Critical Review:
What effects do neurosurgical treatments for generalized dystonia have on speech?

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This critical review examines the effects of two different types of neurosurgical interventions for generalized dystonia, brain lesioning procedures and deep brain stimulation (DBS). Study designs include: single-group post-test only (2), single-group pre-posttest (3), and mixed (between and within) randomized clinical trial (1). Reports on brain lesioning studies showed evidence that surgery had a negative impact on speech. One study reported improved speech after a similar surgery with a different target site. Current studies on DBS showed mixed results reporting no change in speech, or some improvements with the potential for transient dysarthria.

Introduction

Generalized dystonia is part of a group of movement disorders that causes involuntary contractions of opposing muscles. These movements can result in repetitive movements, abnormal postures, and significant discomfort and pain (Albright, Barry, Shafron & Ferson, 2001). One way of classifying dystonia is according to how many anatomical sites it effects, categorizing it as focal, segmental, or generalized. Generalized dystonia can be a primary disorder or secondary to a brain lesion (e.g., due to stroke or cerebral palsy) (Ostrem & Starr, 2008). Generalized dystonia can cause disturbances in speech due to contractions in the muscles used for voicing, articulating, and breathing (Lablance & Rutherford, 1991).

Dystonia and its etiologies are not well understood, therefore most interventions focus on treating the symptoms and not the cause (Adam & Jankovic, 2007). Treatments have evolved over many years and range from oral drugs to neurosurgery. Anticholinergic medications are often used (Ostrem & starr, 2008) and levodopa is successful in some cases (Adam & Jankovic, 2007). Intrathecal baclofen has also proven somewhat successful for some patients (Albright et al., 2001). Initially, surgical procedures for dystonia aimed to create a lesion on the thalamus (Tasker, Doorly & Yamashiro, 1988; Andrew, Fowler & Harrison, 1983) and as techniques evolved, the globus pallidus became the target site (Lin, Lin, Lin, Chang & Lee, 2001). Deep brain stimulation (DBS) involves the implantation of wire contacts into the brain. The contacts are attached to an implantable pulse generator located below the clavicle, and controlled by an external remote (Ostrem & Starr, 2008). DBS of the globus pallidus is now preferred over brain lesioning procedures due to the fact that its stimulus parameters can be adjusted, as opposed to the fixed nature of lesioning effects (Uc & Follett, 2007).

With approximately 1/3 of those with generalized dystonia having dysarthria as a result of the disorder (Cooper, 1976), there is hope that intervention could relieve dystonic movements involving the speech muscles. Due to the large groups of muscles involved in generalized dystonia, treatments do not focus on relieving the spasms in specific groups of muscles. Unfortunately this means that while the treatment may positively affect some muscles groups, it may negatively impact another in terms of function. The speech muscles are commonly reported as being negatively impacted. Side effects of treatment reported in the literature include dysarthria (Andrew, et al., 1983; Tasker et al., 1988) and dysphonia (Cooper, 1977). Other sources cite that speech can be improved following treatment (Albright et al., 2001; Lin et al., 2001).

Objectives

The primary objective of this paper is to critically evaluate the literature on neurosurgical treatments for generalized dystonia that report on speech outcomes after treatment. The secondary objective is to summarize potential outcomes which can be used as background knowledge when providing evidence-based treatment information.

Methods

Search Strategy

Computerized databases SCOPUS, Medline, and CINAHL were searched using the following search strategy: "generalized dystonia" AND (speech OR dysarthria). Articles were limited to those published in English. Abstracts were retrieved for articles which met the search criteria and full articles retrieved for those

which contributed to the purpose of this article. Reference lists were examined from articles retrieved for any further articles which contributed to the purpose of this review.

Selection Criteria

Studies included in this critical review were required to report speech outcomes following neurosurgical treatment for generalized dystonia. Studies examining outcomes for both primary and secondary dystonia were included. Studies that did not report results exclusive to participants with generalized dystonia (i.e., included segmental or focal dystonias in all reported outcomes) were not included.

Data Collection

Results of the literature search yielded papers on two different methods of surgical intervention. Papers from 1977-2001 described results of brain lesioning procedures done on the thalamus and globus pallidus. There were three papers on this topic reporting results of single-group post-test only (2), and single-group pre-posttest (1) study designs. and mixed (between and within) randomized clinical trial (1). Papers from 2005-2007 reported results on deep-brain stimulation of the globus pallidus. Study designs included single-group pre-posttest (2) and mixed (between and within) randomized clinical trial (1).

Results

Results of brain lesioning

Early studies on brain lesioning techniques report negative speech outcomes. Cooper (1977) performed bilateral or unilateral lesions to the ventrolateral nucleus and centrum medianum of the thalamus on 227 patients with primary and secondary generalized dystonia. After a 2-20 (mean 7.9) year follow-up interview was completed, the most commonly reported side effect was dysphonia, which occurred in 18% of patients who had bilateral lesions (n=122). While this study does include a large sample size, these results should be interpreted with caution due to lack of standardized follow-up times and absence of any statistical comparisons

Dysarthria was also found to be a common side effect for those undergoing thalamotomy procedures. Tasker, Doorly & Yamshiro (1988) reported results for 56 patients with primary and secondary dystonia who underwent unilateral and bilateral thalamotomy. A follow-up was completed with each available patient at the time of the study where, among other functions, dysarthria severity was rated by a neurologist on a scale of 0-5. Follow-up times ranged from less than 1 year to greater than 10 years after surgery. They found dysarthria to be a problem following both unilateral and bilateral lesions to the thalamus and included separate results for patients with primary and patients with secondary dystonia. Ten patients with primary dystonia (n=20) had post-operative difficulties with speech, which persisted at follow-up. Seven of these patients had undergone bilateral surgery. Transient dysarthria was observed in four patients with primary dystonia. In patients with secondary dystonia (n=30), four experienced worsened dysarthria, all of whom had undergone a bilateral procedure. Overall, any speech improvements were classified as "minimal." Similar to Cooper (1977), the results of this study should be interpreted cautiously due to its lack of standardized follow-up times and statistical comparisons.

Better speech results were obtained for patients who received surgery targeting the globus pallidus as evidenced by Lin, Lin, Lin, Chang & Lee (2001). Their study included 18 patients with secondary generalized dystonia who received bilateral lesions. The Burke-Fahn-Marsden Dystonia Rating Scale (BFMDRS) is a validated tool commonly used to rate movement in people with dystonia (Burke et al. 1985). It includes a movement scale (based on a motor exam) and a disability scale (based on patient interview) on which to quantify the effects of dystonia (Ostrem & Starr, 2008). Within the movement scale, there is a rating for speech/swallowing movement. Within the disability scale, there is a rating for speech. The BFMDRS was completed at one week, pre-operatively and at a one-year follow-up. A Wilcoxon signed rank test was used to determine significance of their findings. The authors found significant improvement ($p = 0.040$) in movement for speech and swallowing. Improvement in disability for speech was greatest out of all disability scales as 14% of patients ($p = 0.034$) showed sustained improvement at one year post-surgery.

Results of deep brain stimulation

DBS does not appear to have either a positive or a negative impact on speech. The earliest paper to report any speech outcomes following DBS was done by Vidailhet et al. (2005). Bilateral DBS of the posterolateral ventral globus pallidus was performed on 22 patients with primary generalized dystonia. Using a single group pre-posttest design, patients were evaluated in two conditions: with the neurostimulator activated, and with the neurostimulation deactivated. Evaluation was done at three months postoperatively, by an expert who was blind to the condition. In the activated condition, scores were better on all subscales of the BFMDRS, with the exception of speech subscales. A Wilcoxon signed-rank test for matched pairs was used to determine statistical significance. There were no significant differences in the subscale scores between

the activated and deactivated conditions. These same findings were maintained at 12 months post-operatively when scores were compared to preoperative baseline measures. A follow-up single group pre-posttest study was conducted on the same 22 participants (Vidailhet et al., 2007). The researchers found that after three years of neurostimulation, overall movement and disability scores remained significantly improved when compared to historical preoperative measures, yet there were still no significant differences between baseline measures for movement in speech/swallowing (p=0.89) and disability in speech (p=0.40).

There is some evidence that DBS can improve speech. Kupsch et al. (2006) conducted a mixed (between and within) randomized clinical trial on 40 participants with primary segmental and generalized dystonia. All participants received surgery to implant neurostimulators bilaterally in the globus pallidus. Participants were then randomly assigned to one of two groups. One group received neurostimulation, and the other did not ("sham-stimulation"). Participants were blind to their group assignment. The BFMDRS was used to assess patients at three months post-assignment. After this initial follow-up, neurostimulation was activated in the sham-stimulation group and all study participants reassessed after receiving a total of six months of neurostimulation. A Wilcoxon signed rank test was used to determine statistical significance of the findings. At three months post-assignment, improvements on all subscales of the BFMDRS (including speech/swallowing and disability in speech) were significantly better in the neurostimulation group when compared to the sham-stimulation group. When examining outcomes in all participants after six months of stimulation, movement scores for speech/swallowing were not significantly improved from baseline measures (p=0.14), but there was significant improvement in disability scores for speech (p=0.01). Post-hoc comparisons examining differences between participants with segmental and generalized dystonia showed no difference between groups.

This study also provided evidence that, similar to speech results for brain lesioning techniques, DBS may cause dysarthria. Unlike the earlier surgical techniques, these outcomes appear to be transient. Kupsch et al. (2006) reported that 12% (n=40) of those receiving DBS experienced dysarthria, as defined by "slurred but understandable speech". Dysarthria caused by stimulation was eliminated in 4/5 patients by adjusting the stimulation measures. In the remaining patient, it was accepted as a side effect since that particular setting resulted in optimal improvements of other dystonic movements.

Discussion

When considering these results, one must take into account the inherent limitations to summarizing results from such a variety of studies. One limitation is the wide range of subject inclusion criteria which resulted in a heterogeneous population. This makes it difficult to compare results, and to generalizing findings to other people with generalized dystonia difficult. Those studies that reported ages of participants included a range from 11-66 years old (Kupsch et al., 2006; Lin et al., 2001; Tasker et al., 1988; Vidailhet et al., 2005; Vidailhet et al., 2007;). Primary versus secondary etiology of dystonia also contributes to population heterogeneity. Some studies included only participants with primary dystonia (Cooper, 1977; Kupsch et al., 2006; Vidailhet et al., 2005; Vidailhet et al., 2007), while others included only those with a secondary etiology (Lin et al., 2001), and one included both primary and secondary (Tasker et al., 1988). There is evidence that primary and secondary dystonias respond differently to treatments and therefore it may be more appropriate to consider results for these groups separately (Ostrem & Starr, 2008).

Another factor that makes results of some studies difficult to compare and generalize is the range in follow-up times included. The earlier studies did not use standard follow-up times. Cooper (1977) looked at outcomes in patients 2-20 years after surgery. Tasker's group (1988) described their follow-ups as ranging from less than one year to more than 10 years post-intervention. These long spans of follow-up times could alter outcomes. Research has shown that the brain's plasticity and capacity for reorganization can have an impact on function even years after damage to the brain has occurred (Taube, Uswatte, & Elbert, 2002). The four remaining studies (Lin et al., 2001, Kupsch et al., 2006; Vidailhet et al., 2005; Vidailhet et al., 2007) did reassess study participants at standard, preset time points. One difficulty is that the longest follow-up time was three years post-intervention, reported by Vidailhet et al. (2007), which means that long term results for DBS have yet to be studied.

The methods used to measure or report speech outcomes also pose a difficulty for comparing the results of the studies. Severity judgment of dysarthria is subjective and can therefore vary. One study documented speech outcomes as either a presence or absence of dysphonia (Cooper, 1977). Another study used a rating scale from 0-5 to judge severity of dysarthria (Tasker et al., 1988). A number of researchers used the BFMDRS (Kupsch et al., 2006; Lin et al., 2001; Vidailhet et al., 2005; Vidailhet et al., 2007;). Because this scale has been well described in the literature and has been validated

(Burke et al., 1985), studies that use this scale are easier to compare. One difficulty is that none of the studies included in this review reported interrater or intrarater reliability on any of the measurements. Since these rating are subjective, reporting on these factors would make results more compelling.

Levels of evidence

The level of evidence provided by each of these studies also varies. Study design and methodology should be considered when deciding how much weight should be given to the results of a study. The two early single-group post-test only studies on brain lesioning did not include any statistical analysis of their findings (Cooper, 1977; Tasker et al., 1988) and therefore their findings cannot be deemed statistically significant. Cooper's study (1977) does not include the sex or age characteristics of his participants. His methods are also not detailed as he mentions that each patient had between 1 and 7 surgeries, with no breakdown of results according to extent of lesioning. Tasker's group (1988) also excludes some important information. They lost nine participants to follow-up, five of which were "surgical failures" and reasons for the remaining four are unreported. This missing data may have had an impact on results. The nature of these study designs (single-group post-test only) also neglects to report any information on patient functioning before surgical intervention.

As standards for research have improved with time, so has the evidence they present. Lin et al. (2001) produce more compelling evidence since they present their results using valid statistical analysis. However, their selection criteria lessen the strength of their findings. The authors selected the first 18 patients to reach a 12-month follow-up to include in their study. Those who did not reach the one-year follow-up or those who were unavailable may have had less favourable results. In contrast to the earlier studies on brain lesioning, Lin et al. (2001) found improved speech outcomes. Although they did use a different target site, these findings along with their selection criteria make the evidence from this study less compelling than the more recent studies on DBS. Their findings should also be considered with caution due to their small sample size.

One encouraging observation is that the more recent studies, specifically those examining DBS produce more compelling evidence with their results due to careful study design and detailed methodology.
The three studies reporting results of DBS present very compelling results. All three used appropriate statistical tests (Wilcoxon signed-rank test) to determine significance of results. Kupsch's group (2006) used a control group for comparison and Vidailhet et al. (2005, 2007) used each subject as their own control, comparing all results to pre-intervention baseline measures. Missing data was accounted for in all three papers. Overall the three studies on DBS used experimental methods and could be replicated due to careful detailing of their procedures. Level of evidence from these papers could be improved with an increase in sample size.

Articles included in this critical review inadvertently follow the evolution of neurosurgical techniques for generalized dystonia. They begin with brain lesioning techniques targeting the thalamus, moving to similar procedures in the globus pallidus and finally the current preferred method of DBS in the globus pallidus. We can assume that as surgical techniques are refined, they have evolved to provide more control over dystonic movements of the body. The results of this critical review show that favourable results for speech are not as reliable. Early reports of brain lesioning studies reported that surgery to the thalamus had a negative impact on speech (Cooper, 1977; Tasker et al., 1988). One study reported improved speech after similar surgery with a different target site, the globus pallidus (Lin et al., 2001). Current studies on DBS report no change in speech (Vidailhet et al., 2005; Vidailhet et al., 2007) or some improvements with the potential for transient dysarthria (Kupsch et al., 2005). These results are congruent with other findings that point towards speech being controlled differently than other muscles in the body. They contribute to a growing body of literature that shows evidence that some interventions for movement disorders can have favourable outcomes for other muscle groups, while having a negative impact on speech (Kent, 2003).

This review uncovers areas for potential future research related to speech outcomes after treatment for generalized dystonia. Since speech effects of DBS are impermanent, it is possible that they can be adjusted so patients can receive maximum benefit. Current practice is to have programming sessions with the neurosurgeon who implanted the device to adjust the stimulation parameters. There is some evidence that allowing the user a window of adjustment can be beneficial and allow them to change parameters as needed (Romanelli & Heit, 2004). Further research is needed to determine whether it is feasible for patients to control their own stimulation measures to tailor their abilities to different situations. There is also more research needed to see whether favourable results can even be achieved for those who have dysarthria due to dystonia before treatment. Currently DBS is a popular topic to research, yet this review could include only three articles that reported on speech outcomes. Many leave motor control of speech unmentioned. In order to fully

understand the impact that neurosurgical treatments have on speech, studies must be undertaken that examine this area in more depth.

Clinical Implications

While this study shows that trends in neurosurgical interventions for generalized dystonia have changed over time, it is still helpful to know how past treatments have affected patients. The results indicate that brain lesioning procedures often left patients with long-term dysarthria, an impairment for which they may seek speech therapy. Currently, DBS may produce impermanent dysarthria which can be reversed by changing stimulation measures. The literature shows some evidence that it can have positive effects on speech but not all are in agreement. In the future speech-language pathology may be one profession involved in adjusting stimulation frequencies to maximize its benefits for patients.

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