

Critical Review:
What is the evidence for a relationship between Parkinson's disease and dysfluency?

Olivia Tontini, M.Cl.Sc (SLP) Candidate
University of Western Ontario: School of Communication Sciences and Disorders

This review examined the relationship between Parkinson's disease (PD) and dysfluency by looking at re-emerging stuttering, effects of deep brain stimulation, and the excess theory of dopamine. Studies reviewed include one quasi-experimental between groups study, three case-studies, one survey research design and one single group pre-post test. Overall, there appears to be a relationship between Parkinson's disease and dysfluency, however it is a new area of research, and most studies consist of case study information. Future studies involving experimental group designs are required to strengthen the evidence in this area of research.

Introduction

Individuals with Parkinson's disease (PD) often develop a variety of speech disturbances, that may include dysfluency of speech. For example, it has been noted that 16-44% of individuals with Parkinson's disease demonstrate phoneme repetitions (Darley et al, 1975; Logemann et al, 1973, as cited by Adams & Dykstra, 2009). Repeated phonemes usually occur at the beginning of an utterance or after a pause and may be rapid, blurred or prolonged. Dysfluencies in individuals with Parkinson's disease have been compared to their difficulty with initiating walking ("freezing") and shuffling which is evident in their gait (Duffy, 2005). Benke and colleagues have labeled repetitive speech in Parkinson's disease as an "iterative repetitive phenomena", characterized by "variable speech iterations with immediately successive repetitions of syllables, words or phrases" (Benke et al, 2000). Therefore by this definition, stuttering and palilalia can be grouped together however it should be noted that stuttering is a more rare speech disturbance in this population. Palilalia can be characterized as repeating or echoing one's own spoken words and is often seen in postencephalitic Parkinson's disease (Ackermann et al, 1989).

When dysfluency has an adult onset, it is often termed "acquired" or "neurogenic" (Shahed & Jankovic, 2001). Other cases of "neurogenic" stuttering have been observed in individuals with Wilson's disease, progressive supranuclear palsy, brain trauma, brain tumors and others (Shahed & Jankovic, 2001). This review examined studies in which adult-onset of dysfluency was associated with Parkinson's disease as well as the interesting phenomena of re-emergent stuttering. This latter form of stuttering refers to a developmental stutter that resolves in childhood and reemerges after the onset of Parkinson's disease (Shahed & Jankovic, 2001; Lim et al, 2005). The relationship between dysfluency and Parkinson's

disease was also investigated by examining a study involving Deep Brain Stimulation (DBS) and the "excess theory of dopamine". This theory claims that stuttering is associated with excess levels of dopamine in the brain (Goberman & Blomgren, 2003).

Objectives

The primary objective of this paper was to critically evaluate the available literature and to examine the relationship between Parkinson's disease and dysfluency. The secondary objective was to provide evidence-based recommendations about conducting future research and about clinical practice.

Methods

Search Strategy

The data bases PubMed, SCOPUS and MEDLINE were used with the following search criteria: (Parkinson's disease) AND (dysfluency) OR (stuttering) OR (re-emergent stuttering).

Selection Criteria

Selection criterion was focused on studies that examined stuttering or dysfluency in individuals with Parkinson's disease. Other neurogenic disorders were excluded as well as studies that focused on Parkinson's disease but with other speech disorders such as rate or dysarthria.

Data Collection

The papers selected consist of one quasi-experimental between groups study, three case-studies, one survey research design and one single group pre-post test. All studies were published between the years 2000 and 2006.

Results

In a quasi-experimental between groups study, Benke and colleagues (2000) examined repetitive speech in 53 patients with Parkinson's disease. Patients were separated according to the stability of their response to levodopa. One group consisted of 29 patients that had a stable response to levodopa and the other group consisted of 24 patients who were in a more advanced stage of Parkinson's disease and had a series of unstable responses to the medication including motor fluctuations. They examined repetitive speech during five speech production tasks- spontaneous speech, naming when looking at a picture, reading-both normal words and non-words, repetition- both normal words and non-words, and automatic speech. On and off states of levodopa were studied for repetitive speech phenomenon by re-testing seven of the advanced state individuals. The speech samples were recorded and transcribed word by word for analysis.

The results showed that 15 out of 53 patients (28.3 %) had repetitive speech phenomenon. Most of these individuals were in the advanced stage grouping (13/15). A significant correspondence of repetitive speech phenomena existed in patients with long term disease with accompanying fluctuating motor responses to levodopa ($p=0.007$, Fisher's exact test). There were no significant differences between on and off states tested. When examining the specific tasks, picture naming and spontaneous speech generated the highest percentage of repetitive speech. Reading and repeating non-words produced significantly more repetitive speech than normal text ($p=0.013$, 0.046).

This study was successful in highlighting the prevalence of dysfluency in individuals with more advanced stage Parkinson's disease. They did a good job in exploring their participants with respect to neurological testing and selection criteria. In result, they also concluded that repetitive speech phenomena may not necessarily be associated with dementia. Another interesting observation was that all individuals had varying repetitive speech types (palilalia type dysfluencies and stuttering like dysfluencies) displaying that speech dysfluencies may exist as a continuum of speech symptoms in one individual. The study lacked a control group which would have been helpful to compare results to. In addition, the study could have been improved by adding more objective measures such as standardized severity indexes for stuttering.

Dysfluency involving Deep Brain Stimulation (DBS) and Parkinson's disease

This case study describes the effects of deep brain stimulation (DBS) in the subthalamic nucleus on an individual that has Parkinson's disease and a history of developmental stuttering (Burghaus et al, 2006). Burghaus and colleagues (2006) used positron emission tomography (PET scan) to examine the areas of activation in the brain when DBS and levodopa medication were on and off. The stuttering severity instrument (SSI) and the Unified Parkinson's Disease Rating Scale (UPDRS) scores were taken during all conditions.

After surgery for DBS, there was an increase in speech dysfluency. Dysfluency was worse during bilateral stimulation compared to unilateral stimulation. Stuttering decreased when DBS was turned off. Even though stuttering worsened during the DBS on conditions, UPDRS scores showed an improvement in other motor symptoms (rigidity, akinesia and dyskinesias). PET findings showed bilateral speech activation of cortical and cerebellar motor areas in DBS off conditions. Specifically, the right Wernike's area ($z=3.9$), the left supplementary motor area ($z=3.8$), and the left Broca's area and anterior insula ($z=4.4$). In DBS-on conditions z-scores showed significant cerebral blood flow in right primary motor cortex ($z=4.6$) and other left motor areas, left Broca's area and anterior insula ($z=4.2$). The left Wernikes area was not activated during the DBS-on conditions.

This study was effective in using an objective measure to examine the relationship between Parkinson's and dysfluency in one individual with re-emergent stuttering. The pre-and post testing using the SSI and UPDRS allowed for useful comparisons between on and off states of DBS and levodopa with reference to stuttering and motor functioning. Furthermore, the brain imaging techniques with accompanying z-scores allowed for further analysis of the prominent neuro-locations that were dominant during the different states. Lack of a control group for comparison as well as more statistical analysis showing significant results between pre and post testing would increase the validity and reliability of this study.

Re-emergent stuttering in Parkinson's Disease

In a survey research study, Shahed and Jankovic (2001) examined twelve patients with a history of developmental stuttering that had remitted and then re-occurred after developing Parkinson's disease. The UPDRS was used to rate their motor symptoms and the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) was used to obtain a criteria for stuttering. In addition, questionnaires and various scales were used for self-ratings and to obtain

information on their history of stuttering and Parkinson's disease. Averages were calculated and compared from the data received.

Out of 12 initial patients, data was only able to be collected from 6 individuals. Various commonalities existed between the patients regarding their history of stuttering. For example, avoidance behaviors were most prevalent in adult stuttering and the most frequent stuttering characteristics were repetitions of sounds, and syllables at the beginning of words, blocks, physical tension, and an increase in severity with stress. There didn't appear to be an association between severity of childhood stuttering and severity of PD symptoms, however those with higher UPDRS scores were shown to have more severe stuttering in adult-hood. They didn't find any improvement or worsening of stuttering with Levodopa treatment.

Another case of re-emergent stuttering in Parkinson's disease was reported by Lim and colleagues (2005). The study described the stuttering characteristics of a 61-year old man and used UPDRS scores to report the motor symptoms. After receiving medication to treat his Parkinson's disease, motor symptoms were resolved, but stuttering continued.

The survey study by Shahed and Jankovic (2001) obtained relevant information regarding various case history information and characteristics of individuals who have had a history of developmental stuttering that re-emerged after the onset of Parkinson's disease. Considering this is a fairly new area of research, obtaining norms allows for further studies a means for comparison. They were also able to collect information using well-known standardized testing and scales that allowed for appropriate comparisons. Like any other survey research, there are limitations such as a possible lack of validity and reliability because the responses are subject to the patient's opinions and memory of their childhood. In addition, credibility would increase with more subjects involved.

The case study by Lim et al, 2005, was useful in providing another model to demonstrate the relationship between dysfluency and Parkinson's disease. However, like any other case-study, it describes only one individual's condition; therefore it is difficult to see the representativeness in the hypothesis. Some sort of measure of severity of stuttering would have also been helpful in understanding how severe the dysfluency was and if it differed under various speech tasks and medication states.

Excess dopamine theory

Goberman and Blomgren (2003) investigated the excess dopamine theory of stuttering in 9 individuals with Parkinson's disease (6 males and 3 females). Data was collected in the patient's home during four separate sessions. The first session was used for screening (hearing, cognitive). In the next three sessions, the medication level was modified; either the session was conducted 30 minutes before taking morning medication (OFF state), 1h after the patient took medication (ON1 state), or 2 h after taking medication (ON2 state). During the three data collection sessions, participants read the first paragraph of the rainbow passage, and produced a monologue of 3-5 minutes long. Analysis of dysfluencies was achieved as well as obtaining UPDRS scores during each session. To analyze the results, non-parametric Wilcoxon Signed Ranks Tests were used as well as effect size.

The results revealed that 8 of 9 patients were most impaired during their OFF states. Significant differences in percent dysfluencies existed between individuals in their OFF states compared to controls during the monologue task ($p=0.011$). There was no significant differences in percent dysfluencies that existed between participants in their ON and OFF states.

A major advantage to this study was that it took careful measures to ensure proper validity and reliability (ex. they conducted intra-judge and inter-judge measures and took hearing and cognitive screenings to rule out any other influences on the outcomes). They also had a control group to compare percent dysfluencies to which many of the other studies lacked. Their use of non-parametric testing and effect size was also appropriate in analyzing the large variability that existed in the results. Increasing sample size would increase the applicability and taking careful measures such as documenting all medications taken and exact dosages would have allowed for a more detailed analysis.

A case study design by Louis and others (2001) also looked at the effects of levodopa on two individuals who experienced adult-onset dysfluency accompanying Parkinson's disease. One 72-year old man experienced dysfluency including speech freezing while on levodopa (600mg max) that subsided when switched to pramipexole (1.125 mg a day max). Motor symptoms worsened when on pramipexole and cognitive disturbances existed which prompted the physician to switch back to levodopa. The other individual documented in this case study also experienced an increased incidence of speech freezing and dysfluency after taking levodopa (1000 mg max).

In contrast the previous study, the results of this study support the excess theory of dopamine in stuttering. Although the study appears to provide some support for this theory, this study only considered two individuals. Thus, the validity would increase with increasing sample size. In addition, there were no standardized measures or statistical comparisons to allow for appropriate analysis.

Discussion

Although these studies may appear to differ widely in their methodology and outcomes, a series of overall conclusions can be formulated from their findings.

Firstly, the studies that examined dysfluency under varying conditions or tasks had a general consensus that cognitively more demanding tasks elicit a higher percent of dysfluencies (Benke et al, 2000; Goberman & Blomgren, 2003; Louis et al, 2001). More dysfluencies in a “cognitively more demanding task” support the notion that there is a cognitive component to dysfluency in that more neural resources are required to formulate the higher linguistically demanding task (Goberman & Bomgren, 2003). In addition, the study by Benke and colleagues found that the individuals with more advanced stage Parkinson’s disease showed a significantly higher amount of dysfluencies, and dementia was ruled out due to the cognitive testing that was preformed.

When examining the types of dysfluencies present, the results of the papers demonstrate that a variety exists. As mentioned in the study by Benke and others, “a continuum of speech symptoms rather than a uniform profile of speech” may subsist (Benke et al, 2000, pg. 323). With this being said, there still appears to be a prominent prevalence of “speech freezing” which can be compared to “blocks” of speech that is evident in individuals who stutter. The “speech freezing” has been compared to the freezing of gait that is evident in Parkinson’s disease which may indicate an explanation for its prevalence. The other type of dysfluency that appears to be common amongst the studies was palilalia. This speech symptom has been reported in past cases of Parkinson’s disease and is often defined separate to stuttering (Boller et al, 1975, as cited in Louis et al, 2001). Therefore from these studies, individuals with Parkinson’s disease experience variable types of dysfluencies, however the predominance of “speech freezing” and palilalia may exist.

The study by Burghaus and others that examined dysfluency in an individual with Parkinson’s disease after the effects of deep brain stimulation highlighted the importance of the basal ganglia network in the general regulation of motor activity. Previous studies have speculated that DBS functions by modulating the subthalamic nucleus hyperactivity and to improve motor functioning by releasing overinhibited prefrontal basal ganglia projections (McIntyre et al, 2004; Krack et al, 2003, as cited in Burghaus et al, 2006). An explanation for the reversible deterioration of stuttering from the DBS could be the unselective nature of the stimulation that most likely targeted the areas that coincided with the dysfluency (Burghaus et al, 2006). Other studies have also noted this worsening of speech symptoms under DBS coinciding with positive outcomes occurring with other motor functions. A study by Dromey and colleagues, 2000 found disparities between limb and speech improvements after DBS in individuals with Parkinson’s disease. These authors noted that limb and speech motor systems are entirely different in their organization and control (corticospinal versus corticobulbar pathways) (Dromey et al, 2006). Therefore this can explain Burghaus’s findings on stuttering worsening in the individual when other motor functions improved (Burghaus et al, 2006).

The two studies that examined the effects of levodopa on dysfluency showed contrasting outcomes. The study by Goberman and Blomgren demonstrated individuals with Parkinson’s disease having variable dysfluencies from dopamine levels and thus contested that “dysfluency levels are affected by any change (i.e. increase or decrease) in dopamine to the central nervous system” (Goberman & Bomgren, 2003, pg. 65). In the other study, Louis and colleagues mentioned in their paper that “both over- and under-activity of dopamine have been hypothesized to be important, and the role of the dopaminergic system in these forms of dysfluencies is still poorly understood.” (Louis et al, 2001, pg. 563). This being said, the results of their study support the excess theory of dopamine, in that the two individuals they examined showed an increase in dysfluencies after taking levodopa. This contrast in effects on dysfluency from levodopa in PD patients was evident in other papers examined in this review. The results in the paper by Benke et al, 2000, did not support the excess theory of dopamine where the study by Burghaus et al, 2006 did. The effects of dopamine on dysfluency appear to be highly individualistic in individuals with Parkinson’s disease. Further studies are required to understand the neural mechanisms linking dopamine and speech dysfluency in order to comprehend the reasoning towards the varying effects.

Clinical Implications

There appears to be an association between dysfluency and Parkinson's disease. This link is of clinical relevance for various reasons. From a diagnostic perspective, it may be relevant to examine individuals with either adult onset or re-emergent stuttering for basal ganglia disorders (Lim et al, 2005). This importance was emphasized in a case that mistook a 29-year old male that had adult-onset stuttering to have a conversion when in fact he was later diagnosed with a Parkinsonian-like syndrome (Leder, 1996).

Clinical importance also exists when trying to successfully treat individuals with Parkinson's disease for motor disturbances. For example, it was previously mentioned that deep brain stimulation and dopamine drugs have led to an increase in dysfluency when treating individuals with Parkinson's disease for other non-speech motor symptoms (Burghaus et al, 2006; Louis et al, 2001). By having a stronger understanding of the relationship between Parkinson's and dysfluency, treatments such as deep brain stimulation and pharmaceuticals may be able to be modified to control dysfluency while still improving other non-speech motor symptoms.

The etiology of stuttering is not fully understood, and learning more about the relationship between dysfluency and Parkinson's disease can allow further insight into this area and even provide treatment ideas for individuals who stutter. A study by Alm in 2004 describes the relationship between stuttering and Parkinson's by comparing therapy techniques that have been used to treat Parkinson's disease. One study looked at improved motor ability in individuals with Parkinson's disease after they were instructed to consciously attend to specific aspects of their movement (Cunnington et al, 1999, as cited in Alm, 2004).

Recommendations

Although this review does display evidence that a relationship exists between Parkinson's disease and dysfluency, it is still a new area of research and is largely based on case study information. It is imperative that future studies incorporate objective and subjective methods of measuring dysfluency in this population of individuals, as well as increasing sample size and taking appropriate validity and reliability measures. Most of the studies in this review lacked a control group, detailed statistical analysis as well as documentation of valid data such as medication dosage which is vital for creating a thorough analysis. As more quality studies arise, insight may develop on the effect

of medication, namely levodopa, which would allow for more effective patient treatment. In addition, formulation of normative data relating to the types and characteristics of dysfluencies would promote efficient diagnosis for those with Parkinson's disease that experience dysfluency.

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