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A Mini Systematic Review of Subthalamic Nucleus Deep Brain Stimulation as a Treatment for Gait and Dysarthria in Parkinson's Disease

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Abstract

This review investigated the efficacy of subthalamic nucleus deep brain stimulation (STN DBS) as a treatment for gait and dysarthria in patients with Parkinson's Disease. Gait and dysarthria—walking and talking—have a huge impact on a person's day-to-day functioning. Three databases were systematically searched: PubMed, CINAHL, and ComDisDome. Eight articles were found about the two subtopics. It was discovered that although STN DBS effectively treats gait abnormality in Parkinson's patients, it usually exacerbates rather than improves dysarthria. It was concluded that more research needs to be conducted on difference stimulation settings to see if STN DBS can improve gait and dysarthria.

Keywords: dysarthria, gait, subthalamic nucleus, deep brain stimulation, Parkinson's Disease

The Clinical Question

There is a growing body of research literature on the effects of subthalamic nucleus deep brain stimulation (STN DBS) and its effects on the motor ability of patients with Parkinson's Disease. One often-observed symptom of Parkinson's Disease is dysarthria, which is a motor dysfunction affecting speech. Since STN DBS is used to treat motor disability—particularly gait abnormalities—in Parkinson's Disease patients, it is possible that it can also affect dysarthria for these patients. The goal of this review is to address two questions:

1) What is the effect of STN DBS on parkinsonian gait as compared to traditional medication?

2) What is the effect of STN DBS on dysarthria for patients with Parkinson's as compared to no STN DBS?

Background

Population

Parkinson's Disease is a disorder where neurons in the substantia nigra that produce dopamine degenerate (Rouse, 2016). Incidence rates are about 0.3% of the general population and about 1% of the population over 60 years of age in industrialized nations (Nussbaum & Ellis, 2003). The symptoms include tremor, slowed movement, muscle rigidity, and hypokinetic dysarthria—slow and stiff speech movements that result in breathy voice, monotonous pitch, and a variable rate of speech (Rouse, 2016). About 90% of people with Parkinson's Disease also develop some kind of speech disorder according to Pahwa, Lyons, & Kuller, (2007). This results from neurological lesions that affect motor execution of speech (Jones, 2010).

Deep Brain Stimulation

Deep brain stimulation (DBS) is a treatment that involves electrical stimulation of the brain. Electrodes are implanted in the brain and are stimulated by a pulse generator, which

creates an electric charge. Different parameters affect how much brain tissue is affected by the stimulation, such as the pulse amplitude, frequency, and width. Currently, there is no published research documenting permanent side effects or damage observed as a result of DBS (Gielen & Molnar, 2012). The subthalamic nucleus (STN) is the site of stimulation examined in this systematic review. It is one of the three structures comprising the basal ganglia in the brain. According to Rouse (2016), the basal ganglia, along with the substantia nigra of the midbrain, are part of the brain's motor system. The indirect motor pathway that runs through the subthalamic nucleus inhibits movement. It is also important to the fine-tuning of speech motor plans. Damage to this area of the brain can result in rigidity and dyskinesias (Rouse, 2016).

DBS of the STN significantly improves motor function in patients with Parkinson's Disease when medication cannot further improve symptoms (Deep-Brain Stimulation for Parkinson's Disease Study Group, 2001). This is often measured using the Movement Disorder Society-Sponsored Revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS), which is a Likert scale on which patients subjectively rate their motor function, considering issues such as cognitive ability, mood, types and severity of extraneous movements, rigidity, and ability to perform daily activities.

Gait abnormalities are among the primary symptoms of Parkinson's Disease; therefore, they are among the primary targets for treatment via STN DBS. This paper will evaluate the effectiveness of STN DBS in treating the primary motor and motor speech symptoms of PD using the best and most current research.

DBS treats motor dysfunction in Parkinson's Disease (Astrom et al., 2010; Jones et al., 2010; Sauvegeau et al., 2014; Schupbach et al., 2005; Tornqvist, Schalen, & Rehncrona, 2005). Since dysarthria is a motor dysfunction involving the speech mechanism (ASHA, n.d.), it is one

target of treatment in Parkinson's Disease. Dysarthria in Parkinson's Disease patients often includes a monotonous, harsh-sounding voice quality, with impairment in speech articulation (Astrom et al., 2010). One of the goals of STN DBS treatment is to improve these aspects of disordered speech in patients with Parkinson's Disease, resulting in improved speech intelligibility. The efficacy of STN DBS as a treatment for dysarthria is an important question to ask because it affects the quality of life for people with Parkinson's Disease (Schupbach et al., 2005).

The Search for Evidence: Gait

My evidence search on STN DBS and the primary symptoms of PD focused on parkinsonian gait. I used three databases: PubMed, CINAHL, and ComDisDome. My keywords were "deep brain stimulation", "subthalamic nucleus", "Parkinson's", and "gait" for all searches. PubMed initially yielded 178 results, which I narrowed to 18 by excluding all but clinical trials published in the last five years. Fifteen were discarded based on irrelevance (e.g. articles on stimulation of the pedunculopontine nucleus, or on the drug Amantadine rather than DBS). Two of the remaining articles did not have full text available, which I could not get through interlibrary loan due to the limitations of the University of Wyoming student access. This left me with one result (Rocchi et al., 2012). In CINAHL, I found 29 using keywords, 15 of which were published in the last five years. Two of those overlapped with previous PubMed searches. Of the remaining publications, 5 were relevant. Two had no full text, and one was a letter to the editor. This yielded two reviews, which—though ranking relatively high on level of evidence—did not present any new research. Therefore, I discarded all CINAHL results. The ComDisDome keyword search yielded nine results, none of which were published within the last five years. Of those nine, four were relevant. Two had broken or misdirected links to full text

articles, leaving two articles (Shivitz et al., 2006; Van Nuenen et al., 2008). I therefore found a total of three useful articles on DBS STN and parkinsonian gait.

The Search for Evidence: Dysarthria

My initial intent when searching for evidence was to find current research on deep brain stimulation as a treatment for dysarthria. I looked in three databases: PubMed, CINAHL, and ComDisDome, searching for "deep brain stimulation AND dysarthria". In PubMed, I found 96 publications, in CINAHL I found 14 publications, and in ComDisDome I found 15 publications. Since my goal was to find relevant, high quality research studies, I had to narrow my search. Most of the studies I encountered were based on deep brain stimulation as a treatment of Parkinson's Disease (to which dysarthria is related), so I narrowed my search in PubMed to "deep brain stimulation AND dysarthria AND Parkinson's". This resulted in 8 full-text available publications.

As I reviewed my remaining studies, I rejected several of them based on their research objectives. Many of them focused on diseases other than Parkinson's Disease, such as pallidotomy, medullary infarction, and neuronal intranuclear inclusion disease. I also excluded a publication on the acoustic analysis of the speech of people with Parkinson's Disease, because this would not help me determine the efficacy of deep brain stimulation as a treatment for dysarthria.

I ended up with fifteen viable publications between the three databases on deep brain stimulation as a treatment for dysarthria in Parkinson's patients. I rejected one because it was a case study, and my goal was to find the highest level of evidence possible. I rejected three more because they were systematic reviews, not being primary sources. I rejected another one because it was a review of different types of speech evaluations for deep brain stimulation, not a study on

the efficacy of the treatment itself. From my ten remaining studies, I chose five that focused on the same type of deep brain stimulation (subthalamic nucleus, or STN DBS) that were mostly group experiments. Four came from PubMed, and the other one was in both the CINAHL and ComDisDome databases.

Levels of Evidence

The quality of the research design determines its level of evidence. For example, a study with a high level of evidence controls for extraneous variables, has a statistically significant sample size, and potentially determines causality. A study with a low level of evidence has few subjects, does not control for variables, is not generalizable, or is based solely on a clinician's expertise. The higher the level of evidence, the more reliable the results. This is important in evaluating evidence in the field of speech language pathology because clinicians and clients want to know whether a treatment (which are usually already commonly practiced before there is sufficient research on it) is actually efficacious. There is a plethora of research based largely on expert opinion or single case studies in this field, so evaluating the quality of the research is essential in determining how weighty its conclusions are.

The studies in this paper were evaluated for their level of evidence based on twelve criteria. Studies rated "high" received a score of 9-12. "Moderate" studies received a score of 5-8, and "low" studies received a score of 1-4. The criteria and scores for each study are included in the table below.

"High" Level of Evidence

Gait

Effects of STN DBS on step initiation. Rocchi et. al (2012) studied the effect of DBS on step initiation in PD as compared to medication. They measured anticipatory adjustments,

center of pressure, length and velocity of the first step patients took when asked to walk. These measurements were taken in multiple conditions with and without medication, and with and without DBS. The participants included 29 patients with PD randomly assigned to one of two DBS conditions: GPi (globus pallidus) and STN DBS. There were 28 healthy control participants and 9 control participants with PD who did not undergo DBS implantation. The design of the study was group experimental. In all conditions, participants were asked to take two steps from a standing position, which they had to repeat three times. Their performance was scored using the UPDRS-III. Preoperatively, the participants were tested in the *on* and *off* medication conditions. Six months postoperatively the participants were tested in the *off* medication and ON DBS (*off*/ON), *off* medication and OFF DBS (*off*/OFF), *on* medication and ON DBS (*on*/ON), and *on* medication and OFF DBS (*on*/OFF) conditions. The researchers (Rocchi et. al, 2012) found that six months of DBS (regardless of type) could significantly impair step initiation. The level of evidence is high, as there are both randomization of the treatment condition and control groups.

Evaluating the Evidence

	Astrom et al., (2010)	Jones et al., (2010)	Sauvageau et al., (2014)	Schupbach et al., (2005)	Tornqvist et al., (2005)	Rocchi et al., (2012)	Van Nuenen et al., (2008)	Shivitz et al., (2006)
Published in peer-reviewed journal	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Specific testable question	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Control or alternate treatment condition	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Randomized participant assignment	No	No	No	Yes	No	Yes	No	No
Testers blind to condition assignment	Yes	Yes	No	No	Yes	Yes	No	No
Conditions or phases similar	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Tester reliability reported	No	Yes	Yes	No	Yes	No	No	No
Treatment well described	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Treatment fidelity reported	Yes	Yes	Yes	Yes	Yes	Yes	No	No
Outcome measures appropriate	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Statistical significance reported	No	Yes	Yes	Yes	Yes	Yes	No	Yes
Effect size or other measure of practical significance	No	No	No	No	No	No	No	No
Score:	Mod.	High	High	High	High	High	Mod.	Mod.

Level of evidence scores: Low (1-4 "yes" answers), Moderate (5-8 "yes" answers), High (9-12 "yes" answers)

Dysarthria

Motor program maintenance vs. switching. Jones et al. (2010) studied motor programming as it related to DBS in the speech Parkinson's Disease patients. In their introduction, they mention that dysarthria is a neurological problem affecting the motor execution of speech. However, they used speech response times as a measure to evaluate whether motor programming is the aspect of speech affected by DBS rather than just the motor execution. They hypothesized that the effect of DBS on motor programming could explain better speech response times of patients while being stimulated. Their three research questions were comparing speech maintenance versus switching, speech maintenance with DBS on versus off, and speech switching with DBS on versus off.

This was a within-group repeated measures experiment. The method used in this study to examine response time was to prime participants with words on a monitor, telling them to prepare to say the word when it flashed up again. The same word flashed on the screen most of the time, but with a variable incidence the word would switch, requiring the participants to restart the motor programming process. The time it took for the participants to correctly produce the word on the screen was measured for motor program "maintenance" (keeping the initial word in mind and preparing to say it) versus motor program "switching" (having to prepare to say a different word other than the one used to prime them). This was studied for both "on" and "off" stimulation conditions (Jones et al., 2010).

There were 12 participants: nine males and three females. Seven of them had STN DBS, while the other five had a different type, which—admittedly—does not entirely line up with my research question: the effect of STN DBS on dysarthria in Parkinson's Disease. Since not all

participants had bilateral DBS, only the effect of left-hemispheric DBS was studied; the right electrode was left off for the study in the participants that had bilateral DBS. All participants had Parkinson's Disease and suffered from slight to moderate dysarthria. They had a mean age of 61.3 years, with a standard deviation of 2.39 years (Jones et al., 2010).

Most—but not all—words were produced correctly; so only the ones that were produced correctly were included in the statistical analysis in the findings. There was a statistically significant difference between motor program maintenance versus switching, which showed that all participants responded faster in maintenance, regardless of the stimulation condition. There was also a statistically significant difference within speech maintenance between "on" versus "off" stimulation, which showed that "on" produced faster responses. There was not a statistically significant difference between "on" versus "off" in motor program switching. In a post-hoc analysis of STN DBS versus the other type of DBS, it was found that there was not a statistically significant difference between them (Jones et al., 2010).

This study rated "high" on the level of evidence scale (see Table 2). The experimental design exhibited a high level of control; tester reliability and treatment fidelity were reported, and the testers were blind to the stimulation conditions. They employed a randomized response-priming program and calculated speech response time with a device worn near the larynx, which was an appropriate measure to assess the motor programming involved in speech. However, the weaknesses were that the sample size was small (twelve participants), and they were self-enrolled rather than randomly selected. There was no statement of practical significance, but the data were all evaluated for statistical significance (Jones et al., 2010).

Vowel articulation with STN DBS. This study (Sauvageau, et al., 2014) looked into the speech articulation of patients with Parkinson's Disease and STN DBS. They did this by

acoustically measuring vowels and the impact of coarticulation (the effect of adjacent consonants on the production of a vowel) on them. The rationale behind using this measure to evaluated speech was that articulation requires fine motor control, and coarticulation is an example of very subtle changes in the production of a vowel that can have a fairly large impact on intelligibility.

This study had a within-group repeated measures experimental design. Each participant was recorded reading a text with STN DBS stimulation on, and was evaluated for dysarthria by two speech-language pathologists. Afterwards, all participants underwent two evaluations on different days: one for "on" DBS stimulation and one for "off", both under the patient's normal dose of antiparkinsonian medication. The "on" recordings were made at home under normal, everyday circumstances for the patient. The "off" recordings were made at a hospital at least one hour after DBS had been turned off. The researchers performed acoustic analysis of different consonant-vowel combinations for each condition (Sauvageau et al., 2014).

There were eight participants: five female and three male. All of them had Parkinson's Disease and were taking antiparkinsonian medication. They all had mild to severe dysarthria, as diagnosed by two speech-language pathologists. Participants had established DBS parameter settings that worked for them for at least six months (Sauvageau et al., 2014).

Sauvageau et al. (2014) found that STN DBS increased vowel articulation without affecting duration, which they concluded was a result of STN DBS improving the range of motion for articulation. An ANOVA statistical test was run, and it found that the difference between "on" versus "off" conditions was statistically significant. The researchers admitted that the small sample size (8 people) made it difficult to generalize. They also stated that vowel articulation is only one aspect of speech intelligibility. They concluded that dysarthria could be

affected—positively or negatively—by STN DBS, and that the affect it has depends on how the DBS settings are optimized.

This study rated "high" on the level of evidence scale (see Table 2). The specific, testable question this study investigated was: What is the effect of STN DBS on speech articulation in Parkinson's Disease patients with dysarthria as compared to no stimulation? The measures used to study articulation were very precise because they involved acoustic analysis of vowels with computer programs. The sample size, however, was small (only eight participants), so this is a preliminary study. Also, the testers and the participants were not blind to the stimulation conditions. There was a problem with ecological validity because the "on" testing was done in the participants' homes, while the "off" testing was conducted in the hospital, which added an extraneous variable. The data were examined for statistical significance, but no measure of practical significance was stated (Sauvageau et al., 2014).

A five-year follow up. This longitudinal study by Schupbach et al. (2005) examined the long-term outcomes of STN DBS on Parkinson's Disease patients by conducting a five-year follow up of patients after implantation. The researchers primarily evaluated the effect of the treatment on the participants' motor performance. However, they also examined the treatment's effect on everyday life and any observed adverse side effects, of which one was its effect on speech.

The researchers (Schupbach et al., 2005) used a group experimental design, but lacked a control group. There were systematic evaluations at several points across the five years: 1 month prior to the STN DBS implantation surgery, 6 months after, 2 years after, and 5 years post-surgery. Participants were scored for motor function based on different scales for Parkinson's Disease function. They were evaluated for both "on" and "off" antiparkinsonian medication, and

for "on" and "off" STN DBS, resulting in four treatment conditions. The participants were given ample time for each treatment to kick in (between 1 and 12 hours, depending on the treatment condition), and all conditions were tested on the same day.

The participants in this study consisted of thirty-seven people with Parkinson's Disease: 24 males and 13 females. At the time of surgery, the mean age way 54.9 years with a standard deviation of 9.1 years. Attrition was a problem in this study because six patients died for various reasons over the course of the five years, and one moved to a different location. Thirty-seven participants were in the initial evaluation, and thirty participated through to the final evaluation (Schupbach et al., 2005).

The researchers found that STN DBS maintains its improvement in Parkinson's Disease patients for at least five years post-operation. The outcomes were put into multiple groups by type; a Bonferroni correction was performed, and the results were all statistically significant. However, although this improvement was maintained, dysarthria was one of several symptoms of Parkinson's Disease that regressed slightly over the course of the study. Though the researchers claim that this permanent effect on speech function is probably due to STN DBS, they also noted that it could have also been a result of the antiparkinsonian medication. Therefore, Schupbach and colleagues (2005) found that STN DBS could reduce parkinsonian motor disability while negatively affecting dysarthria.

This study rated "high" on the level of evidence scale (see Table 2). It had the largest sample size of any of the five studies discussed in this review: 37 participants. They consisted of all the patients assessed in the researchers' center following bilateral STN DBS implantation surgery. Another unique feature of this study was that it was longitudinal, following 30 of the 37 participants from one month prior to surgery all the way through to five years after the surgery.

However, the testers were not blind to stimulation conditions, and no measures for tester reliability were reported (Schupbach et al., 2005).

Electrical parameter settings. Researchers (Tornqvist, et al., 2004) examined the effect of different STN DBS parameter settings on the intelligibility of speech. Because DBS is a treatment that can be adjusted to best benefit the patient, the researchers wanted to study what settings generally produced the best speech outcomes for the participants. They evaluated the DBS' frequency, amplitude, and localization, and they looked at these settings' effect on rate and intelligibility of speech.

There were ten participants: eight males and two females. All participants had Parkinson's Disease and had been implanted with bilateral STN DBS a few years prior to the study. Three of the patients had also undergone a different type of Parkinson's Disease surgery prior to being implanted with DBS. The participants were required to be fluent Swedish speakers (since the study was conducted in Sweden) and had to be aware of disturbances in their own speech. They excluded people who suffered from dementia and those who did think they could complete the tests. There was no control group because the patients were their own reference for speech intelligibility without DBS. The median age at the time of implantation was 65 years, with an interquartile range of 61-68 years (Tornqvist et al., 2004).

All participants were examined with a video laryngostroboscopy and compared to a reference group without Parkinson's Disease of similar age (60-77 years) to the experimental group. The researchers (Tornqvist et al., 2004) did not find any anatomical abnormalities in the participants; they did find some minor problems (such as vocal fold tremor in two participants), but found similar incidences of problems in the reference group.

This study design was a within-group, repeated measures, experimental design. The participants were each assigned to all conditions at some point, and the order of these conditions was randomized. All tests were conducted at least eight hours after the participants' antiparkinsonian medication had been withdrawn. For each sample, the participants had to read a Swedish text, followed by nonsense sentences, while being recorded. The researchers (Tornqvist et al., 2004) turned DBS on, off, and changed the amplitude and frequency settings for each sample, with a total of eleven different parameters being tested in random order. The participants were blind to the condition of their stimulation. A panel of listeners (including equal numbers of professional speech pathologists and nonprofessionals with normal hearing) who were also blind to the testing condition transcribed the participants' discourses and rated them for intelligibility; the mean of these scores was calculated. The participants also judged their own speech intelligibility using a rating scale.

A few data points were missing because individual patients could not complete the test. However, they found that DBS "on" had a negative impact on speech intelligibility, with statistical significance. They also found that higher amplitudes than the normal settings adversely affected speech, while decreased amplitude had no effect. Lower frequency than the normal setting seemed to improve speech intelligibility, and a higher-than-normal frequency had no effect on speech. There was no significant difference in the location of the electrodes between patients, or in the rate of speech. Interestingly, all participants rated their own speech as worse than did the panel of listeners. The researchers concluded that STN DBS can adversely affect speech, so the settings need to be optimized for each individual to reduce the treatment's affect on intelligibility (Tornqvist et al., 2004).

This study rated "high" on the level of evidence scale (see Table 2). One of the requirements for enrollment in the study was self-perceived speech difficulties, which is rather subjective, and could have biased the results. The sample size was small, only ten participants, so the findings are difficult to generalize. The study's strength was that there was a high level of experimental control; tester reliability and treatment fidelity were both reported, the testers were blind to the condition, and the data were evaluated for statistical significance (Tornqvist et al., 2004).

"Moderate" Level of Evidence

Gait

Bilateral STN DBS improves postural control. Shivitz et. al (2006) studied the effect of STN DBS on postural stability in patients with PD versus anti-parkinsonian medication. There were 28 participants in this study (Shivitz et. al, 2006). The mean age was 58.4 years with a standard deviation of 8.2 years. Participants were tested beforehand for peripheral neuropathies and vestibular disease that may affect the results. Each participant was tested in the *off* medication state before implantation of DBS, *on* medication with ON DBS (on/ON), and the *off* medication and ON DBS (off/ON). Therefore there were no groups; each participant was his or her own control in the preoperative *off* medication state, to which postural stability in subsequent conditions was compared.

The design of this study was group experimental, though it has characteristics of a single subject experiment. Each participant underwent multiple conditions, with within-subject comparison. However, the results of all subjects were averaged together.

Each subject was tested preoperatively in the *off* medication state according to the Sensory Organization Test (SOT) and scored according to Computerized Dynamic Posturography (CDP) and Unified Parkinson's Disease Rating Scale (UPDRS). The SOT involved placing the standing subject in a chamber and measuring their balance response to changes in the visual and proprioceptive environment. The subjects were again tested 6-12 months postoperative in the on/ON and off/ON states.

The participants in this study demonstrated significant improvement in postural stability with STN DBS. Researchers also reported some improvement with medication, though it was not statistically significant. The level of evidence of this study is moderate for several factors. The participation assignment was not randomized, as they were selected from an existing pool of patients with bilateral STN DBS who consented to participate in the study. In addition, the testers were not blind to the experimental conditions of the participants. There were neither measures of treatment fidelity nor of tester reliability reported. Despite these weaknesses, the study's strengths were that is was peer-reviewed, had control conditions, and reported statistical significance.

Postoperative gait deterioration. Van Nuenen et. al (2008) studied the long-term effect of STN DBS on gait in patients with PD. The 55 participants with PD had all undergone STN DBS. A questionnaire was sent asking the participants about their perception of their quality of movement, as measured by a global outcome score (GOS), both pre- and postoperatively. It was sent to patients who had been implanted with STN DBS at least six months prior.

The researchers (Van Nuenen et. al, 2008) found that there was an improvement in GOS, but a significant proportion of participants experienced a perceived deterioration of gait. The

deterioration, however, was delayed; significant differences were only observed after at least six months.

The level of evidence of this study is moderate, as it is both retrospective and subjective. It is retrospective because the researchers sent a questionnaire to the participants asking about their past changes in movement ability. It is subjective because the participants reported their perception of changes in gait; there were no objective measures employed. The patient selection was not randomized; the researchers chose to include all patients that had undergone STN DBS implantation within a certain time frame at two neurosurgical centers. There was no tester blinding, tester reliability, or treatment fidelity reported as the research consisted only of a questionnaire. The results were not evaluated for statistical significance. However, the strengths of this study are that it was peer-reviewed and that they had a control condition, though this condition was assigned retrospectively based on the groups observed by the researchers during data analysis.

Dysarthria

Speech intelligibility and movement during DBS. Astrom et al. (2010) studied the effects of different settings for DBS, such as exact anatomical position in the STN and amplitude. This study was part of a larger study on the effects of STN DBS on speech intelligibility and movement (Tripoliti et al., 2008). Astrom et al. (2010) focused on the effect of the electric field generated by the DBS electrodes on speech intelligibility and movement. This involved looking at the qualities of the electricity being used for DBS (such as amplitude) and how it related to anatomy. They detailed the anatomical placement of the electrodes within the STN for each participant to try to examine the effects of the STN DBS on speech.

There were 10 participants (eight males and two females) with advanced Parkinson's Disease who had received bilateral DBS in the STN (Astrom et al., 2010). The mean age of the group was 59 years with a standard deviation of 7 years. The researchers divided the participants into three groups, depending on the level of speech intelligibility impairment they demonstrated with a 4-volt DBS amplitude setting compared to no DBS: group A being a high level of impairment, group B being a moderate to slight level of impairment, and group C being no impairment.

The design for the Astrom et al. (2010) study was difficult to determine. Even though there was a small sample size (10 participants), the participants were placed *post-hoc* into three groups based on speech intelligibility. There were only three data points per participant ("off", "on 2 volts", and "on 4 volts"), but there was no averaging between the groups. The groups were discussed in the data analysis descriptively. The design could be best described as a group descriptive study. The participants underwent a magnetic resonance image (MRI) scan to determine and model the precise location of each individual's DBS electrodes in the STN. In addition to the scan, at least 6 months after implantation surgery of the electrodes, an assessment was conducted of the intelligibility of each participant's speech during no stimulation, low-, and high-amplitude stimulation, with a fifteen-minute resting period in between each setting. This assessment consisted of prolonged vowel phonation as well as an extemporaneous monologue, and was scored by calculating the percent of words transcribed correctly.

The researchers' (Astrom et al., 2010) findings were that STN DBS could improve movement in patients with Parkinson's Disease. However, speech intelligibility seemed to suffer from STN DBS. In particular, high-amplitude stimulation affected the speech intelligibility of the participants negatively. The researchers postulated that poor intelligibility was induced by

stimulating the fasciculus cerebellothalamicus of the brain, and thus was a side effect of the treatment. The researchers did not run any tests of inferential statistics, so it is difficult to determine whether the findings could be generalized to the population of patients with Parkinson's Disease.

This study rated "moderate" on the level of evidence scale (see Table 2). It was published in a peer-reviewed journal. The design was experimental, using a specific *a priori* testable question: What is the effect of the anatomical position of STN DBS on speech intelligibility and movement as compared to no DBS? One particular strength in the study was that the testers were blind to the stimulation condition. However, participants were chosen for the study based on reported affects of STN DBS on their speech intelligibility, so the sample was not random. Also, there were only ten participants, so it is difficult to generalize to the population. Statistical and practical significance were not reported for this study (Astrom et al., 2010).

"Low" Level of Evidence

I did not include any research articles with a "low" evidence rating in this paper. In my search procedures, I narrowed down articles by choosing ones that rated higher on the level of evidence scale. Examples of the types of articles that I rejected that may have been classified as "low" were case studies, letters to the editor, and clinical opinion publications.

The Evidence-Based Decision

In this systematic review, I sought to discover whether subthalamic nucleus deep brain stimulation (STN DBS) is an efficacious treatment for gait abnormalities and dysarthria in patients with Parkinson's Disease. In the studies that I examined concerning gait (Rocchi et al., 2012; Shivitz et al., 2006; Van Nuenen et al., 2008), the researchers found that although DBS

can improve postural stability, it tends to worsen gait in the long term. In the studies I examined concerning dysarthria (Astrom et al., 2010; Jones et al., 2010; Sauvageau et al., 2014; Schupbach et al., 2005; Tornqvist et al., 2005), the researchers suggest that dysarthria is a side effect of STN DBS that is usually negatively affected by stimulation, but can be positively affected, depending on the electrical parameters optimized for the individual patient (see Table 1).

Even though gait is one of the primary treatment targets of STN DBS, the evidence I reviewed was mixed. The two articles that were specifically about gait (Rocchi et al., 2012; Van Nuenen et al., 2008) both implied that gait was worse after six months of STN DBS in patients with Parkinson's Disease. Rocchi et al. (2012) found that step initiation was significantly impaired after six months, and Van Nuenen et al. (2008) found that gait quality has a delayed deterioration after six months of DBS. However, Shivitz et al. (2006) found that DBS improves postural stability—an important component of gait. Unlike the dysarthria research, none of these researchers examined different parameter settings for DBS besides on/off. Further research could be conducted to explore the effect of different STN DBS settings on parkinsonian gait.

It is important to note that the findings of all five studies on dysarthria (Astrom et al., 2010; Jones et al., 2010; Sauvageau et al., 2014; Schupbach et al., 2005; Tornqvist et al., 2005) suggest that dysarthria and speech intelligibility are sensitive to the effects of STN DBS (see Table 1). This shows that there is an underlying correlation between STN DBS and dysarthria. However, the treatment does not consistently have a positive effect on dysarthria. Four of the studies (Astrom et al., 2010; Sauvageau et al., 2014; Schupbach et al., 2005; Tornqvist et al., 2005) concluded that while STN DBS improved motor ability, it could also have a negative effect on speech. Two of those studies (Sauvageau et al., 2014; Tornqvist et al., 2005) also said that STN DBS could have a positive effect on speech, depending on how the electrical

parameters were set. The Sauvageau et al. (2014) study was rather narrow in its focus, only investigating the effect of STN DBS on vowel articulation, which is a small component of speech. The Tornqvist et al. (2005) study looked more holistically at its effect on speech intelligibility; however, there were only ten participants, and documented improvement in only one out of eleven of their electrical parameter conditions. Even though all studies pointed clearly to STN DBS having an effect on speech, the evidence for STN DBS being as an effective dysarthria treatment is inconclusive.

According to Jones et al., (2010), it is seemingly counterintuitive that DBS—a treatment that improves motor dysfunction—could at the same time exacerbate dysarthria, which is a motor dysfunction in the orofacial mechanisms. The researchers argue that perhaps the reason for this is because dysarthria actually results from a disability in motor programming rather than motor execution. This is a possibility because, according to their results, there was a statistically significant improvement in the maintenance of a speech motor program (the ability to repeat a word multiple times in a row) when the stimulation was "on" as opposed to when it was "off". Their results suggest that speech reaction time is improved by DBS. The limitation of this approach to studying the negative effects of DBS on dysarthria is that reaction time is only a small component of speech. However, further investigation should examine whether dysarthria is primarily a motor programming issue rather than a motor execution issue.

Based on the findings of Tornqvist et al. (2005) on different electrical parameters of STN DBS, speech intelligibility can either be positively or negatively affected by stimulation, depending on how the electrical parameters are uniquely set for the individual patient's needs. Sauvageau and colleagues (2014) reinforced this finding, suggesting that certain aspects of speech, articulation in particular, need not suffer from STN DBS, but could even benefit from it.

As previously stated, this evidence is inconclusive, so it is worth further investigation into what aspects of STN DBS can minimize the treatment's negative effects on speech.

Anatomical placement of the electrodes for STN DBS is another important consideration, according to Astrom et al. (2010). They found that some patients suffered less from speech impairment than others, and some did not demonstrate any speech impairment. However, this study was more descriptive than experimental, so the effects of electrode placement on the outcomes of STN DBS need to be further studied in order to understand more fully how anatomical placement affects dysarthria in patients with Parkinson's Disease.

The long-term effects of STN DBS are not well known; however, Schupbach et al. (2005) suggest that though the treatment's effect on motor ability remains positive over time (five years), it can exacerbate dysarthria. Of the study's original thirty-seven participants, six died. The cause of death in two of the patients could possibly have been related to complications surrounding STN DBS, so it is important to consider whether or not the treatment is worth the trouble. It has an adverse affect on speech as compared to no stimulation. Many of these patients were also on antiparkinsonian medication, so perhaps patients remaining on this medication without STN DBS would be a better alternative.

Based on the eight studies (Astrom et al., 2010; Jones et al., 2010; Sauvageau et al., 2014; Schupbach et al., 2005; Tornqvist et al., 2005; Rocchi et al., 2012; Shivitz et al., 2006; Van Nuenen et al., 2008) taken together, the level of evidence is moderate-high (see Table 2). With the exception of Astrom et al. (2010) and Van Nuenen et al. (2008), all the studies had a within-group repeated measures experimental design. All of the evidence seemed to suggest that though the primary focus of STN DBS treatment was to improve motor function in patients with Parkinson's disease, it actually exacerbated gait abnormalities and dysarthria. With this in mind,

a different approach needs to be taken to treating gait and dysarthria in patients undergoing STN DBS. Apart from further investigation into how to best optimize the electrical parameters of STN DBS to reduce its negative effects on gait and speech, the logical next step is to seek out complementary treatments to STN DBS that can improve both areas.

Conclusion

The evidence from these eight studies suggests that STN DBS is not an efficacious treatment for gait or dysarthria in patients with Parkinson's Disease. Even though DBS is primarily meant to treat movement disorders in Parkinson's Disease, it appears that stimulation of the STN only improves some aspects of movement (i.e. postural stability) while adversely affecting gait and speech intelligibility. Though this adverse effect can be minimized—or even eliminated—through proper optimization of the electrical parameters of DBS in the case of dysarthria, these studies suggest that the effect cannot be successfully reversed to improve gait or dysarthria.

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