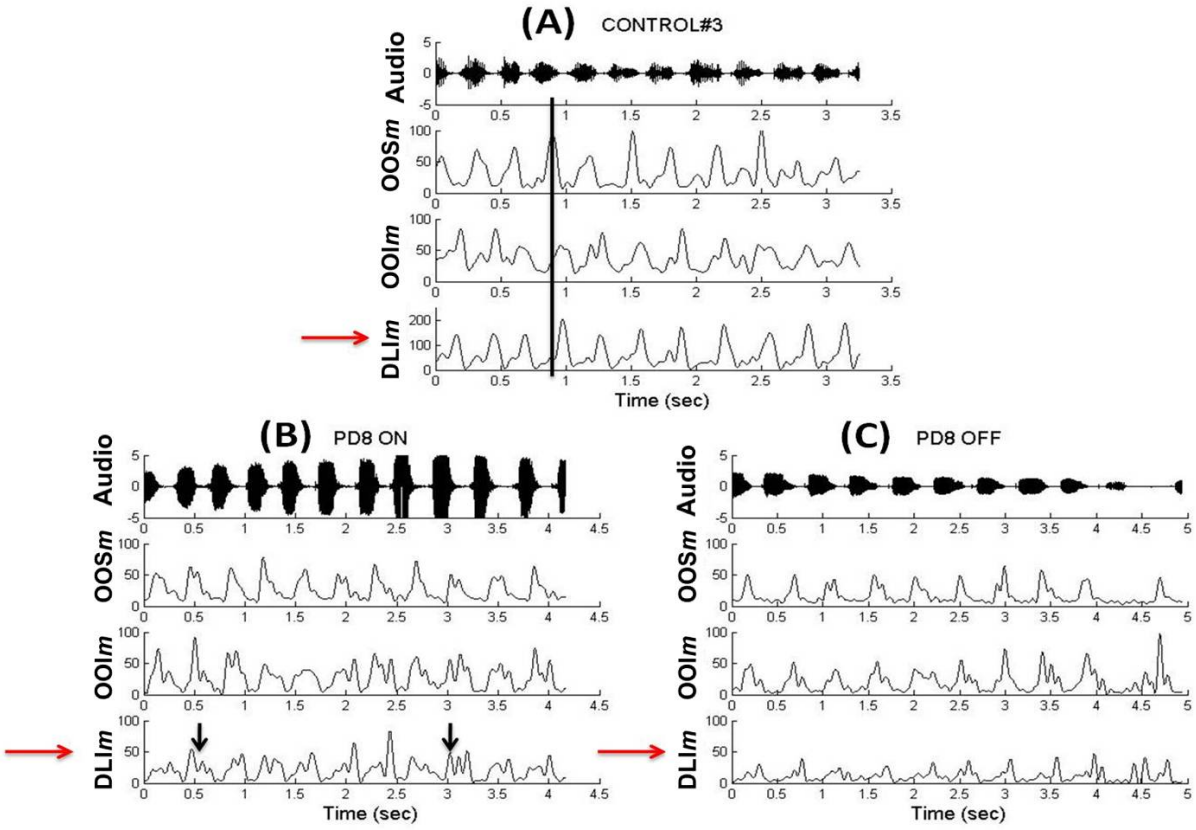

Figure 35. Patterns of integrated IEMG activity in the OOS*m*, OOI*m*, and DLI*m* muscles during "pa" syllables produced by (A) Control, (B) PD ON, (C) PD OFF groups at 3.5 Hz.

CHAPTER IV: DISCUSSION

The results of this investigation provide a quantitative description of the perioral stiffness in relationship to labial kinematics and associated IEMG patterns in individuals with PD. Specifically, at the biomechanical level, perioral stiffness was different between normal controls and individuals with PD, which is consistent with existing descriptions that characterize clinical rigidity symptoms in limb motor control. When there was a high level of perioral stiffness, there was also increased IEMG activity at rest. It was also determined that elevated perioral stiffness is negatively correlated to the amplitude of labial movement in individuals with PD. These findings provide evidence of a cause-effect relation between perioral stiffness and labial hypokinesia. Pharmacological effect was also noted in perioral stiffness, labial kinematics, and IEMGs characteristics. There was a direct relationship between speech rate and labial kinematic measurements across groups. These and other findings are consistent with a variety of motor theories. The remainder of this section contains the concluding statements about the results, each followed by a discussion.

A1. Orofacial Biomechanics: Tonic IEMG RMS during perioral stretch

1. Linear function of OOS*m* and OOI*m* IEMG RMS confirmed the non-participatory nature of the experimental task.

Because PD is a central mechanism disease, the design of this current study was to test the non-participatory ("passive") stiffness during perioral stretches. Electrophysiological monitoring of perioral IEMG was used to verify that voluntary and/or reflexive muscle activation did not contaminate the stiffness measure. Both OOS*m* and OOI*m* IEMG RMS activity levels were remarkably stable across interangle span for all groups. This confirmed the absence of reflex activity during perioral stretches and suggests that the growth in stiffness as a function of interangle span is presumably due to a combination of elastic forces generated by muscle and

connective tissue, and abnormally high levels of central tonic drive to motoneurons within the facial motor nucleus.

2. Modulation of the tonic IEMG muscles activity by Levodopa treatment supports the idea of up-regulation in the basal ganglia circuit.

Tonic IEMG muscles activity presented in the perioral system can be modulated by dopaminergic treatment in individuals with PD. At first, we demonstrated the classic notion that PD patients showed excessive IEMG activity at rest. We found that, IEMG activity in PD patients was greater than those in the control group. This difference was increased nearly three-fold after the administration of prescribed Levodopa treatment, especially in the OOI*m*. This shows an up-regulation of the dopaminergic treatment effects in the basal ganglia-cortical circuit, whereby administration of dopamine reduced excitation of GPi/SNr and activation of thalamocortical activity, in turn, an increased excitation to the cortical cortices.

The increased of OOI*m* IEMG after Levodopa treatment seen in this current investigation may positively impact postural control for the orofacial structure, as commonly observed in the limb muscles. One of the motor signs resulting from PD is difficulty in limb postural control (Cioni, Richards, Malouin, Bedard, & Lemieux, 1997), which can be improved by dopaminergic treatment (Frank, Horak, & Nutt, 2000). In fact, an injection of the monoamine precursor L-Dopa on rats resulted in a marked increase in postural tonic IEMG activity in extensor muscles (Navarrete, Slawinska, & Vrbova, 2002). This increase in postural extensor tonus was sufficient for the rats to maintain a standing posture with the pelvis raised above ground. Similar to the muscular stiffness that is essential to the regulation of posture and interjoint coordination (Nichols, 2002), skilled motor behavior, such as speech, also requires muscular stiffness in order to achieve greater prediction of movement and end-point accuracy. Hence, basal ganglia, in

addition to regulating muscle tone and energizing muscle activation, also are critical for postural function in the orofacial system.

When comparing the upper and lower lip IEMGs for PD and control participants, the OOI*m* consistently showed greater tonic activity compared to the OOS*m*. This observation is consistent with the antigravity function of the OOI*m* for postural control of the lower 1/3rd of the face (Barlow & Rath, 1985; Seibel & Barlow, 2007). A similar pattern of antigravity postural control is apparent in the mandibular system where stiffness is the sum of forces arising from both passive viscoelastic properties of connective tissue and muscle (Peck, Sooch, & Hannam, 2002) and descending input to the trigeminal motor nucleus to produce tonic activity among the jaw-closing muscles (Goldberg & Derfler, 1977).

A2. Orofacial Biomechanics: Modeling of the perioral stiffness

3. Multilevel regression modeling of the perioral stiffness shows significant differences in perioral stiffness across the groups, indicating that there is clinical rigidity affecting both the limb and orofacial muscles of individuals with PD.

The findings on perioral stiffness in the present study are consistent with previous studies on orofacial and limb muscular rigidity in PD patients. Perioral stiffness in the upper and lower lips was found to be greater in four PD subjects than those in the control group (Hunker, et al., 1982). Seibel (2003) reported PD patients showed significant differences of lateral tangential interangle lip stiffness when measured with a digitally-controlled linear servo motor. Specifically, four out of seven PD subjects exhibited improvements in their perioral stiffness functions during the medication ON state. It is apparent that muscular stiffness in PD is not limited to limb or axial muscles, nor a manifestation of muscles endowed with muscle spindle afferents since perioral muscles do not contain these mechanoreceptors (Folkins & Larson, 1978; Lovell, Sutton, & Lindeman, 1977).

Because perioral muscles lack muscle spindles, the derived perioral stiffness does not support the hypothesis that rigidity is solely the result of increased gamma motor drive to muscle spindles (Burke, et al., 1972; Rushworth, 1964), as observed in the limb studies. The fact that perioral muscles are attached directly to the integument of the skin in the lower face and the absence of spindle end-organs (Folkins & Larson, 1978), points to the probable role of cutaneous and deep mechanoreceptor activity in modulating proprioceptive cues in the regulation of movement in the perioral region (Pinto et al., 2004). The slow adapting mechanoreceptor, pseudo-Ruffini corpuscle ending, has been shown to encode stretch and directional information (Johansson & Olsson, 1976). A high density of stretch-sensitive slow adapting mechanoreceptive units that exhibit similar physiological properties as the Ruffini ending have been found in the transitional zone of the lips region (Johansson, Trulsson, Olsson, & Westberg, 1988; Nordin & Hagbarth, 1989) may be important for proprioception in the perioral region (Barlow, 1987). However, we did not test the proprioception in the perioral system and therefore we could not derive any conclusion regarding the theory that bradykinesia and rigidity manifest in PD patients are related to abnormal processing of the mechanoreceptor sensory inputs (Tatton, Eastman, Bedingham, Verrier, & Bruce, 1984).

Regardless of medication state, the elevated perioral stiffness demonstrated by the PD group was consistent with Caligiuri's (1987) and Hunker's (1982) findings. However, both studies used a linear function to derived mean stiffness coefficients rather than a quadratic regression technique, as we utilized in the present study. Moreover, previous studies measured the perioral stiffness at the lips midline position while our current study measured the interangle (lateral) region. Muscles of the lower face can produce complex deformations and have a complex arrangement with the integument of the facial skin (Blair & Smith, 1986; Müller &

MacLeod, 1982; Müller, et al., 1985). Considering the underlying dynamics (position end point, force end point, rate of force change, velocity, etc.) of the orofacial muscles, we modeled the perioral stiffness with 2nd order equations that better represent the low-mass viscoelastic perioral system. Our findings suggest that a quadratic increase in perioral stiffness with interangle span appears to be a very robust pattern across all groups. The differences between slopes across groups became greater as the perioral stretches increased; this highlight the underlying dynamic anatomy differences between subjects (see Figure 22). This quadratic slope is likely to change as the disease advances, indicating a greater perioral stiffness level at a later stage of disease. We have noticed previously in a case study of a moderate-severe PD subject that the slope was approximately 7 times greater than a control prior to anti-PD medication intake (Chu, Barlow, Kieweg, & Lee, 2010). This biomechanical modeling using regression techniques fits the complex structures of the orofacial subsystem (Müller, et al., 1985).

This investigation showed that a quantitative metric of stiffness is useful in revealing changes in tonic motor neuron drive that may change due to medication status, and disease progression. The ability to evaluate the efficacy of pharmacological intervention using the face-referenced OroSTIFF device supports Müller's (1985) view that assessment of perioral stiffness could provide a useful set of biomarkers to clarify the effects of progressive neuromotor disease and to test hypotheses concerning articulatory dynamics.

4. High tonic IEMG associated with elevated perioral stiffness may serve as postural control for the orofacial system in early stage of PD.

It might be anticipated that dopaminergic treatment would reduce the perioral stiffness within the PD group, yet the PD participants in this investigation demonstrated a greater quadratic function slope after the administration of Levodopa. These findings are in apparent contradiction to previous orofacial biomechanics and electromyographic studies which focused

on the neurophysiology of speech articulators that found a beneficial effect of Levodopa (Leanderson, et al., 1971; Nakano, et al., 1973). However, the finding in the current study that perioral stiffness increased during the ON state corresponds with the increased tonic OOI*m* IEMG (as mentioned in Discussion section A1). Just as the control of limb stiffness as an important strategy for maintaining adjustments during movements, changes in the perioral stiffness and tonic IEMG may be used to maintain positional control and stability of the mandible during speech production and mastication. For example, normal subjects were able to maintain positional stability during wrist movements by elevating muscle coactivation levels, thereby increasing the magnitude of joint stiffness (De Serres & Milner, 1991). This finding supports the common observation in PD muscle activity that an increase in the tonic IEMG activity level is accompanied with elevated muscular stiffness (Marsden, 1982).

It is possible that elevated background tonic IEMG in early stage of PD contributes and modulates postural alignment so that it does not also resist intended movements. The fact that the overall labial kinematics measurement improved after medication intake supports this view. In the limb movement, stiffness is thought to be important because it contributes to positional stability in response to unexpected loads and appears to play an important role in the control of posture and movements (Horak, Dimitrova, & Nutt, 2005). The perioral system- a spring-like property of the neuromuscular system- plays an important role in sharpening the system's behavior and influencing the neural control of movements. Measurements of the jaw stiffness during speech and non-speech tasks have shown the ability of normal subjects to modify jaw stiffness in order to maintain postural stability in the presence of external loads (Shiller, Houle, & Ostry, 2005). Shiller and colleagues (2002) found that the pattern of jaw kinematic variation during simple consonant-vowel-consonant utterances was associated with the spatial pattern of

jaw stiffness. Our findings that up-regulation of perioral stiffness is associated with slight improvement in labial kinematics performance in the PD ON group (compare to PD OFF) represents a powerful means by which the nervous system attempts to maintain mechanical stability during speech production.

Despite the fact that basal ganglia play an important role for postural control, the central mechanism underlying postural coordination is unknown. Besides the classic motor symptoms (i.e., rigidity, tremor, bradykinesia), individuals with PD show abnormalities in gait and posture (Horak, et al., 2005; Winogrodzka, Wagenaar, Booij, & Wolters, 2005). It is not clear to what extent these postural problems are secondary to the clinical symptoms of rigidity and/or bradykinesia in limb and orofacial systems.

5. There was a correlation between perioral stiffness and hypokinesia in individuals with PD, indicating that rigidity and hypokinesia may arise from the same pathophysiology.

The present findings confirm the perioral stiffness-hypokinesia relationship in individuals with PD, specifically in the 5 Hz speech rate condition during ON state. The finding that perioral stiffness-hypokinesia did not show a significant correlation at the $[LL+J]_y$ and at slow rate of speech production raises the following concern. First, it suggests that a fairly large change in speaking rate (i.e., 5 Hz) may be required before a correlation in the perioral stiffness will be observed. Second, it also suggests that there may be differences across structures (i.e., UL_y and $[LL+J]_y$) in terms of the extent to which a given rate of speech will be associated with a particular change in stiffness profile. The OroSTIFF device we utilized to sample the interangle perioral stiffness measured composite of force and interangle displacement during perioral stretches. Therefore, no data is available to determine the passive stiffness-hypokinesia correlation relative to upper lip and lower lip independently. Future study will consider redesigning the equipment in order to address this question.

All of the evidence in our findings points to a general "down-scaling" of speech production in individuals with PD. There was also a disproportionate decrease in displacement amplitude relative to speech rate, which may have contributed to the speaking rate-dependent velocity reduction in PD. This disproportionate decrease in displacement amplitude may due to active rigidity. Recall that passive perioral stiffness was measured in this study. Hence, no data are available to address the contribution of active rigidity to the rate dependent kinematics change.

The current finding is in contrast to a previous report on labial stiffness in PD (Caligiuri, 1987). Using a linear motor transducer, Caligiuri (1987) reported increased labial stiffness for upper and lower lip muscles in twelve PD subjects. However, no apparent relationship between labial rigidity and the decrement in the range of lip movement was found. The inconsistencies may be attributed to the distinct level of analyses provided by the different methodologies. Stiffness coefficients were derived in the previous study while the present study utilized a definite perioral stiffness score at 12 mm of the interangle displacement. However, we do not suggest that deriving perioral stiffness at 12 mm interangle span is the perfect method to correlate with motor aberration in PD. Future study could model the perioral stiffness and hypokinesia relationship using high-level statistical methods, such as structural equation modeling technique.

Taken together, our findings support the hypothesis that elevated perioral stiffness and movement decrements arise from the same pathophysiology- dopaminergic deficits in the basal ganglia circuit. With a high stiffness-hypokinesia correlation (r = 0.69) shown in our study, evaluating this relationship with a larger sample of subjects at different stages of PD could identify a stronger perioral stiffness-hypokinesia relationship.

B1. Labial Kinematics

1. The presence of hypokinesia and bradykinesia occurred in all x-y-z dimensions of the articulatory movements, indicating a reduction of activation to the motor cortex for appropriate motor commands.

The hypokinesia and bradykinesia commonly reported for PD limb movements was also observed in the present study for the orofacial system. Consistent with previous studies (Caligiuri, 1987; Forrest & Weismer, 1995; Forrest, et al., 1989), hypokinesia and bradykinesia were evidenced in $[LL+J]_y$ movements of the PD speakers in this investigation. As a group, PD speakers had very limited $[LL+J]_y$ movement compared to the control group. For both opening and closing gestures, $[LL+J]_y$ displacements and velocities produced by the PD speakers were approximately half of those produced by the control. These findings support the "scaling" model proposed by Marsden (1982). He proposed that in addition to abnormalities of proprioceptive feedback, there was also a failure to generate an adequate motor signal due to basal ganglia deficits, leading to hypokinesia and bradykinesia.

Consistent with previous work (Hughes & Abbs, 1976; Kuehn & Moll, 1976), we found that the LL+J achieved higher velocities than the UL over greater ranges of displacement during speech production. Dynamics studies have shown that the lower lip generates more stable and higher rates of force than the upper lip (Barlow & Netsell, 1986). Indeed, the lower lip generates a maximum force that is three times greater than for the upper lip (Barlow & Rath, 1985). It is logical to assume that the lower lip, because of its dominant kinematic role during speech, may manifest proportionately greater deficits in kinematic measures following basal ganglia dysfunction. The jaw muscles are endowed with muscle spindles, which provide proprioceptive control to the system. Because impairment of the basal ganglia results in decreased cutaneous sensory input to the orofacial structure (Schneider, Diamond, & Markham, 1986, 1987), PD

patients may adopt a strategy by maintaining the jaw in a fixed position while speaking, thereby contributing to hypokinesia.

A considerable amount of information has been reported regarding the labial function in individuals with PD (Caligiuri, 1987; Hirose, et al., 1981). The current investigation revealed similar main effects for the participants, but the present study is the first to characterize PD perioral kinematics during speech in 4-dimensions using infrared tracking of facial flesh points. The pattern of hypokinesia was apparent in all three dimensions (x-, y-, and z-). In general, both normal and PD subjects showed a similar movement trend that had greater movement magnitude in the inferior-superior (y), followed by medial-lateral (z), and then anterior-posterior (x) dimensions. This trend signifies that PD subjects have intact basal ganglia-thalamocortical-brainstem circuit similar to those of control group, however, there is a functional deficit in this link. This disturbance must arise in the projection from the GPi/SNr via the thalamus to the primary motor, premotor area and the supplementary motor cortex. The cortical areas control the initiation, direction, and force during movements (Alexander, DeLong, & Strick, 1986). The fact that PD subjects were able to produce accurate speech tokens by reducing range of motion as a compensatory skill and to manifest similar movement trend in x-y-z dimensions as those of control group indicated that a cortical pathway is intact in these PD patients. However, a reduction in the thalamocortical activation due to loss of dopaminergic neurons may prevent the motor cortex from generating appropriate commands, resulting in hypokinesia.

Theoretically, the inferior-superior (y) dimension acts as the primary articulator movement to control for changes in the shape and function of the vocal tract. Note that the medial-lateral (z) and anterior-posterior (x) dimensions reported in the present study accumulate a very small range of movement (range 0.68mm-2.15mm) for the control group, with a smaller

range in the PD group. Hence, comparing the distinct movement displacement and velocity may not be an appropriate method to test the difference between dimensions given that x-z movements consistently show smaller movements compared to the *y*-dimension. Future study should examine the relation between x-y-z-dimensions during speech production to characterize the dynamic changes of orofacial movements due to disorders.

If the basal ganglia play a role in the suppression of unwanted movement during the execution of a movement, then, performance in the lateral movement should be smaller than the anterior-posterior movement. However, this was not the case in our findings. One possible reason might be that lateral and anterior-posterior movements involve different neural circuits and different muscle synergies. Lateral jaw movements have been found to have different cortical representation than the vertical jaw closing representation in the motor cortex (Hoffman & Luschei, 1980). Certainly, PD affects the central programming of functionally related muscles involved in voluntary movements.

The results of this study support the idea that PD does not alter only one dimension of articulator movement but rather affects several dimensions of the evolving speech movement. Similar to the inferior-superior (y) findings, the anterior-posterior (x) and medial-lateral (z) displacements were decreased as speech rate increased. This finding is consistent with both control (MEAN $[LL+J]_y$ at 2 Hz= 13.9mm, 5 Hz= 10.5mm) and PD groups (PD OFF MEAN $[LL+J]_y$ at 2 Hz= 8.6mm, 5 Hz= 6.4mm) (see Appendix G, H, and I for details). Future investigation will be required to determine the central neural representation of anterior-posterior (x) and medial-lateral (z) dimensions in oromotor control during speech.

2. There does not appear to be a difference between opening and closing gestures of speech production.

It was speculated that potential differences between opening and closing labiomandibular gestures may provide new insight into the central control mechanisms in individuals with PD. The literature suggests that closing and opening movements are fundamentally different actions operating under different constraints and that closing movements are more difficult to control than opening movements (Gracco, 1988; Gracco & Lofqvist, 1994). Contrary to previous reports describing articulatory closing movements as having higher peak velocities than articulatory opening movements (Forrest, Weismer, & Turner, 1989), the present results showed non-significant differences between opening and closing gestures when PD and control speakers produced "pa" syllables. This discrepancy may be due to the speech task, whereby Forrest et al. (1989) utilized the sentence "Buy Bobby a Puppy" while simple repetitive repetition of "pa" syllables was used in this current report. The kinematic patterns for different articulators varied depending on the phonetic context surrounding the target sound (i.e., sipping vs. sifting) and whether one (i.e., safe) versus two consonants (i.e., safety) were produced in sequence (Gracco & Lofqvist, 1994). It may be possible that no significant different between the opening and closing gestures when comparing on the same consonant-vowel ("pa") task, but comparing different consonant-vowel combinations may show differences between opening and closing gestures.

3. Both PD and control subjects were able to coordinate their articulatory movements as a function of speech rate. However, PD subjects showed a greater extent of displacement reduction.

The present findings indicate that hypokinesia is consistently present as a function of speaking rate in individuals with PD. Since the basal ganglia appear to regulate temporal-spatial aspects via thalamocortical modulation, one would expect speech rate abnormalities in

individuals with PD. Indeed, the present study revealed that lip movements for "pa" syllables at slow, normal, and fast speaking rates were significantly reduced in amplitude and velocity. As speech rates increase, the movement amplitude and velocity reduced in a greater magnitude. PD subjects showed a disproportionate compression of labiomandibular displacement scaling as a function of speech rate, particularly evident at the 5 Hz production rate. That is, while both control and PD subjects reduced displacement amplitude with increased speaking rate, the magnitude of this reduction was greater for the PD subjects.

Our results are consistent with limb findings in PD in which there is a significantly reduced capacity to accurately scale amplitude when the velocity demands are increased (Horak, Dimitrova, & Nutt, 2005; Montgomery, Nuessen, & Gorman, 1991). An adaptive velocity scaling mechanism affords the healthy speaker to adjust agonist drive for opening/closing gestures as a function of speech rate to preserve intelligibility, loudness control, and suprasegmental features of the speech signal. Our PD patients show a pattern of scaling the articulatory movement in a limited range of motion in order to produce the target speech movements as speech rates increase.

It is generally thought that reduced articulatory movements of PD patients may appear to be slow as the movement is less for a given amount of time. As speech rate increases, movement displacement and movement time decrease (Caligiuri, 1989). Future study should quantify the movement duration to better describe if the PD patients are actually hypokinetic rather than just slow during speech production.

Decreased lip movement velocities have been found during speech (Hirose, et al., 1981), which contradict clinical perception of an abnormally fast speech rate in individuals with PD. These findings confirm former studies indicating that there is a tradeoff between demands on

speech rate and movement amplitude (Ackermann, et al., 1997; Ackermann & Ziegler, 1991; Caligiuri, 1989), as well as the presence of bradykinesia in PD (Forrest, et al., 1989). This observation suggests that speaking rate may be an important control variable that contributes to articulatory hypokinesia in PD.

4. Administration of Levodopa treatment influences the basal ganglia-thalamocortical circuit that permits scaling of movement.

Consistent with previous findings that Levodopa has a positive effect on lip function (Cahill et al., 1998; Nakano, et al., 1973), phonation (Goberman, Coelho, & Robb, 2002), and word/sentence intelligibility (De Letter, Santens, Estercam et al., 2007; De Letter, et al., 2005), the present investigation demonstrated the increased labiomandibular kinematic performance (amplitude, velocity) following administration of Levodopa. The observed $[LL+J]_y$ movement displacement during PD ON was amplified compared to the medication OFF state. The net positive effect of Levodopa therapy on labiomandibular kinematics was approximately 24% in the amplitude domain. For example, the mean closing amplitude for PD OFF subjects ($\overline{X}$ = 7.48mm) increased by 24% during ON state ($\overline{X}$ = 9.90mm), relative to control ($\overline{X}$ = 13.02mm) at the 3.5 Hz speaking rate.

This finding supports the theory that scaling of movement could be achieved by a combination of inhibition of the GPi/SNr neurons via the direct pathway and excitation of these output cells via the indirect pathway in the basal ganglia circuit. The balance between these two pathways may modulate the amount of disinhibition of thalamocortical neurons, providing a mechanism by which the movement can be scaled to achieve end-point accuracy (DeLong, 1990). Our findings provide evidence of "down-scaling" in individuals with PD, resulting in hypokinesia. We expect to see a greater deficit in the ability to scale movement as the disease

advances. Clearly, the ability to scale movement to meet changes in task demands (rate, loudness) is an important aspect of speech motor control.

B2. Spatiotemporal Stability (STI)

1. PD subjects in this investigation showed a stable motor behavior in the UL_y and $[LL+J]_y$.

In contrast with previous findings of normal speakers (Smith, et al., 1995), adults who stutter (Smith & Kleinow, 2000), and PD subjects (Kleinow, et al., 2001), the current investigation found no group effect on both syllables and sentences production associated with STI measurements. This result indicates that individuals with PD may recruit an existing coordinative organization that is highly stable despite the elevated perioral stiffness and reduced amplitude of movement. This finding is consistent with their perceptual speech intelligibility score that showed highly intelligible speech production. It may also be possible that these patients' spatial-temporal motor control of speech was preserved due to the relatively mild stage of PD.

The current findings differ from the STI patterns reported by Kleinow and colleagues (2001). The inconsistencies may be attributed to the different methodologies. While Kleinow et al. (2001) measured the STI by asking PD subjects to read phrases ("Buy Bobby a Puppy") at different loudness levels, we used a metronome pace to control for the speech rate, which provided an external cue to the subjects during speech production. External cues given to address loudness and articulation have been shown to modulate speech behavior in individuals with PD. For example, background noise was found to elicit increases in loudness, although individuals with PD did not increase loudness to the same extent as age-matched adults when reading the rainbow passage (Ho, Bradshaw, Iansek, & Alfredson, 1999). In addition, the patients in our study were in the mild stage of PD while the subjects in the Kleinow et al. (2001)

ranged from mild to moderate, with two out of eight subjects who were not classified by the Hoehn and Yahr stage. These discrepancies further emphasize the necessity to carefully classify subjects' stage of disease in order to provide the most comprehensive description of PD motor behavior changes in future investigation.

We initially expected that all "pa" and rainbow passage STI values would have increased as a function of speech rate, particularly in the PD OFF group. However, we only found a speech rate effect in the "pa" speech task. The "pa" speech task is a simple voluntary movement for the subjects to execute compared to the rainbow passage task. Both tasks were practiced with the metronome pace prior to the examination. Consequently, all subjects may have well learned the motor patterns on both tasks. If the basal ganglia provide a mechanism to mediate cognition and language, as well as speech motor control, then performance of the longer sentences may be affected by the demands placed on the production system. However, this was not the case.

It should be emphasized that STI is a composite measure of spatial and temporal variability over repeated motor behaviors (Wohlert & Smith, 1998). Therefore, the specific changes of the articulatory kinematic patterns cannot be derived from the STI value. In order to understand the underlying articulatory compensatory strategies in individuals with PD, this investigation takes into consideration the effects of speech modulations on independent measures of spatial and temporal characteristics using kinematic measurements. When compared to the control group, PD subjects showed both decreased amplitude and velocity in lip movement (Caligiuri, 1987) and jaw movement (Svensson, et al., 1993). Therefore, combining both measures of motor stability (i.e., STI) and kinematics is useful to understand the coordinative organization of speech motor control pattern in PD.

C. EMGs

1. Significant reduction of the IEMGs amplitude magnitude in PD subjects indicating that reduction in the thalamocortical activation prevents the motor cortex from generating appropriate commands.

Although perioral muscle activation patterns during speech production are altered in individuals with PD, they were able to maintain the general feature of reciprocity between OOI*m* and DLI*m* muscles. This finding indicated that their ability to activate appropriate muscles for speech production was preserved. Interestingly, significant differences were found in the muscle activation amplitude magnitude between the OOI*m* and DLI*m* muscles. Similar observation was also evidenced in a study whereby the bursts of IEMG activity in the agonist muscle did not increase in magnitude for the larger amplitude movements during attempted rapid elbow flexion (Hallett & Khoshbin, 1980). These authors speculated that the PD subjects were not able to sufficiently "energize" agonist muscles during high velocity, ballistic movements. Therefore, additional IEMG bursts are needed to produce rapid movement of required amplitude. This pattern of IEMG activation was also observed among the perioral muscles sites among PD subjects in our study.

One explanation that describes the changes of IEMG patterns in PD speakers is the abnormality in the descending commands sent to motor neurons. These abnormal commands might originate in the motor cortex or other areas receiving input from the basal ganglia. Delwaide et al. (1991) proposed that reticulospinal pathway is disinhibited in PD, resulting in abnormal descending influences on the spinal cord interneurons. This, in turn, changes the reciprocal activation and alters the tonic state of motor neurons. A reduction in the thalamocortical activation may prevent the motor cortex from generating appropriate commands, hence, smaller IEMG amplitude was observed. Our findings support the fact that muscular

abnormalities in PD appear to be "coded" in the central nervous system due to neural changes in the basal ganglia rather than any deficits in the peripheral motor system.

From a physiological standpoint, decreased muscle activation amplitude in PD is considered to be the result of an inability to recruit motor units sufficiently for movement control. These lower amplitude muscle action potentials have been interpreted as weakness in the neuromuscular control signals in PD subjects (Netsell, et al., 1975). Netsell et al. (1975) suggested that this weakness is of neurogenic origin rather than muscle contractile weakness, muscular weakness, or problems at the neuromuscular junction. The fact that IEMG patterns change after administration of Levodopa treatment, as seen in our study, provides evidence that muscle activation amplitude is modulated by central mechanisms.

Motoneuron degeneration and death appear to be a process that occurs in normal aging. Because PD is a progressive disease that often affects the elderly population, one could debate that some of the change in motor unit pattern activity in PD could due to neuronal loss. However, this was not the case in our present findings.

The inability to produce the required amount of EMG activity in one single burst may account the observed hypokinesia in PD. The multiple EMG burst pattern has been observed in the wrist flexors/extensors among individuals with PD (Kumru, Summerfield, Valldeoriola, & Valls-Sole, 2004) and elbow (Berardelli, Dick, Rothwell, Day, & Marsden, 1986; Hallett & Khoshbin, 1980). Our findings in the perioral muscles support the previous literature that mainly focused on the upper limb, which reveals that the initial burst of IEMG is ineffective to generate and complete the oromotor task. Therefore, PD patients compensate by generating subsequent bursts until the lip opening or closure gesture is executed, and this appears to account for the bradykinesia (slowness) of movement execution.

Limitations

We found that the effect of Levodopa on the labial kinematic measures provide a parsimonious account for the varied findings in PD speech. Meanwhile, these initial results are limited by sample size and clearly need to be investigated in large-scale study to account for the different clinical signs and patients' respond to Levodopa treatment as the disease advances. The most obvious limitation of this study is the PD selected subjects, which consists of both rigid and tremor dominant clinical signs. It is conceivable that individuals with more advanced PD who manifest more significant impairments in different orofacial biomechanics and speech profiles will show different responses to Levodopa treatment. Therefore, the direct effects of Levodopa in up-scaling labial kinematics may depend upon the pre-existing pattern of dysarthria of a patient's profile.

A common assumption is that improvement of the primary symptoms of tremor, rigidity, and bradykinesia with dopaminergic medication will translate into improved speech. The present study along with previous reports appears to counter this notion. It is clear that there is considerable individual variation nested within the null group and future analysis should anticipate this pronounced variability. Most of the patients tested in the present study demonstrated an average of 95% or higher speech intelligibility, yet, neuromotor status changed substantially for these individuals as measured by kinematics and IEMG analyses. In the current study, all PD subjects were able to compensate their articulatory movements (at reduced movement displacement) in order to achieve speech targets. It appears that there is greater capacity for motor compensation at early stage of PD. However, as the disease progresses, the motor reorganization "window" progressively narrows, resulting in degraded speech intelligibility, significant reduction in articulation movements, loudness, and pitch. The extent by when PD patients are no longer able to effectively compensate for speech control is uncertain.

Future studies should include longitudinal design to classify the speech motor reorganization patterns at different stages of PD to address this question.

The current findings underscore the importance of examining individual differences within individuals with PD. For group comparison between variables, we simply pooled and contrasted test results with controls. Follow-up study could examine the differences within subject's pre-post Levodopa treatment for careful assessment and longitudinal study using repeated measures technique.

Evidence from behavioral-motor studies showed that basal ganglia generate internal cues for the beginning and sequential portions of a movement (Georgiou et al., 1993; Marsden, 1982, 1990). PD patients showed improvement with external cues using an illuminated pathway (Georgiou, et al., 1993). While these observations have been made mainly for the musculoskeletal system, studies suggest that PD patients have the capacity to speak with normal volume using attention-driven cues (i.e., instructions regarding volume level) (Ho, Bradshaw, Iansek, & Alfredson, 1999), or instructions such as "Think Loud" (Ramig, Sapir, Fox, & Countryman, 2001), or directions to consciously slow them down (Kempler & Van Lancker, 2002). Recall that a metronome was used in the current study to pace the subjects during speech production, and this external cue may provide an aid to planning, initiating, and monitoring the speech gesture, therefore reducing the demands placed on the basal ganglia.

The lower lip appeared to a better choice than the jaw for a stable measure of articulatory performance as the jaw movements were more variable during speech production (Forrest, et al., 1989). In this current study, we analyzed the LL+J movement instead of analyzing the lower lip and jaw independently. Using cineradiography, one study found that the standard deviation between the vertical positions of a chin marker and a point identified on the mandibular bone is

variable across subjects (Kuehn, Reich, & Jordan, 1980). This standard deviation was reported to be as high as 1.28mm during speech. In our pilot investigation, we also found a mean of 2mm (SD=0.3mm) during speech when measuring the jaw movement using an incisal bite block during syllable production. It is likely that the lower lip pulling the skin overlying the chin is accounting for some of the positional deviation. Therefore, we limited the labial kinematics measurement to the UL and LL+J in this investigation. Future efforts will be directed toward quantifying potential positional errors associated with flesh-point tacking methods.

General Conclusions

The results from this study contribute to the understanding of orofacial biomechanics and associated hypokinesia in individuals with PD speech production. Our findings suggest that the basal ganglia, in addition to regulating muscle tone and energizing muscle activation, also are critical for orofacial postural control. The complex interactions between the biomechanical constraints on the perioral system and constraints on muscle activation imposed by the basal ganglia pathology result in hypokinesia and bradykinesia in individuals with PD. Although perceptually no differences in individual speech dimensions were observed, perhaps other forms of objective assessment would be more sensitive to changes in labial kinematics not detected by the ears of examiners. The findings in the current study further support administration of a complement of perceptual and objective (i.e., biomechanics, kinematics, or electrophysiology) outcome measures. The following states the general findings derived from this investigation:

1. High baseline muscle tone was apparent in PD subjects from their high background IEMG activity. Administration of Levodopa increased tonic IEMG, which may serve postural control purposes for the orofacial system.

2. There were significant differences in perioral stiffness across the groups, indicating that there is clinical rigidity affecting both the limb and orofacial muscles of individuals with PD.

3. There was a perioral stiffness-hypokinesia relationship in the UL_y structure, specifically at a high speech rate level (5 Hz). This finding suggests that perioral stiffness contributes to hypokinesia and these two symptoms may result in part from a common neural substrate.

4. Articulatory displacement and velocity changes significantly across groups, indicating that individuals with PD compensate elevated perioral stiffness by scaling the articulatory movements. In fact, PD subjects showed smaller articulatory displacement amplitude and velocity, especially during the high speech rate condition.

5. There was no difference in STI across the groups, indicating that the temporal motor control stability is preserved in these patients. The non-significant finding of reciprocal activity across groups support the idea that temporal organization is preserved in PD.

6. There was significant difference in the agonist-antagonist muscles amplitude, indicating that the amount of activity to achieve a target is limited in PD and that an apparent compensation for the decreased muscular activation was used to evoke additional cycles to accomplish the task.

7. The results of this investigation provide a quantitative description of perioral stiffness, labial kinematics, and IEMG patterns of individuals with PD, which not only advances knowledge regarding these measurements, but begins to provide a normative baseline from which to capture the severity of dysarthria in PD in the future.

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Appendix A. Perceptual survey for speech judges.

Subject's File ID: _____

Examiner: _____

Instruction to the Examiner: Identify the speech characteristics noted during the speech sample.

	Normal	Mild	Moderate	Severe	Very Severe
Reduced Loudness	1	2	3	4	5
Monotonicity	1	2	3	4	5
Breathiness	1	2	3	4	5
Articulatory Precision	1	2	3	4	5
Speech Rate	1	2	3	4	5
Hoarseness	1	2	3	4	5
Severity of Dysarthria	1	2	3	4	5
Comments					

Appendix B. Hearing screening threshold (dB SPL) at 500, 1000, 2000, and 4000 Hz for control and PD participants. The "R" denotes right ear while "L" denotes left ear.

		Threshold level (dB SPL)			
Control		500 Hz	1000 Hz	2000 Hz	4000 Hz
C1	R	30	30	30	35
	L	30	30	30	40
C2	R	30	30	30	30
	L	30	30	30	30
C3	R	30	30	30	30
	L	30	30	30	30
C4	R	30	30	30	30
	L	30	30	30	30
C5	R	30	30	30	30
	L	30	30	30	30
C6	R	30	30	30	30
	L	30	30	30	30
C7	R	30	30	30	30
	L	30	30	30	60
C8	R	30	30	30	30
	L	30	30	30	30
C9	R	30	30	55	65
	L	30	45	55	65
C10	R	30	30	35	40
	L	30	30	35	50

		Threshold level (dB SPL)			
PD		500 Hz	1000 Hz	2000 Hz	4000 Hz
PD 1	R	30	30	30	30
	L	30	30	30	30
PD2	R	35	35	35	35
	L	40	40	40	40
PD3	R	30	30	30	35
	L	30	30	30	35
PD4	R	30	30	30	30
	L	30	30	30	30
PD5	R	30	30	30	60
	L	30	30	30	60
PD6	R	40	45	55	65
	L	40	45	55	65
PD7	R	30	30	30	50
	L	30	30	30	65
PD8	R	60	30	30	60
	L	60	30	30	60
PD9	R	30	30	30	50
	L	30	30	30	45
PD10	R	30	30	30	30
	L	30	30	30	30

Appendix C. Detailed parsing rules for the "pa" syllable task.

The following rules were followed to systematically select the "pa" for analysis:

1. All data collected from each subject using Cortex-64 (version 2.0.0.900) were exported into *.c3d format.
2. Using the SMASH program, the extraneous head movement of all markers was corrected.
3. In order to select the beginning and ending points of the syllable trains, the inferior-superior (y-axis) dimension of the lower lip velocity signal zero-crossing points was used to define the beginning (positive slope) and ending (negative slope) points of each syllable trains.
4. The first and the last peaks of the syllable trains were disregarded.
5. The next five error-free consecutive repetitions at 2 Hz productions, 10 repetitions for 3.5 Hz, and 15 repetitions for 5 Hz were selected for analyses. Therefore, a total of 30 samples at each speech rate were selected for statistical comparison.

Speech Task	Task Repetitions	Number of Parsing Syllables	Total of Parsing Syllables
pa @ 2 Hz	6	5	30
pa @ 3.5 Hz	3	10	30
pa @ 5 Hz	2	15	30

6. The selected syllables were saved in .txt and export into a LabVIEW™ 8.6 program that allows the user to detect the syllable peaks and export to MATLAB®.
7. The MATLAB® program was used to calculate the UL and LL+J displacement and velocity of opening and closing gestures.
8. All x-, -y-, z- dimension of selected "pa" trains were analyzed.

Appendix D. Detailed parsing rules for "pa" syllable-STI

A second analysis proposed for this study was to calculate the STI for the "pa" syllable:

1. Only the inferior-superior (y-axis) dimension of the UL_y, $[LL+J]_y$ was selected for STI analysis.
2. Using the SMASH program, the extraneous head movement of all markers was corrected.
3. The inferior-superior (y-axis) dimension of the lower lip velocity signal zero-crossing points were used to define the beginning (positive slope) and ending (negative slope) points of the syllable trains.
4. The first and the last peaks of the syllable trains were disregarded.
5. The next five error-free consecutive repetitions at 2 Hz productions, 10 repetitions for 3.5 Hz, and 15 repetitions for 5 Hz were selected for analyses. This procedure ensured that each speech rate had an equal total of 30 samples for statistical analysis comparison.
6. The raw data of the UL_y, and $[LL+J]_y$ were exported to .txt format for STI analysis.

Appendix E. Detailed parsing rules for sentences task.

The sentences "When the sunlight strikes raindrops in the air, they act as a prism and form a rainbow." were used for analysis. The first phrase ["when the …..air"] and the second phrase ["they act….rainbow"] of the rainbow sentence were selected for comparison.

To systematically select the sentences for the STI analysis, the following rules were followed:

1. All data collected from each subject using Cortex-64 (version 2.0.0.900) are exported into *.c3d format. For the first phrase, the parsing begin at the starting acoustic signal of /wh/ ["when"] and ending at the vowel /ae/ ["air"]. The second phrase begins at the /th/ ["they"] and ends at /o/ ["rainbow"].
2. Using the SMASH program, extraneous head movement of all markers was corrected.
3. All movement traces were amplitude- and time-normalized using SMASH software (Green, 2008). Amplitude normalization was achieved by dividing each movement trace by its standard deviation. Subsequently, the linear temporal normalization was achieved by interpolating each signal to 1000 points using a commercially available cubic spline fit algorithm (MATLAB®).
4. The raw data of the UL_y, and $[LL+J]_y$ were exported to .txt format for STI analysis.
5. A total of five repetitions of the rainbow passage at three different rates were selected for analysis.

Appendix F. Parsing rules for IEMG analysis.

The following rules are followed to systematically select the "pa" EMGs for analysis:

1. All raw EMGs data collected from each subject using Cortex-64 (version 2.0.0.900) were exported into *.c3d format.
2. All raw EMGs data were in-line with the selected "pa" kinematic analysis.
3. Using the SMASH program, the raw data of the OOS*m*, OOI*m*, and DLI*m* EMG signals were adjusted to zero offset (detrend), full-waved rectified (second panel) and low pass filter to create "envelope".
4. The EMG signals low-pass cut off are as follows:

Speech Rate	Low-pass cut off
2 Hz	0.18Hz
3.5 Hz	0.40Hz
5 Hz	0.55Hz

5. These integrated EMG (IEMG) files were exported as .txt format and fit into a custom written MATLAB® program to generate amplitude ratio/phase polar plots.

Appendix G. Means (*SD*) of the amplitude and velocity variables: CONTROL

	Closing						Opening					
	2 Hz		3.5 Hz		5 Hz		2 Hz		3.5 Hz		5 Hz	
Variable	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*
Amplitude												
UL_x	0.68	0.32	0.74	0.40	0.67	0.36	0.71	0.31	0.72	0.36	0.72	0.45
UL_y	1.21	0.81	1.82	1.33	1.54	1.23	1.01	0.86	1.80	1.33	1.52	1.20
UL_z	1.20	0.37	1.38	0.55	0.98	0.47	1.09	0.27	1.38	0.57	0.98	0.46
$[LL+J]_x$	1.54	0.87	1.84	1.04	1.62	0.74	1.62	1.04	1.78	1.08	1.55	0.81
$[LL+J]_y$	13.94	3.16	13.02	3.50	10.53	3.63	14.12	3.24	13.04	3.51	10.55	3.62
$[LL+J]_z$	2.01	1.61	2.15	1.62	1.54	1.10	2.10	1.71	2.13	1.60	1.50	1.11
Velocity												
UL_x	7.90	2.71	9.02	5.24	9.00	4.46	7.76	2.24	9.10	4.23	8.79	4.10
UL_y	12.64	7.25	16.93	11.51	19.22	17.29	8.50	7.04	21.00	16.37	23.21	16.27
UL_z	11.73	3.40	15.00	6.85	13.59	6.12	8.37	2.00	13.07	6.07	12.96	6.39
$[LL+J]_x$	12.52	3.66	20.32	10.39	21.41	11.20	15.32	9.66	17.93	10.94	19.52	10.71
$[LL+J]_y$	93.65	48.80	124.22	44.30	139.44	43.99	131.40	44.33	134.90	52.38	135.88	43.97
$[LL+J]_z$	16.93	10.63	21.90	14.83	22.28	15.45	19.32	12.36	23.38	15.32	21.61	14.31

Appendix H. Means (*SD*) of the amplitude and velocity variables: PD ON

	Closing						Opening					
	2 Hz		3.5 Hz		5 Hz		2 Hz		3.5 Hz		5 Hz	
Variable	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*
Amplitude												
UL_x	0.63	0.31	0.60	0.25	0.49	0.12	0.59	0.28	0.60	0.26	0.53	0.23
UL_y	0.99	0.58	1.03	0.39	0.73	0.35	0.90	0.53	1.01	0.37	0.71	0.33
UL_z	0.69	0.35	0.68	0.26	0.60	0.26	0.67	0.34	0.65	0.24	0.59	0.25
$[LL+J]_x$	1.09	0.62	0.87	0.30	0.71	0.26	1.03	0.50	0.86	0.27	0.67	0.24
$[LL+J]_y$	11.13	2.78	9.90	3.17	8.19	3.03	11.15	2.70	9.91	3.18	8.20	3.01
$[LL+J]_z$	1.28	0.55	1.40	0.66	1.12	0.69	1.34	0.54	1.35	0.64	1.08	0.67
Velocity												
UL_x	6.66	2.19	6.98	1.95	6.39	1.66	6.68	1.62	6.96	2.15	6.81	2.15
UL_y	8.78	4.47	11.92	5.85	10.34	5.45	7.77	3.96	8.48	3.67	8.85	4.30
UL_z	6.36	2.02	7.46	2.52	8.55	4.08	7.03	2.37	6.83	3.02	8.05	3.88
$[LL+J]_x$	10.06	4.46	9.53	2.36	9.29	2.77	9.73	2.43	9.57	2.18	9.42	3.61
$[LL+J]_y$	75.81	28.60	90.74	32.69	113.09	42.01	87.58	15.67	96.61	29.45	103.19	37.19
$[LL+J]_z$	10.80	3.34	12.30	5.16	15.45	8.26	12.37	3.03	15.55	6.50	16.06	9.45

Appendix I. Means (*SD*) of the amplitude and velocity variables: PD OFF

	Closing						Opening					
	2 Hz		3.5 Hz		5 Hz		2 Hz		3.5 Hz		5 Hz	
Variable	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*
Amplitude												
UL_x	0.47	0.12	0.50	0.18	0.42	0.08	0.47	0.15	0.50	0.18	0.44	0.08
UL_y	0.85	0.45	0.71	0.37	0.50	0.17	0.76	0.35	0.70	0.37	0.49	0.16
UL_z	0.62	0.21	0.62	0.17	0.44	0.10	0.66	0.29	0.62	0.21	0.43	0.10
$[LL+J]_x$	0.74	0.39	0.73	0.29	0.70	0.28	0.76	0.33	0.75	0.27	0.71	0.25
$[LL+J]_y$	8.58	2.99	7.48	3.18	6.44	2.60	8.63	2.96	7.52	3.20	6.46	2.57
$[LL+J]_z$	1.27	0.67	1.31	0.68	0.94	0.59	1.45	0.75	1.35	0.70	0.94	0.59
Velocity												
UL_x	4.98	1.28	5.61	1.99	6.23	1.05	4.89	1.34	5.67	1.88	6.52	1.32
UL_y	7.15	4.21	9.39	5.68	7.59	3.39	6.34	3.81	6.02	2.83	6.64	2.35
UL_z	5.83	0.93	6.91	1.56	7.16	3.27	6.27	1.92	6.79	3.21	7.15	3.41
$[LL+J]_x$	7.25	2.85	7.85	2.56	9.65	4.22	7.61	2.11	8.88	3.10	9.81	3.00
$[LL+J]_y$	54.52	26.82	71.10	30.95	97.24	46.66	68.23	19.91	75.24	34.68	89.12	40.85
$[LL+J]_z$	10.34	4.02	11.81	4.72	12.61	7.70	13.45	5.20	16.74	8.58	13.92	8.36

Appendix J. Summary of paired-samples *t*-test for UL and LL+J variables.

Group		Variable	*t*	*p*
CONTROL	Amplitude	$UL_x - [LL+J]_x$	-7.73	0.0000
		$UL_y - [LL+J]_y$	-23.78	0.0000
		$UL_z - [LL+J]_z$	-4.66	0.0000
	Velocity	$UL_x - [LL+J]_x$	-7.09	0.0000
		$UL_y - [LL+J]_y$	-18.80	0.0000
		$UL_z - [LL+J]_z$	-5.86	0.0000
PD ON	Amplitude	$UL_x - [LL+J]_x$	-5.05	0.0000
		$UL_y - [LL+J]_y$	-22.95	0.0000
		$UL_z - [LL+J]_z$	-6.49	0.0000
	Velocity	$UL_x - [LL+J]_x$	-6.45	0.0000
		$UL_y - [LL+J]_y$	-20.41	0.0000
		$UL_z - [LL+J]_z$	-6.48	0.0000
PD OFF	Amplitude	$UL_x - [LL+J]_x$	-7.43	0.0000
		$UL_y - [LL+J]_y$	-18.20	0.0000
		$UL_z - [LL+J]_z$	-7.02	0.0000
	Velocity	$UL_x - [LL+J]_x$	-8.34	0.0000
		$UL_y - [LL+J]_y$	-15.02	0.0000
		$UL_z - [LL+J]_z$	-6.74	0.0000

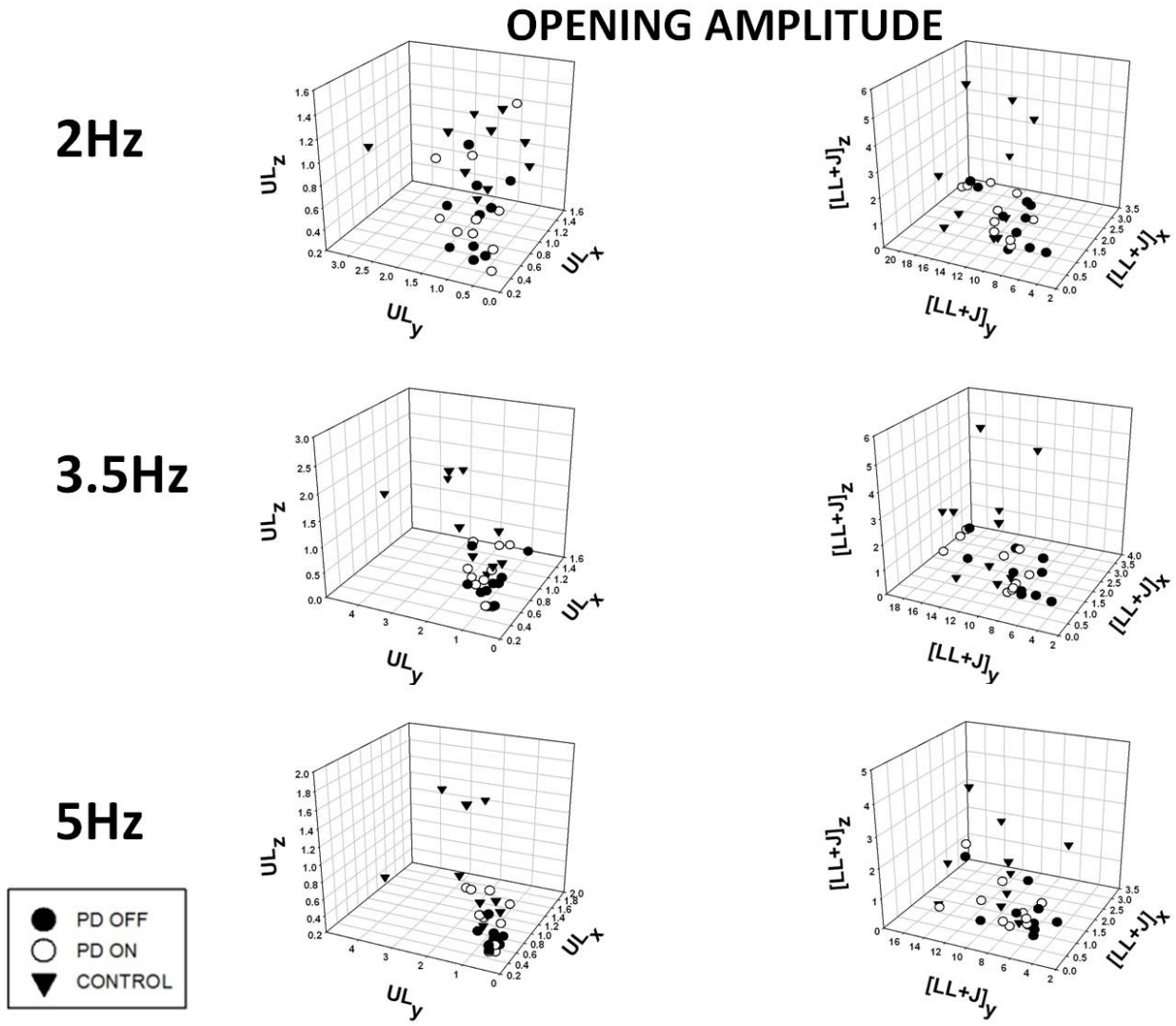
Appendix K. Summary of Wilks' lambda test: Amplitude

Variable	*df*	*F*	*p*
Group	12	14.57	0.0000*
Gesture	6	0.16	0.9875
Speech rate	12	3.15	0.0003*
Group x Gesture	12	0.03	1.0000
Group x Speech rate	24	1.11	0.3267
Gesture x Speech rate	12	0.07	1.0000
Group x Gesture x Speech rate	24	0.04	1.0000

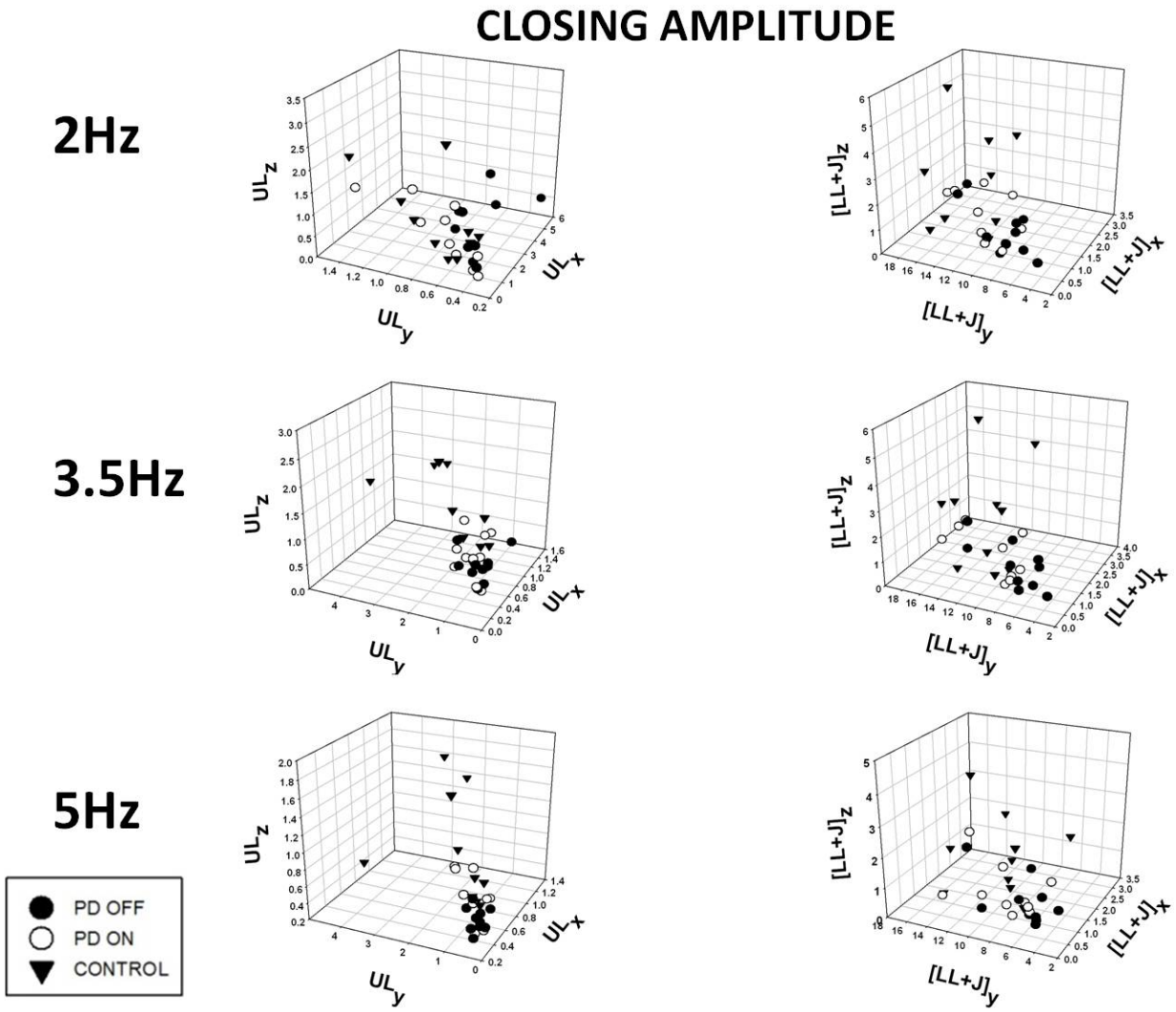
Appendix L. Summary of Univariate Analyses of Variance: Amplitude

Source	*df*	*F*	*p*	*Partial* η^2
DV=Amplitude UL_x				
Group	2	11.79	0.0000*	0.1270
Gesture	1	0.05	0.8234	0.0003
Speech Rate	2	0.98	0.3764	0.0120
Group × Gesture	2	0.02	0.9804	0.0002
Group × Speech Rate	4	0.19	0.9443	0.0046
Gesture × Speech Rate	2	0.11	0.8974	0.0013
Group × Gesture × Speech Rate	4	0.04	0.9971	0.0010
DV=Amplitude UL_y				
Group	2	19.80	0.0000*	0.1964
Gesture	1	0.23	0.6343	0.0014
Speech Rate	2	2.23	0.1112	0.0268
Group × Gesture	2	0.02	0.9817	0.0002
Group × Speech Rate	4	2.08	0.0858	0.0488
Gesture × Speech Rate	2	0.11	0.8977	0.0013
Group × Gesture × Speech Rate	4	0.01	0.9997	0.0003
DV=Amplitude UL_z				
Group	2	58.43	0.0000*	0.4191
Gesture	1	0.12	0.7306	0.0007
Speech Rate	2	6.79	0.0015*	0.0774
Group × Gesture	2	0.08	0.9271	0.0009
Group × Speech Rate	4	1.56	0.1875	0.0371
Gesture × Speech Rate	2	0.02	0.9839	0.0002
Group × Gesture × Speech Rate	4	0.10	0.9815	0.0025
DV=Amplitude $[LL+J]_x$				
Group	2	39.78	0.0000*	0.3293
Gesture	1	0.02	0.8762	0.0002
Speech Rate	2	1.05	0.3512	0.0128
Group × Gesture	2	0.03	0.9707	0.0004
Group × Speech Rate	4	0.87	0.4824	0.0211
Gesture × Speech Rate	2	0.02	0.9776	0.0003
Group × Gesture × Speech Rate	4	0.04	0.9966	0.0010
DV=Amplitude $[LL+J]_y$				
Group	2	38.71	0.0000*	0.3234
Gesture	1	0.01	0.9339	0.0000
Speech Rate	2	12.76	0.0000*	0.1361
Group × Gesture	2	0.00	0.9986	0.0000
Group × Speech Rate	4	0.33	0.8548	0.0082
Gesture × Speech Rate	2	0.00	0.9979	0.0000
Group × Gesture × Speech Rate	4	0.00	1.0000	0.0000
DV=Amplitude $[LL+J]_z$				
Group	2	8.84	0.0002*	0.0984
Gesture	1	0.03	0.8560	0.0002
Speech Rate	2	3.32	0.0387*	0.0393
Group × Gesture	2	0.03	0.9728	0.0003
Group × Speech Rate	4	0.20	0.9373	0.0049
Gesture × Speech Rate	2	0.09	0.9175	0.0011
Group × Gesture × Speech Rate	4	0.00	1.0000	0.0001

Appendix M. 3D opening gesture of movement displacements for UL and LL+J.
Note that the control group tended to demonstrate greater displacements across anterior-posterior (x), inferior-superior (y), and medial-lateral (z) dimensions compared to the PD group.



Appendix N. 3D closing gesture of movement displacements for UL and LL+J.



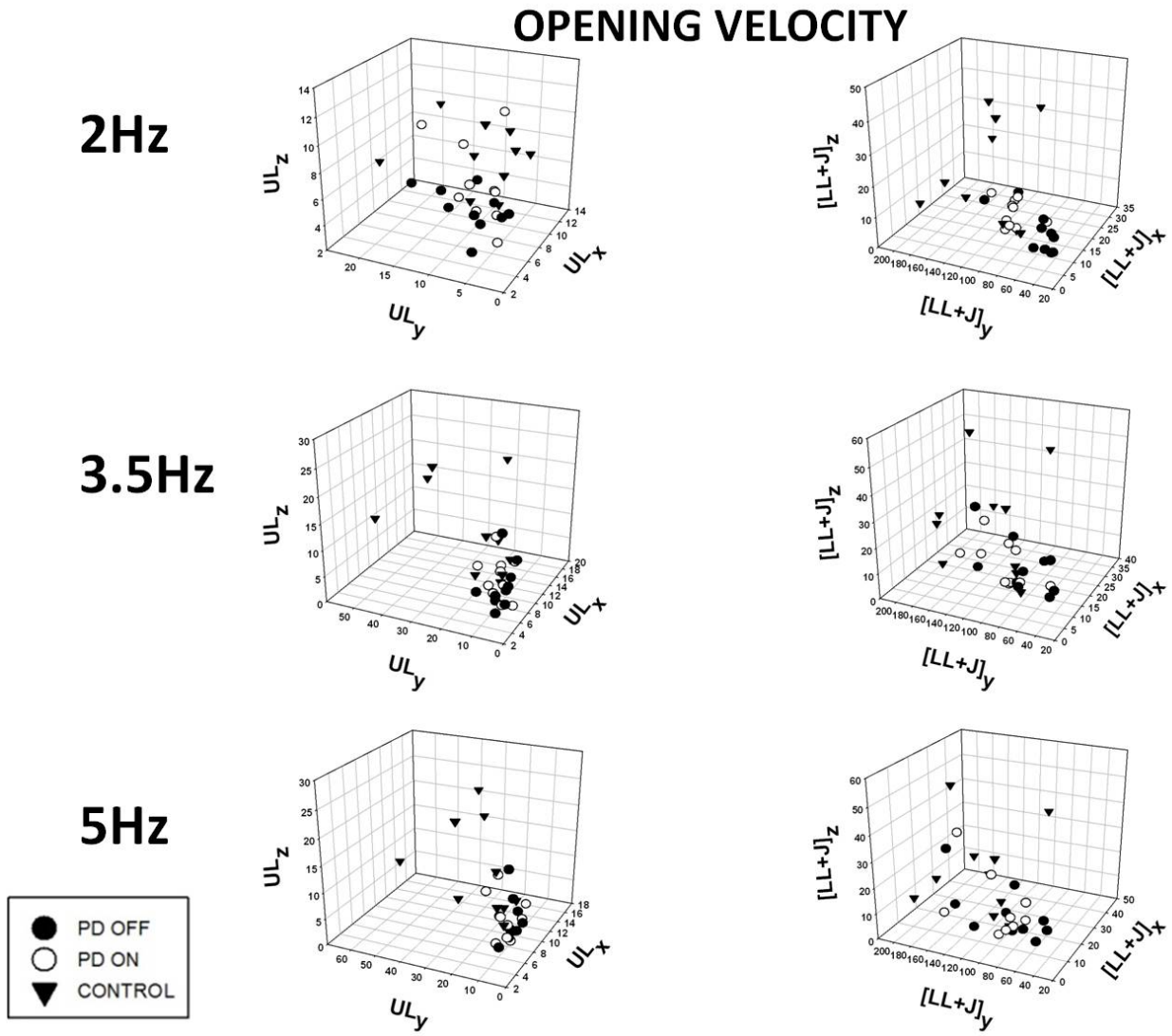
Appendix O. Summary of Wilks' lambda test: Velocity

Variable	*df*	*F*	*p*
Group	12	11.03	0.0000*
Gesture	6	1.29	0.2651
Speech rate	12	2.14	0.0145*
Group x Gesture	12	0.83	0.6211
Group x Speech rate	24	1.22	0.2158
Gesture x Speech rate	12	0.64	0.8089
Group x Gesture x Speech rate	24	0.30	0.9995

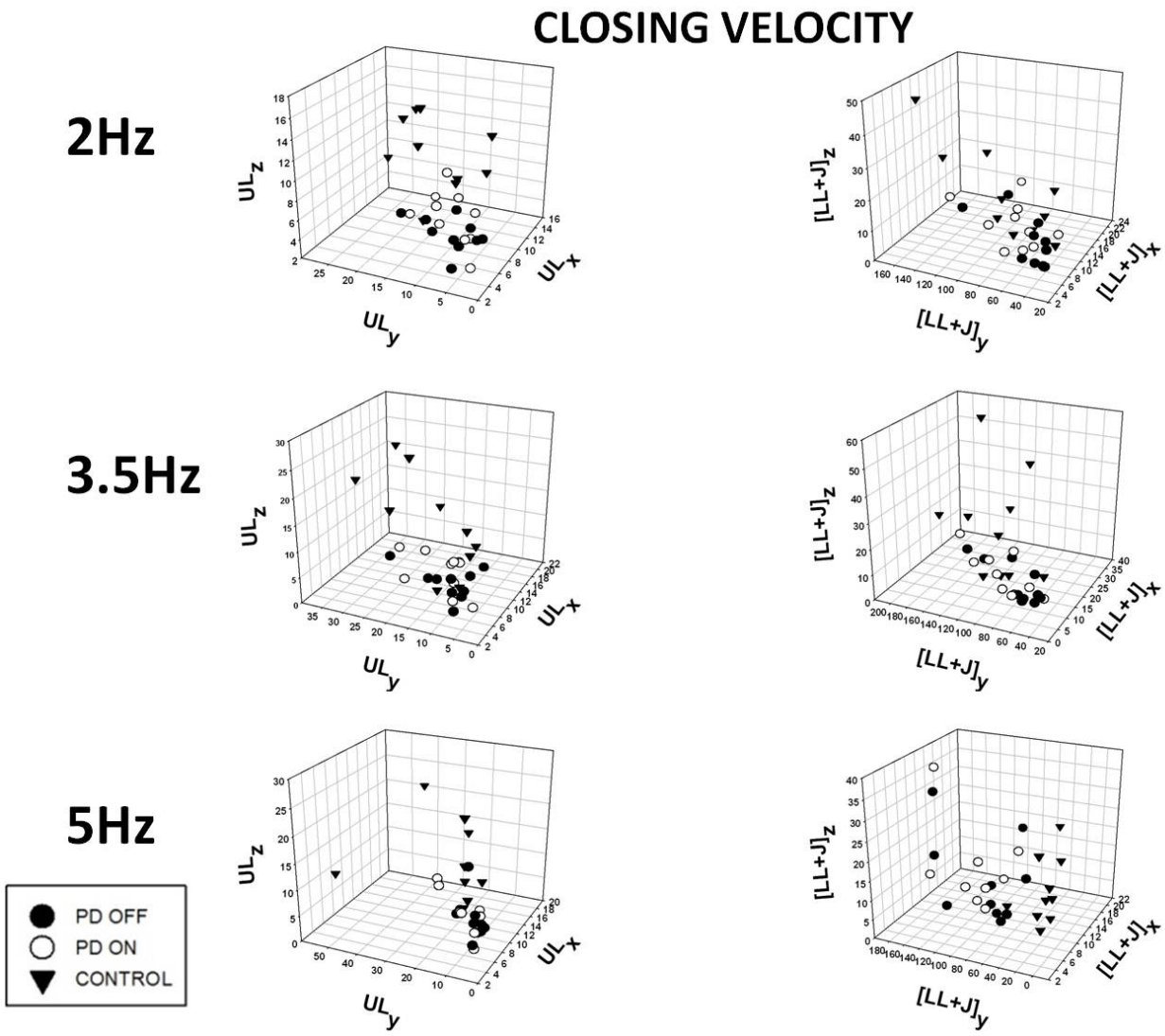
Appendix P. Summary of Univariate Analyses of Variance: Velocity

Source	*df*	*F*	*p*	Partial η^2
DV=Velocity UL_x				
Group	2	18.26	0.0000*	0.1839
Gesture	1	0.01	0.9120	0.0001
Speech Rate	2	1.68	0.1904	0.0203
Group × Gesture	2	0.03	0.9704	0.0004
Group × Speech Rate	4	0.54	0.7042	0.0132
Gesture × Speech Rate	2	0.03	0.9723	0.0003
Group × Gesture × Speech Rate	4	0.03	0.9987	0.0006
DV= Velocity UL_y				
Group	2	21.89	0.0000*	0.2127
Gesture	1	0.40	0.5294	0.0024
Speech Rate	2	4.36	0.0143*	0.0511
Group × Gesture	2	0.70	0.4988	0.0086
Group × Speech Rate	4	2.39	0.0531	0.0557
Gesture × Speech Rate	2	0.33	0.7193	0.0041
Group × Gesture × Speech Rate	4	0.74	0.5645	0.0180
DV= Velocity UL_z				
Group	2	39.07	0.0000*	0.3254
Gesture	1	1.35	0.2469	0.0088
Speech Rate	2	4.59	0.0115*	0.0536
Group × Gesture	2	1.26	0.2867	0.0153
Group × Speech Rate	4	1.30	0.2727	0.0311
Gesture × Speech Rate	2	0.07	0.9331	0.0009
Group × Gesture × Speech Rate	4	0.37	0.8299	0.0090
DV= Velocity $[LL+J]_x$				
Group	2	40.87	0.0000*	0.3354
Gesture	1	0.00	0.9919	0.0000
Speech Rate	2	3.17	0.0445*	0.0377
Group × Gesture	2	0.10	0.9052	0.0012
Group × Speech Rate	4	1.92	0.1102	0.0452
Gesture × Speech Rate	2	0.27	0.7639	0.0033
Group × Gesture × Speech Rate	4	0.42	0.7932	0.0103
DV= Velocity $[LL+J]_y$				
Group	2	27.09	0.0000*	0.2506
Gesture	1	1.48	0.2249	0.0091
Speech Rate	2	7.97	0.0005*	0.0896
Group × Gesture	2	0.50	0.6076	0.0061
Group × Speech Rate	4	0.13	0.9712	0.0032
Gesture × Speech Rate	2	2.06	0.1308	0.0248
Group × Gesture × Speech Rate	4	0.15	0.9637	0.0036
DV= Velocity $[LL+J]_z$				
Group	2	11.97	0.0000*	0.1288
Gesture	1	1.92	0.1674	0.0177
Speech Rate	2	2.06	0.1303	0.0248
Group × Gesture	2	0.17	0.8411	0.0021
Group × Speech Rate	4	0.23	0.9240	0.0055
Gesture × Speech Rate	2	0.33	0.7172	0.0041
Group × Gesture × Speech Rate	4	0.04	0.9975	0.0009

Appendix Q. 3D opening gesture of movement velocities for UL and LL+J.
Note that the control group tended to demonstrate greater velocities across anterior-posterior (x), inferior-superior (y), and medial-lateral (z) dimensions compared to the PD group.



Appendix R. 3D closing gesture of movement velocities for UL and LL+J.
Note that the control group tended to demonstrate greater velocities across anterior-posterior (x), inferior-superior (y), and medial-lateral (z) dimensions compared to the PD group.



Appendix S. Means (*SD*) of the UL_y and $[LL+J]_y$ STI for "pa" production.

		2 Hz		3.5 Hz		5 Hz	
GROUP	**Variable**	***M***	***SD***	***M***	***SD***	***M***	***SD***
CONTROL	UL_y	32.72	5.47	33.63	3.34	32.11	3.59
	$[LL+J]_y$	24.23	7.38	29.13	4.66	30.84	3.05
PD ON	UL_y	32.41	6.63	31.74	6.50	30.02	6.15
	$[LL+J]_y$	25.44	7.24	27.62	6.35	33.83	5.16
PD OFF	UL_y	32.22	6.72	33.51	6.06	30.06	5.84
	$[LL+J]_y$	24.68	5.89	26.48	4.57	32.07	3.92

Appendix T. Means (*SD*) of the UL_y and $[LL+J]_y$ STI for the rainbow passage.

		2 Hz		3.5 Hz		5 Hz	
GROUP	**Variable**	***M***	***SD***	***M***	***SD***	***M***	***SD***
CONTROL	UL_y (a)	26.57	5.93	26.52	5.16	29.70	4.23
	UL_y (b)	28.37	2.32	26.38	2.98	28.37	5.03
	$[LL+J]_y$ (a)	28.77	4.67	28.54	5.47	30.26	4.84
	$[LL+J]_y$ (b)	24.65	4.40	26.25	3.49	25.28	4.60
PD ON	UL_y (a)	25.59	6.53	24.29	5.08	24.56	8.33
	UL_y (b)	23.53	7.09	22.69	6.12	20.75	6.59
	$[LL+J]_y$ (a)	29.62	6.58	28.45	6.03	28.69	8.00
	$[LL+J]_y$ (b)	23.20	6.76	22.16	6.06	20.43	6.21
PD OFF	UL_y (a)	28.15	5.37	24.84	3.65	27.62	7.79
	UL_y (b)	23.61	5.81	22.64	5.78	20.96	7.79
	$[LL+J]_y$ (a)	29.78	5.42	27.22	5.60	29.60	6.40
	$[LL+J]_y$ (b)	23.09	4.59	23.91	4.72	21.29	7.09