THE EFFECTS OF LSVT® LOUD AND LSVT® CLEAR ON VOWEL PRODUCTION IN STN-DBS SUBJECTS WITH IDIOPATHIC PARKINSON'S DISEASE

by

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The Effects of LSVT® LOUD and LSVT® CLEAR on vowel production in STN-DBS Subjects with Idiopathic Parkinson's Disease

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ABSTRACT

Idiopathic Parkinson Disease (PD) is a neurodegenerative movement disorder that affects an estimated 1 in 1000 people worldwide. The associated speech disorder is characterized by reduced movement in the speech mechanism and reduced loudness. Lee Silverman Voice Treatment (LSVT® LOUD) has been shown to be an effective therapy for treating parkinsonian voice. In recent years, a surgical intervention-deep brain stimulation of the subthalamic nucleus (STN-DBS)—has been used to treat the movement symptoms associated with PD. It has been suggested that this procedure changes the characteristics of the voice and speech. The precise effect that STN-DBS has on speech is still being studied. This study uses acoustic analysis to compare the speech of subjects with PD with subjects with PD who have undergone STN-DBS. It addresses the following questions: 1) Compared to PD subjects, do PD subjects who have bilateral STN-DBS improve after LSVT? 2) Do two additional weeks of treatment affect the outcome? And 3) does the nature of the additional treatment (traditional LSVT LOUD vs. LSVT LOUD/CLEAR) affect treatment outcome? Six people (1 female, 5 males) with PD and bilateral STN-DBS made up the experimental group. The control group was part of a larger study of people with PD conducted by the same research group. Euclidean distances of the difference in formant frequencies, and vowel duration between F2 /i/ and F2 /i/ were compared pre- and post-LSVT, and after two additional weeks of therapy. The subjects were divided into two groups of three for the two additional weeks, one group receiving two extra weeks of traditional LSVT LOUD and the other group receiving an experimental articulation treatment called LSVT LOUD/CLEAR. Results found no significant differences pre-post, after two additional weeks (6 week), or across treatment groups. Clinical implications and limitations are discussed.

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CHAPTER I

BACKGROUND

Idiopathic Parkinson's disease (PD) is a neurodegenerative disorder that affects an estimated 1 in 1000 people worldwide. It is characterized by resting tremor, rigidity, movement disorders such as bradykinesia (slowed movement) and hypokinesia (reduced movement), postural insufficiency and disordered speech (dysarthria) (Marsden, 1994). These symptoms are associated with a degeneration of dopaminergic brain stem nuclei in the substantia nigra pars compacta. The cause of this cell death is as yet unknown. Though at this point in time life expectancy in people with PD is close to that of the general population, PD is insidious and the worsening symptoms over time have a profound impact on the patient's quality of life (Marsden, 1994).

Disordered speech is commonly seen in PD. Symptoms include reduced loudness (hypophonia), change in vocal quality, monopitch and monoloudness, reduced stress, rapid speech rate, short rushes of speech, imprecise consonants, inappropriate silences, and reduced overall intelligibility (Darley et. al, 1969). These symptoms combined are often referred to as hypokinetic dysarthria, and hypokinetic dysarthria is considered to be "the dysarthria of Parkinson's disease" (Duffy, 2005).

Hypokinetic dysarthria was previously thought to be the result of a "discoordination of the articulators" (Canter, 1965). More recent research, however, suggests that the speech involvement in PD is related to the hypokinesia that affects the entire body (Ackerman, 1991; Yunusova, 2008). Ho et. al. (1998), in their comprehensive study of 200 PD patients, found that voice was affected first, followed by fluency and articulation. The voice disorder and volume reduction could be clearly correlated with other movement phenomena in PD, such as

micrographia (miniaturized handwriting), and reduced stride length (Ho, 1998). In later stages of PD, articulation was affected as well, with patients showing similarly reduced movement in their articulators. PD subjects are often described as speaking more quickly than healthy speakers, but this perception seems to be a result of the monopitch and monoloudness that are a part of the scaling down of the movements in the laryngeal tract (Tjaden, 2000).

Parkinsonian speech has been described as "slurred" and imprecise (Yunusova, 2008). In hypokinetic dysarthria, low vowels and diphthongs tend to be more affected (Yunusova, 2008; Forrest, 1989), and stops and affricates tend to be the most affected of the consonants (Logemann, 1981; Canter, 1965). In consonants, manner of production is the first aspect to change, with stop-plosives, affricates and fricatives being the first affected (Logemann, 1981). Studies have shown specific acoustic measures of abnormal articulation in people with PD. Dromey and Ramig (1995) report longer frication duration and increased rise time for the consonants "s" and "sh" in people with PD than in healthy adults. Tjaden and Wilding (2004) describe significant differences in first moments for the consonants */t/*, */k/*, and */s/* in PD subjects, compared to healthy adults. Sapir et. al. (2007) showed that PD subjects differ significantly from healthy subjects when their second formant (F2) of the vowels */i/* and */u/* are compared (F2*i*/F2*u*). Tjaden and Wilding (2004), and Sapir et. al. (2007) describe smaller vowel space in people with PD.

LEE SILVERMAN VOICE TREATMENT

In 1995, Ramig, Bonitati, Lemke and Horii described the Lee Silverman Voice Treatment (LSVT® LOUD), which went on to be the first treatment for Parkinsonian voice disorder with level one evidence for efficacy. LSVT is unique in that it is an intensive voice therapy (delivered

for 60 minutes in 16 sessions over the course of 4 weeks) that focuses on one parameter: loudness. Loudness is a global parameter that, when increased, affects all of the subsystems involved in speech (Dromey, Ramig, 1998). Increased loudness requires greater effort from the respiratory subsystem, as well as increased glottal competence, and increased movement in the articulatory subsystem. As such, the cue of loudness, though a simple cue for the client to focus on, has a complex effect on the entire speech system (Fox et. al., 2006).

Although the principles of neuroplasticity were not well-known at the development of LSVT/LOUD, the treatment is consistent with many of the now widely disseminated principles (Fox et, al. 2006). The Principles of Neuroplasticity refers to a set of rules that affect the ability of the brain to change, and the damaged brain to repair itself (Kleim, Jones, 2008). LSVT takes advantage of the principles of intensity, saliency, and complexity.

One of the principles of neuroplasticity is Intensity Matters. It has been shown that intensive practice promotes neurological change (Kleim and Jones, 2008). LSVT is an intensive therapy; the client meets with the clinician 16 times over the course of four weeks. During the 60-minute sessions, the client engages in high-effort, highly repetitive vocal exercise. Furthermore, the client is given home practice, to be done once a day on days that he or she had therapy, and twice a day on off days (Ramig et. al. 1995). Redundancy in therapy tasks *trains* the client to use his or her loud voice, rather than keeping them reliant on cueing from the clinician, and increases generalization (Sapir, 2007).

Complexity Matters is another principle of neuroplasticity. It has been shown that complexity of practice promotes neurological change (Kleim and Jones, 2008). Although the cue used in LSVT is a simple one: Be Loud, its effects are complex. The complexity comes from the multiple subsystems that are affected during with increased loudness. Increased

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loudness requires increased effort from all three of the speech subsystems: the respiratory, phonatory, and articulatory subsystems. These three systems work together in a complex, highly orchestrated manner(Sapir, et. al. 2007). Therefore, the seemingly simple act of increasing loudness is actually physiologically highly complex. The program also utilizes increasing complexity in therapy materials, starting with single words, and working up to paragraphs and conversational speech. The therapy also includes multi-tasking, so that the loud voice may generalize out of the therapy room into the complexity of every-day life, such as holding a conversation in a crowded room (Fox et. al, 2006).

The principles of neuroplasticity also show that more salient material is more likely to promote neurological change (Kleim and Jones, 2008). In parkinsonian voice, the voice is not quiet because the person with PD is physically unable to be louder, but because of a decreased movement overall and an erroneous self-perception of loudness. People with PD often say that their speech is fine, and that the people they communicate with need to get hearing aids. This is because they perceive that they are speaking with the same amount of effort as before, and that their voice is as loud as it was before, even though to their listeners they are speaking much more softly (Fox, 2002). Dromey and Adams (2000) refer to this as a "sensory processing deficit", suggesting that PD causes an impairment in the individual's self-perception. To remedy this, LSVT focuses on "recalibration" of the system. Clients are taught that their voice is indeed softer than it was previously, and in order to bring it back to normal loudness, they must increase their effort. Because of their altered perception, people with PD often do not believe the clinician that their voice is too quiet, and when speaking in stimulated loud voice, they feel as though they are shouting (Fox et. al., 2002). LSVT capitalizes on the principle of saliency to change this erroneous self-perception (Fox et. al, 2006). LSVT incorporates "carry-over

assignments" that have the client use his or her "loud voice" in daily activities and with loved ones. In doing so, they hear from people they care about that their voice has improved. The salience of hearing that their loud voice "sounds so good" or "is the voice I fell in love with" is key to generalization of the therapy (Fox, 2002).

LSVT AND ARTICULATION

The cue "Be Loud" seems to have specific benefits beyond the principles of neuroplasticity outlined above. Specifically, LSVT has been shown to improve function in PD subjects beyond improved voice; after completing LSVT, PD subjects are more intelligible (Dromey and Ramig, 1998; Neel, 2009; Ramig et al. al. 1995; Sapir et. al. 2007). There is undoubtedly a correlation between loudness and intelligibility; however, there are studies that have found that the increased intelligibility post-LSVT comes from more than just increased loudness. Articulation has been shown to improve with LSVT as well. Dromey and Ramig (1998) showed decreased variation from token to token in the articulatory measures of semitone standard deviation and fundamental frequency when the subject uses increased vocal loudness. Sapir et. al. (2007) described changes in vowel space, second formant of the vowels /i/ and /u/, and increased "vowel goodness" in subjects post-LSVT. While Tjaden and Wilding (2004) also looked at vowel space and first moment characteristics of consonants, they could not make a clear connection between acoustic measures and intelligibility. Ramig and Dromey (1995), on the other hand, found that post-LSVT, subjects had decreased frication and rise times, closer to those of healthy adults. Increased vowel space area (Spielman, Ramig, Story, Fox, 2000), and improved vowel formants (Borrie, et. al., 2007; Sapir et. al. 2007) have also been shown in subjects post-LSVT. Wenke, et. al. (2010) showed that LSVT improves vowel space, vowel

formants, and first moment measures in subjects with non-degenerative dysarthria. LSVT/LOUD clearly has an undeniable impact on articulation, which contributes to the overall increase in intelligibility.

LSVT traditionally focused specifically and intensely on the cue of "Be Loud", with an increase in vocal loudness at the primary goal. Recently, the research group that developed LSVT/LOUD has pioneered a similarly intensive therapy program that addresses articulation instead of loudness. LSVT ARTIC maintains the same principles of training improved speech via intensity and high-effort tasks. The tasks in LSVT ARTIC focus on maximum enunciation instead of loudness. Preliminary studies show that LSVT ARTIC improves articulation parameters, such as vowel space area and Disorder-Specific Vowel Articulation Index, but does not improve loudness (Spielman et. al, 2010). One preliminary study also showed that where LSVT/LOUD improves laryngeal function, LSVT ARTIC may in fact have a negative impact on vocal fold closure (Hannon et. al., 2010). LSVT ARTIC is a new treatment technique, and more research is needed to determine its efficacy in treating hypokinetic dysarthria. LSVT LOUD/CLEAR was the precursor experimental treatment to what is now called LSVT ARTIC, and the two programs are based on the same principles.

CHAPTER II

HISTORY OF THE TREATMENT OF PARKINSON'S DISEASE

SURGICAL TREATMENT

In the early 1940s, Russell Meyers discovered that surgical removal of parts of the pallidum had a positive effect on extrapyramidal diseases (Meyers, 1959). This inspired a handful of neurosurgeons to try treating Parkinson's disease with pallidotomy (Laitinen, 1992). In 1947, Spiegel, et. al. pioneered a stereotactic technique using the injection of chemicals and three-point targeting on a Cartesian plane to lesion very specific parts of the brain (Krauss, 1996). By targeting the anterodorsal part of the pallidum, neurosurgeons could provide some temporary relief for the rigidity associated with PD (Laitinen, et. al. 1992). Lars Leskill in Lund, Sweden, noted that the results of pallidotomy were unsatisfactory, and experimented by changing the site of the lesion. He varied the site of the lesion in different patients, and found that the best results came from lesions in the postero-medial part of the pallidum. He then made variations to find the minimum size of lesion needed for optimal outcome. The result was consistent beneficial effect on all three of the primary symptoms of PD: tremor, rigidity and hypokinesia, with relatively little occurrence of negative side effects or recurrence of symptoms. The procedure, however, showed no significant effect on the dysarthria associated with PD (Svennilson, 1960). With evidence provided by Svennilson's careful and comprehensive study, pallidotomy became the first successful treatment for parkinsonism. In spite of this evidence, there was debate within the neurosurgical community about the best location to lesion for treatment of PD (Goetz, 1996), and through further experimentation, Hassler and Riechert (1954)

found that lesioning of the venterolateral thalamus produced dramatic results in the treatment of tremor. Because of this, thalamotomy became the most popular treatment for PD, with even Leskill changing over in spite of verbalized statements that pallidotomy seemed more effective (Laitinen, 1992). This debate was cut short, however, in the 1960s, with the discovery of Levadopa.

THE AGE OF LEVADOPA

In the 1960s, Ehringer and Hornykiewicz showed that Parkinson's disease is a result of dopamine depletion (Hornykiewicz, 1966), and the search for a treatment turned to the use of dopamine imitators. Hornykiewicz's research group in Vienna and Barbeau in Montreal simultaneously and independently reported on the use of D, L, dihydroxyohenylalanine (Levadopa), the immediate precursor to dopamine, to treat the symptoms of Parkinson's disease (Barbeau, et. al., 1969). Early short term, small trial studies with low doses showed mixed results or very little therapeutic effect (McGeer, 1964; Greer, 1963). However, subsequent larger randomized control studies began to show promising results in the treatment of parkinsonism with Levadopa. In a controlled trial by Cotzias et. al., 8 out of 16 patients receiving 13 to 16 g of Levadopa daily showed dramatic improvement in all parkinsonian symptoms (Cotzias, 1967), and a large-scale double-blind study by Yahr et. al. showed that in spite of significant side effects, 3-8mg daily of Levadopa significantly increased functioning in 91% of trial subjects (Yahr et. al, 1969). With these promising results corroborated over the next decade, Levadopa replaced neurosurgery as the most promising and most popular treatment for PD. It did not halt the progress of parkinsonism, but it made a dramatic difference in the quality of life for patients who were taking it (McDowell et. al., 1970). The study by Yahr et. al. did, however, outline

many of the significant side effects of Levadopa treatment., including nausea, vomiting, anorexia, postural hypotension, cardiac effects, psychological and sleep disturbances, and involuntary movements. These involuntary movements affected more than 60% of the patients in the trial, and began after the patients had been taking high doses of Levadopa for an extended period of time (Yahr, 1969). This was one of the first indications of one of the major drawbacks of treatment with Levadopa.

The main side effects that were eventually found with use of Levadopa were gastrointestinal upset, mental disturbances such as confusion and psychosis, and motor complications. GI upset tended to occur early in the treatment with Levadopa, and was rarely bad enough to discontinue treatment (Barbeau, 1969). Psychiatric side effects of Levadopa treatment include confused state seemingly related to toxicity, visual hallucinations, and depression. Dementia has been reported as a possible side effect, specifically with impairments to short-term visual and verbal memory (Shaw, 1980). The motor complications that result from taking Levadopa include: end-of-dose deterioration (wearing-off effect), unpredictable mid-dose changes from mobility to disability ("on-off" effect), involuntary movements (dyskinesia), and painful fixed posture of one or more of the limbs upon waking (early morning dystonia). These motor complications tend to not begin until the patient reaches optimal doses for treatment of parkinsonian symptoms, and they begin between 5 and 15 years after the patient starts taking Levadopa (Miyawaki et. al., 1997). Though they disappear as dosage is reduced, for many patients they begin to reappear at lower and lower dosages (Barbeau, 1969). The wearing-off effect is generally the first to be seen, starting 5 years after onset of treatment. It is characterized by a sudden drop in effectiveness of the medication. Patients report that they can "feel" the medication ceasing to function toward the end of a dosage period (Miyawaki et. al., 1997). The

length of time that the medication remains effective also shortens with the duration of treatment, sometimes down to only an hour or two of effective time per dose, and additional doses merely cause dyskinesia. This effect has been reported as affecting as many as 52 percent of patients after six years of treatment (Shaw et. al, 1980).

The "on-off" effect refers to a sudden change from mobility to severe parkinsonian symptoms, sometimes in a matter of seconds (Miyawaki et. al. 1997). These fluctuations occur mid-dose, and can oscillate incredibly rapidly: as many as ten distinct cycles over the course of half an hour. During the off periods patients might suffer visual hallucinations, profound depression, stupor and dystonia (Shaw et. al., 1980). Levadopa induced dyskinesias occur at different periods during the medication cycle, including between doses, and are highly varied. They may include choreoform movements of the face, tongue, jaw, head and extremities (Barbeau, 1969); "jerking" movements during sleep; and focal spasms (Shaw, 1980). This was the first major motor side effect to be noted during early Levadopa trials, and was reported in more than 60% of patients in early clinical trials (Yahr, 1969, Barbeau, 1969). Early morning dystonia is characterized by a painful fixed posture, generally in the foot or the leg, and associated with more general akinesia before the first dose of the day (Miyawaki et. al., 1997).

DEEP BRAIN STIMULATION

When the debilitating nature of the side effects of Levadopa came to light in the 1980's, there was a resurgence of research of neurosurgical treatments. In 1992, Laitinen revived Leskill's previous work in stereotactic surgery, and reported marked improvements in rigidity, hypokinesia, dysarthria, gait, and Levadopa-induced dyskinesias when using stereotactic techniques to induce lesion in the posteroventral lateral portion of the globus pallidus (Laitinen,

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1992). Further research found mixed but generally positive results with unilateral pallidotomy, most of the improvement being evident on the side contralateral to the surgery (Goetz, 1996). Advances in technology since the 1950's allowed for neurosurgical treatment of PD to be taken in different directions during this "renaissance" of interest in the pallidotomy. These include the striatal transplantation of fetal mesencephalic tissue, and deep brain stimulation (Goetz, 1996).

It is currently thought that the symptoms of PD result from flawed input from the basal ganglia to the motor cortex. In the healthy brain, the subthalamic nucleus (STN) receives inhibitory signals from the globus pallidus externum (GPe), as well as excitatory signals from the cortex. This complex balance of excitatory and inhibitory signals controls the excitation of the motor cortex, resulting in movement (DeLong, 1990). In PD subjects, degeneration of dopaminergic cells in the Substantia Nigra pars compacta leads to a dearth of dopamine in the system (Bergman and Deuschl, 2002), causing excessive inhibition of the GPe, and therefore excessive inhibition of the STN. This leads to excessive inhibition in the thalamus, which causes reduced excitation in the motor cortex. This reduced excitation in the motor cortex is thought to result in the "scaling down of movement" that can be seen in the symptoms of PD: bradykinesia, rigidity, tremor, postural instability, and hypokinetic dysarthria (DeLong, 1990; Lozano, Dostrovsky, Chen and Sashby, 2004). Other theories suggest that the basal ganglia contribute to movement by facilitating desired motor programs and inhibiting undesired motor programs (Mink, 1996; Mink and Thach, 1993).

Early in the study of neurosurgery as a treatment for parkinsonism, it was found that stimulation of the sub-thalamic nucleus caused a reduction in tremor. In the early 1990s it was postulated that implants to stimulate the sub-thalamic nucleus could be a highly effective treatment for parkinsonian symptoms. The first clinical trials of the technique of Deep Brain

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Stimulation were pioneered in the mid-1990's (Krauss, 1996, Benabid, 1996). Deep Brain Stimulation is the implantation of electrodes deep within the brain. The surgery involves drilling a hole in the skull, and slipping an electrode strip through the brain matter until it rests in the desired location(Koller, 1997); the electrode strip is controlled by a pulse generator implanted subcutaneously in the chest. Similar to a pacemaker, this pulse generator is then used to adjust the pulse frequency of the implant for maximum efficacy (Krauss, 1996; Koller, 1997). In early DBS patients, the electrode strip was implanted against the ventral intermediate nucleus (VIM) of the thalamus. These studies showed similar results to thalamotomy, with the greatest improvement seen in tremor reduction. The added benefits over thalamotomy were the reversible nature of the procedure, the ability to optimize stimulus settings for maximum efficacy, and the increased ability to perform bilateral stimulation without the morbidity seen in bilateral thalamotomy (Koller, 1997). Although early studies showed a significant reduction in parkinsonian tremor, pallidotomy was still reported as the preferable procedure, because it affected more of the essential parkinsonian symptoms than stimulation of the VIM (Koller, 1997). Subsequent studies found that electrical stimulation of the sub-thalamic nucleus (STN) was as effective at alleviating the movement disorder associated with parkinsonism as pallidotomy, with all of the above-listed added benefits (Houesto, 2000). Stimulation of the STN quickly became the preferred procedure (Jones, 2007), and STN-DBS was presented as a good alternative to medication in patients who respond well to Levadopa, but who find the associated dyskinesias to be debilitating. (Houesto, 2000).

As time and research went on, however, it was found that DBS also comes with a host of side effects, including cognitive dysfunction, depression, social maladjustment, and impaired articulation (dysarthria) (Ferrara, 2010). Suicide rates with STN-DBS are significantly higher

than those in the age-matched general population (Voon et. al. 2008). Cognitive impairments with bilateral stimulation have been reported, especially during complex tasks. Cognitive-motor performance in multi-tasking situations is significantly degraded during bilateral stimulation, impacting every-day functioning such as driving and decision-making (Alberts et. al. 2008). While motor functioning was clearly improved with STN-DBS, quality of life indicators like occupational function, interpersonal relationships, leisure activities, and living conditions did not improve (Ferrara 2010), and in some patients, cognitive and psychological parameters worsened (Alberts 2008, Voon 2008).

SPEECH EFFECTS OF STN-DBS

Determining the intelligibility of people with STN-DBS has been and continues to be a tricky process. There are varying reports about the effects of STN-DBS on speech, and researchers have used a wide variety of parameters in their assessment of speech intelligibility in these subjects. As such, there is considerable disagreement about the effects that STN-DBS has on speech and voice.

D'Alatri et. al. (2008), Pinto et. al. (2003), and Gentil et. al (2000) all report improvement of speech parameters with STN-DBS. D'Alatri et. al. (2008) used acoustic analysis to determine voice quality of 12 subjects. Parameters used were the Multi-dimensional Voice Parameter protocol from *Kay Elemetrics*, which measures jitter, shimmer, and noise-toharmonic ratio during sustained phonation. This group also used "voice and tremor", "intonation stability" and diadochokinetic rate protocols to assess voice quality. Intelligibility was assessed using item 18 of the Universal Parkinson's Disease Rating Scale (UPDRS). Based on these protocols, they reported significant improvement in speech and voice parameters with STN- DBS. Pinto et. al. (2003) used items 18-31 of the UPDRS to assess speech and communication of 26 PD subjects with STN-DBS. They also took force measurements of the lips and tongue during non-speech tasks. All measurements were compared between stimulation on, and stimulation off conditions. Pinto et. al. found that both force parameters and UPDRS scores improved with STN-DBS on. Gentil et. al. (2000) also used the UPDRS rating scale, item 18 to assess intelligibility in 16 subjects with STN-DBS. They also measured force generated by the lips and tongue during non-speech and speech activities, as well as performed acoustic analysis of the following parameters: duration, pause detection, fundamental frequency, jitter, shimmer, and relative intensity during sustained phonation; and repetitive speech tasks. Based on these assessments, they also found improvement in objective voice parameters with STN-DBS on.

The above studies all claim some improvement in speech parameters with STN-DBS. Assessing intelligibility based entirely on item 18 of the UPDRS scale provides a very limited view of the subjects' speech intelligibility. Furthermore, the objective parameters were based primarily on non-speech tasks, which give very limited information about actual speech and articulation. In spite of these findings, other studies have found that patients tend to rate their own speech as worse with STN-DBS turned on and that, in spite of reported improvements in individual voice and speech parameters, there is an overall worsening of speech with STN-DBS turned on (Klostermann et. al, 2007). The reason for this perceived worsening of speech has been difficult to pin down, because it seems to vary from subject to subject (Pinto, 2005; Tripoliti, 2006). Higher amplitude DBS settings tend to degrade intelligibility (Tornqvist, 2005), and left side stimulation, rather than bilateral stimulation, profoundly degrades articulation and prosody, which has a significant effect on intelligibility (Santens, 2003). Putzer et. al. (2008) analyzed voice onset time, frication, and formant frequencies as acoustic measures of this reported decrease in intelligibility, while Gentil et. al. (1999) described DBS patients' speech as "slurred."

Iulianella, Adams and Gow (2008) did a comprehensive meta-analysis of eight studies on the effects of STN-DBS on speech. Seven of the eight studies were group studies, with 6-20 subjects, and one was a single-subject case study. Of these eight studies, six reported no beneficial effect of STN-DBS on speech, and four found negative effects. Negative effects reported included reduced maximum phonation time, reduced intensity of sustained phonation, reduced intelligibility, reduced prosody, and reduced articulatory accuracy. Two studies found positive effects on speech from STN-DBS, but one of them was a single-subject case study, and the other provided insufficient statistical analysis to support its findings. Thus, Iulianella, Adams and Gow report that there is currently very little support for beneficial effects of STN-DBS on speech, and there is preliminary evidence for negative effects. The study also concludes that there is a relatively large degree of variation in speech effects across subjects with STN-DBS.

Several studies have shown that STN-DBS may actually have a negative impact on speech and intelligibility. Santens et. al. (2003) reported that in seven patients with bilateral STN-DBS, there were significant speech discrepancies based on lateralization of stimulation. Reading of a 200-word passage and sustained phonation were evaluated for prosody, articulation, speech intelligibility, quality of voice, loudness, and speech rate. Tasks were performed in four conditions: bilateral stimulation on, stimulation off, left-hemisphere stimulation only, and righthemisphere stimulation only. It was found that, compared to other conditions, left hemisphere stimulation had a significantly negative effect on prosody, articulation, and speech intelligibility. Right hemisphere only stimulation had no significant effects compared to bilateral off. In this study, there was no significant worsening of speech with bilateral stimulation on. Rousseaux et. al. used the UPDRS and a dyskinesia scale to assess global effects of STN-DBS. To assess dysarthria specifically, all seven subjects were evaluated by qualified SLPs using the Lille Dysarthria Test, which includes a subtest dedicated to articulation and phoneme analysis, as well as a subtest for intelligibility. Three of the seven subjects showed significant worsening of dysarthria with STN-DBS on, especially when they were not receiving medication. A study by Tornqvist et. al. (2005) found that DBS parameter settings have a strong effect on speech intelligibility. 10 subjects read a standard running text and five nonsense sentences with their DBS adjusted at 11 different settings. Four of the subjects showed significant worsening of intelligibility with STN-DBS on, with settings optimized. Higher amplitude settings and higher frequency caused significant deterioration in all subjects. This study suggested that adjusting settings to optimize motor benefit may, in some individuals, cause a negative effect in speech. Therefore, DBS parameter settings may potentially be optimized for a beneficial effect in motor control, while minimizing the negative effect on speech. Tripoliti (2010) found that speech intelligibility decreased by 14.4% one year after DBS implantation when off-medication, and by 12.3% when on medication. Furthermore, this study found that intelligibility in DBS subjects did not improve after LSVT, and in fact 4 out of 10 subjects decreased in intelligibility following LSVT. This study gives preliminary data that LSVT may be an ineffective treatment for the speech disorder associated with STN-DBS.

Clearly, the effect of STN-DBS on speech is still debatable, and with appropriate parameter settings, the negative effects on speech may be minimized. In order to understand more thoroughly the role that STN-DBS has on speech production and intelligibility, more research is needed. Furthermore, because subjects with STN-DBS have different speech characteristics than the hypokinetic dysarthria seen with PD, methods of treating parkinsonian

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voice must be studied with respect to the changes that come from STN-DBS. This study aims to begin addressing some of these research demands.

CHAPTER III

METHODS

The present study uses acoustic analysis to measure the dysarthric features of speech in people with STN-DBS. Acoustic analysis is a useful measure because acoustic variants, specifically the relationship between the frequencies of F1 and F2, are directly related to the shape of the oral cavity and the placement of the articulators (Honda and Kusakawa, 1997). This study uses the Euclidean distance between /i/ and /I/ (EDiI), and vowel duration of /i/ and /I/ to compare individuals with PD (PD subjects) to individuals with PD who have bilateral STN-DBS (DBS subjects), as a means of beginning to understand the differences in the dysarthria between the two populations. This study addresses the questions:

- 1. Compared to PD subjects, do DBS subjects improve after traditional LSVT?
- 2. Do two additional weeks of treatment improve treatment outcomes in DBS subjects?
- 3. What is the difference between two additional weeks of LSVT LOUD vs. two weeks of LOUD/CLEAR?

RATIONALE

The voice disorder associated with idiopathic Parkinson Disease (PD) relates to a scaling down of the movements of the entire body. Lee Silverman Voice Treatment (LSVT LOUD) systematically trains the global parameter of loudness, and in so doing increases the intelligibility of people with hypokinetic dysarthria. LSVT LOUD also has a positive impact on articulation, as described previously (Ramig and Dromey, 1995).

Intelligibility of DBS subjects takes on different characteristics from those generally seen in PD subjects. While some studies show no worsening of speech parameters post-DBS (D'Alatri et. al. 2008, Pinto et. al. 2003), patients tend to rate their own speech as worse with deep brain stimulation turned on (Klostermann, 2007). The reason for this perceived worsening of speech has been difficult to pin down, because it seems to vary from subject to subject (Pinto, 2005; Tripoliti, 2006). Klostermann et. al. (2007) found that while individual speech parameters seem to either stay the same or improve with DBS on, there is an overall worsening of speech, and Gentil et. al. (1999) described DBS patients' speech as "slurred." Acoustic analysis may be used as a means of addressing these articulatory differences. Furthermore, it may be a valuable means of measuring treatment efficacy, and measuring the effects of LSVT LOUD and LSVT LOUD/CLEAR as compared to PD subjects.

Acoustic analysis of the first and second formant frequencies (F1 and F2) has been used as an accurate means to describe vowel production. F1 and F2 frequencies have been shown to change as the shape of the vocal tract changes to create different speech sounds. Generally, as the tongue moves forward, F2 increases and F1 decreases. As the tongue moves backward, F2 decreases. When the tongue is elevated, F1 decreases, and when the tongue is lowered F1 increases (Sapir et. al, 2010). Therefore /i/, a high front vowel, is expected to have a low F1 and a high F2, whereas /I/, a mid front vowel is expected to have a higher F1 and a high F2. The relationship between F1 and F2 of two different vowels has been used to show that vowels tend to centralize—to become more similar to one another—in dysarthria (Sapir et. al. 2007).

The Euclidean distance formula is used to measure the difference between F1 and F2 frequencies for different vowels. A larger ED between the vowels /i/ and /I/ theoretically indicates a larger difference between the production of the two vowels. Dysarthric speakers are expected to have a smaller Euclidean distance between the two vowels (Neel, 2008). /i/ and /I/ are produced in close proximity to one another. Therefore, a significant difference in acoustic

measures pre- and post-treatment should indicate that the Euclidean distance between /i/ and /I/ has a significant impact on speech intelligibility. Because of their close proximity, the difference between /i/ and /I/ may play a more substantial role in speech intelligibility than two vowels that are further apart, like /i/ and /u/.

Vowel duration has also been described as a means of expressing vowel quality, and is positively correlated with well-identified vowels (Neel, 2008). Neel includes it in her list of 5 global acoustic characteristics for the study of vowels. It offers another global measure for understanding the production of dysarthric speech.

PARTICIPANTS

The participants in this study were six individuals (5 male, 1 female) with Idiopathic Parkinson's Disease, all of whom had undergone surgery for bilateral deep brain stimulation of the subthalamic nucleus (STN-DBS). At the time of data collection, they were between 54 and 69 years of age (Mean: 60), and had been diagnosed with PD 5 to 15 years previously (Mean: 9.6). Time since surgery was 6 months to 3 years (Mean: 15 months). All participants were rated for severity of articulation impairment and voice impairment, both on a scale of 0-5, with 0 = no impairment and 5 = severe impairment. (See Table 1.)

Tabl	le 1	: I	DBS	Sub	jects:

Subject	Gender	Age at data collection	Years since diagnosis	Articulation Severity	Voice Severity	Months since surgery
DBS-5	F	57	14-15	0	4	36
DBS-6	М	59	5-6	3	2	8
DBS-7	Μ	67	10	4	3	12-13
DBS-8	Μ	69	11.5	0.5	3.5	6
DBS-9	Μ	54	8	1.5	1	18
DBS-10	Μ	56	8	0.5	2	10

Most participants kept their stimulator settings and medication steady for the course of the treatment. DBS-5 changed her settings to home parameters around weeks 5 and 6 of the study, and DBS-7 stopped taking his morning Mirapex dose between pre- and post- recordings. Both commented that they did not think the changes had any effect on their speech.

The control group consisted of PD subjects from a larger study on Parkinsonian speech and voice conducted by the same research group. They received LSVT LOUD by the same clinicians and on the same timeline as the STN-DBS subjects, though they did not undergo the additional two weeks of treatment. They were medicated at the time of the study, and medication was constant throughout the study. As with the STN-DBS subjects, they were rated on a scale of 1-5 for voice severity and articulation severity. Demographics for the control subjects can be seen in Table 2.

DATA COLLECTION

Data were collected seven times during the study: three data points before treatment (PRE), two data points after four weeks of LSVT LOUD (POST), and two data points after two additional weeks of either LSVT LOUD or LSVT LOUD/CLEAR (6 weeks). Data were collected at the National Center for Voice and Speech (NCVS) in Denver, CO. Data were collected using an AKG C410 unidirectional head-mounted condenser microphone, placed 8 cm from the participant's lips. The microphone was calibrated at 30 cm, using a Bruel and Kjaer Type 1 Sound Level Meter (model 2238). Data were collected in an Industrial Acoustics Company (IAC) sound treated booth. Data were recorded directly into a computer using the Kay

Elemetrics CSL 4300 (Kay Elemetrics Corp., Lincoln Park, NJ) hardware. The target passage (The Rainbow Passage) was presented via computer screen.

		Age since		Voice	
Sex	Age	Diagnosis	Stage	Severity	Artic Severity
Μ	60	4	2	2	2
F	72	8	3	4.5	1.5
F	63	28	2.5	3.5	4.5
М	60	4.5	1.5	2	1
М	73	1	2.5	1	1
М	67	1	1.5	1	1
М	69	1.5	2	1	0.5
М	65	4	2.5	1.5	2
М	82	8	3	3	1
М	74	8	2.5	1.5	0.25
М	66	0.7	2	2.5	1
М	60	6	2	3	0.25
М	71	2	1.5	2	0
F	63	2	2	2.5	0.5
м	40	5	2	2.5	0.5
M	49	3	3	2.3	0.5
Μ	85	1	2.5	3.5	0.25

Table 2: Parkinson's Disease Control Subject Demographics:

TREATMENT

All treatment was delivered by two speech-language pathologists (SLPs) expert in the delivery of this therapy. Treatment consisted of four weeks (16 sessions) of LSVT LOUD. Each subject then received two more weeks (8 sessions) of additional therapy (24 sessions total). Three subjects continued with traditional LSVT LOUD, and three participated in LSVT LOUD/CLEAR.

LSVT LOUD/CLEAR varies from LSVT LOUD in that it adds a focus on articulation. The cues are both "BE LOUD" and "BE CLEAR." Tasks are delivered in a similar manner to traditional LSVT, with a high degree of repetition, and a hierarchy of difficulty. Differences between LSVT LOUD and LSVT LOUD/CLEAR can be seen in Table 3.

Task	LSVT LOUD	LSVT LOUD/CLEAR
Daily Task #1	15 repetitions maximum	5 repetitions maximum sustained
	sustained phonation.	phonation, followed by maximum
		over-enunciated "tuh" and "kuh,"
		5 repeats each.
Daily Task #2	Maximum fundamental frequency	Maximum over-enunciated
	pitch range: "high and low	"tuh/kuh", "nuh/guh", "oo/ee"
	glides". 15 repeats each.	pairings in one breath, 5 repeats
		each.
Daily Task #3	Maximum speech loudness in	Maximum speech loudness and
	functional phrases. Model:	enunciation in functional phrases.
	LOUD	Model: LOUD, CLEAR
Hierarchal Drills	Clinician model: LOUD	Clinician model: LOUD and
		CLEAR
Cues	Be LOUD!	Be LOUD, be CLEAR!

Table 3: LSVT LOUD vs. LSVT LOUD/CLEAR:

Participants were grouped according to need. The three participants with the highest articulation severity scores (DBS-6, DBS-7 and DBS-9) participated in LSVT LOUD/CLEAR, and the others participated in two additional weeks of LSVT LOUD (See Chart 1)

Chart 1: Subject Groups



DATA ANALYSIS

Analysis was done using TF32 Time Frequency Analysis software. The vowels /i/ and /I/ as found in the context of the Rainbow Passage (Fairbanks, 1960) were analyzed for duration, and ED of the F1 and F2 frequencies. Three tokens each for the sounds /i/ and /I/ were taken from the rainbow passage for analysis (see Table 4). The microphone files were calibrated to remove any change in loudness across data recording sessions. To obtain vowel duration, the distance was measured from the onset to the offset of the vowel. Formant frequencies were measured at 30ms around the midpoint of the vowel. Midpoint of the vowel was determined by measuring the length of the vowel, from the zero-crossing of the first regular glottal pulse to the zero-crossing of the last regular glottal pulse, and dividing by two. Euclidean distance was calculated with the formula: sqrt((F1i-F1u)^2+(F2i-F2u)^2).

Table 4: Vowel Tokens:

Vowel	Word Token	Sentence
/i/	these	"These take the shape of a long round arch"
/i/	people	"People look but no one ever finds it"
/i/	Hebrews	"To the Hebrews it was a sign"
/I/	division (stressed syllable)	"The rainbow is a division of white light"
/I/	his	"When a man looks for something beyond his reach"
/I/	it	"Some have accepted it as a miracle"

Reliability

20% of data points were analyzed by two second-year students in speech and language pathology, to check inter-rater reliability. They received the same training on the software and analysis procedures, and analyzed the data points separately. Test-retest reliability was checked by measuring data from multiple pre- and post-data collection sessions, to measure within-speaker variability across days. Intra-rater reliability was checked by re-measuring 20% of the data. T-test for intra-rater reliability was T=0.732, and T-test for inter-rater reliability was T=0.51 for Duration i-I, and T=0.71 for EDiI. Reliability was acceptably high to consider the data analysis reliable.

CHAPTER IV

RESULTS AND DISCUSSION

STATISTICAL ANALYSIS

Initially, a repeated measures ANOVA was run between the individual tokens of each vowel to determine whether they should be pooled for further comparison. It was found that the duration and F1 and F2 frequencies of the tokens "it" and "these" varied significantly from the other tokens in their respective sets. Thus, data were pooled in two different ways for further analysis. One set of data pooled all three of the tokens from each vowel, and those were used to calculated duration i-I and EDiI. The other set of data omitted the tokens "it" and "these" from the calculations. "Hebrews" and "people" were pooled to use for the /i/ tokens, and "his" and the second syllable of "division" were pooled to use for the /I/ tokens. Two partially repeating measures ANOVA reports were run on each of these pooled data sets: one to determine statistical differences in the difference of duration between i/i and I/ (duration i-I), and one to determine statistical differences in the Euclidean distance between i and I (EDiI). This led to four reports: duration i-I with three pooled tokens (dur3), duration i-I with two pooled tokens (dur2), EDiI with three pooled tokens (ED3) and EDiI with two pooled tokens (ED2). Measures were compared between PD and DBS subjects pre-treatment and post-treatment. Measures were also compared within the DBS group pre-post, and after 6 weeks. The DBS groups LSVT LOUD and LSVT LOUD/CLEAR were also compared pre-post and after 6 weeks. No statistically significant differences were found for either measure in any condition.

DISCUSSION

The first question addressed in this study was: Compared to PD subjects, do DBS subjects improve after traditional LSVT LOUD? In order to compare DBS subjects with PD subjects after LSVT, they must first be compared before LSVT. There were no significant differences found between the PD control group and the DBS groups in the pre-treatment condition, making them good groups to compare for treatment effects. The lack of difference may be because the measure used was invalid to capture the nature of the articulation deficits in these two populations, or because there was in fact no difference in the production of these two vowels between the groups pre-treatment. There was also no significant difference between the two groups post-treatment. The measure was chosen based on the theory that Euclidean distance could be a valid measure to describe the production of vowels in dysarthria. However, at the time of this study the validity of the EDiI measure had not yet been verified. Based on this study alone, there was no significant improvement for either the DBS or PD subjects post-LSVT. Because there have been many studies showing that PD subjects improve in intelligibility and articulation after LSVT LOUD, it can be assumed that the measure was not valid, rather than that the treatment was ineffective.

It should be noted that the PD and DBS groups were substantially different in composition. The PD subjects came from a larger study by the same research group as the DBS subjects. Data on the PD subjects were only collected four times, rather than the seven times that data were collected for the DBS subjects. The PD subjects participated in two pre-treatment and two post-treatment data collection sessions. No data were collected for the PD subjects after 6 weeks. Therefore, a partially repeated measures ANOVA had to be run on the data, which is a less rigorous measure than what could have been used had the two groups had the same number of data collection points. Furthermore, the data for the PD subjects were analyzed by a different person than the DBS subjects. Both people analyzing the data were trained together, and interrater reliability was found to be high, but this still must be taken into account.

The second question addressed in this study was: Do two additional weeks of treatment improve treatment outcomes in DBS subjects? Two additional weeks of treatment were found to have no significant effect on the articulatory measures in this study. As with the previous research question, this could be for a variety of reasons. It is possible that no significant differences were found because no significant improvements were made after two additional weeks of treatment. However, it is the author's opinion that this would be a hasty conclusion.

Because this research question addresses two groups that underwent the same treatment, had the same number of data points taken, and were analyzed by the same researcher, the conclusions drawn from this research question can be considered more sound than those drawn from the previous question. However, the measure remains questionable. The speech of DBS subjects is often referred to as "slurred" (Gentil et. al., 1999). Though "slurred" is an imprecise term, it generally connotes increased coarticulation rather than a change in vowel production. A measure based on consonant production or coarticulation might therefore provide a more accurate picture of the speech changes in DBS subjects than the present vowel measure.

The measure could also be improved by taking data from sentences specifically created to target articulation. The tokens in this study were chosen from the Rainbow Passage for two reasons. The fluent reading of the Rainbow Passage provides tokens from continuous speech, theoretically closer to conversational speech and therefore theoretically more representative of functional speech than sentence-reading tasks. The Rainbow Passage was also chosen because this study compliments another current study which uses the same tokens to test whether

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Euclidean Distance is an accurate measure for articulatory improvement, based on the PD subjects used as controls in this study. The Rainbow Passage was a common data point between the two studies. Future studies that don't hold these considerations may be better served to use sentences created to gauge articulatory accuracy rather than the Rainbow Passage.

The third question addressed in this study is: What is the difference between two additional weeks of LSVT LOUD vs. LSVT LOUD/CLEAR? The two additional weeks of LSVT LOUD were developed under the theory that some subjects who do not respond as well to the traditional 4 weeks of LSVT may benefit from two additional weeks of "calibration". "Calibration" is the component of LSVT that trains the subject to increase his or her habitual vocal effort to incorporate the increased effort necessary to be heard with PD. The comparison of two extra weeks of LSVT LOUD with LSVT LOUD/CLEAR was trying to answer the question of whether two weeks of calibration were more or less effective than two weeks with a focus on articulation (as described above). For the measures used in this study, no significant results were found to distinguish two additional weeks of LSVT LOUD vs. two weeks of LSVT LOUD/CLEAR. As with the above questions, the lack of significant results may more likely point to the inappropriateness of the measure rather than a lack of change in the subjects. No conclusions can be drawn at this time as to the efficacy of the two additional weeks of LSVT, or to the efficacy of two weeks of additional calibration compared with two weeks of LSVT LOUD/CLEAR.

Sometimes in a small data set although there are no significant group results, there may be individual trends that suggest change not seen in the group results. Examining the data for these subjects shows that not only is there no significant group trend, there are also no apparent individual trends. It was theorized that if the subject's articulation improved, the Duration of i-I

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would increase, and the EDiI would decrease, both measures indicating an increase in difference between the production of the two vowels. As can be seen in Table 3, and in the charts in Appendix A, DBS-8 shows a consistent increase in EDiI, and DBS-10 shows a consistent decrease in EDiI when the data within treatment condition are averaged. DBS-8 also shows a consistent increase in Duration i-I when the data within treatment condition are averaged.

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Subject	Session	Avg. Duration i-I	Avg. EDil
DBS-5	pre	9.478	411.979
DBS-5	post	12.774	509.358
DBS-5	6 wk	6.87	486.297
DBS-6	pre	-9.665	357.499
DBS-6	post	12.041	292.43
DBS-6	6 wk	-8.617	342.538
DBS-7	pre	21.164	402.248
DBS-7	post	-11.28	383.986
DBS-7	6 wk	36.999	428.192
DBS-8	pre	-64.898	89.304
DBS-8	post	-66.848	114.202
DBS-8	6 wk	-44.769	136.691
DBS-9	pre	-29.962	478.376
DBS-9	post	-10.053	449.266
DBS-9	6 wk	-13.008	495.787
DBS-10	pre	-21.925	362.607
DBS-10	post	-47.812	348.574
DBS-10	6 wk	-42.109	321.522

Interestingly, EDiI outcomes after 6 weeks correlated closely to months since surgery, with subjects furthest out from surgery having the highest EDiI values and subjects with more recent surgery having lower EDiI values. This trend was seen both PRE and after 6-weeks. This finding indicates that months past STN-DBS surgery might be a positive predictor of treatment outcomes, with a longer duration of STN-DBS use correlating to a better treatment outcome.

In her undergraduate honors thesis about these same subjects, Isa Down (2010) found that there was a perceptual improvement in intelligibility in all six subjects after four weeks (16 sessions) of LSVT LOUD, though no significant improvement after the additional two weeks. This finding indicates that although the present study finds no significant differences between the pre, post, and 6 week conditions, there is nevertheless a perceptual improvement pre- to posttreatment. Furthermore, this study found that loudness (measured by Decibels Sound Pressure Level: dB SPL) improved post-LSVT for all subjects. Two of the three LSVT LOUD/CLEAR subjects noted improved articulation at 6 weeks. One LSVT LOUD subject increased in loudness at 6-weeks, and all three subjects reported that they felt like the two additional weeks had helped "stabilize" their loud voices.

When listening to the data files, there are perceptual differences in the production of consonants. Specifically, the subjects who scored more poorly in articulation (DBS-6, DBS-7 and DBS-9) had a perceptual difference in their production of stop consonants (/p/, /b/, /t/, /d/, /k/, /g/). A study analyzing frication and voice onset time in the stop consonants of DBS subjects may have more success in identifying the acoustic reasons for the difference in intelligibility pre and post-LSVT LOUD. Other subjects (specifically DBS-5), had a perceptual difference in the production of liquid consonants (/l/, / μ /). As with the stop consonants, a formal assessment of liquid production pre- and post-treatment may potentially yield more informative findings than the present vowel analysis. Because of the wide variation of speech production in STN-DBS subjects, the use of several different consonant measures in the same study seems more likely to provide a useful description of DBS speech than a study that focuses on a single acoustic measure. There is much work still to be done to come up with a clear understanding of the effect that DBS has on speech, and what treatments are effective in improving intelligibility in these people.

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CONCLUSION

This study attempted to use an unverified measure to determine treatment efficacy in a group of subjects that is highly varied and still relatively unstudied. It is very important that studies be done to gather as much information not only about speech with DBS, but also about the effect of treatments on STN-DBS speech. Just as important, though, is that a valid measure be found that can accurately identify differences in articulatory production in STN-DBS subjects, and that can tie articulatory production to intelligibility. This study did not address the subject of intelligibility at all, instead using objective measures to determine changes in articulatory production. The measure used in this study, however, does not seem to be the most sensitive measure for this population, and its accuracy should be verified in future studies. As with so many areas of speech and language pathology, more research is needed to determine the differences between parkinsonian and DBS speech, as well as the efficacy of treatments for these speech deficits.

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APPENDIX A CHARTS OF CHANGES ACROSS CONDITIONS IN DURATION I-I AND EDII

LSVT LOUD subjects are designated in blues, and LOUD/CLEAR subjects are designated by oranges and reds. PD controls are the black lines. PD controls had only two data collection points: pre and post.



