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Critical Review: Effect of Levodopa (L-dopa) medication on speech intelligibility and articulation in individuals with Idiopathic Parkinson's Disorder (IPD)

Amanda Baker
M.Cl.Sc (SLP) Candidate
University of Western Ontario: School of Communication Sciences and Disorders

This critical review examined the effects of Levodopa (L-dopa) medication on speech intelligibility and articulation in individuals with Idiopathic Parkinson's Disorder (IPD). The study designs reviewed included non-randomized within-groups pre-posttest (5) and randomized within-groups pre-posttest (1). Overall, the evidence suggests improvements in intelligibility and articulation post L-dopa therapy in patients with IPD. Included in this critical review are recommendations for future research as well as implications for clinical practice in the field of speech-language pathology.

Introduction

Idiopathic Parkinson's Disease (IPD) is a neurological degenerative disease associated with damage to the basal ganglia. As a result, there is a loss of dopaminergic cells in the substantia nigra leading to a reduced amount of dopamine released from the putamen (Duffy, 2005). Cardinal motor symptoms associated with IPD include rest tremor, akinesia (bradykinesia), rigidity and loss of postural reflexes. Typically, patients with IPD will develop hypokinetic dysarthria as well. Such speech changes can include reduced loudness, abnormal voice quality, reduced prosodic variation, abnormal rate of speech, imprecise consonant placement and overall reduced speech intelligibility. (Duffy, 2005; De Letter, Santens, & Van Borsel, 2005; De Letter et al., 2007b). It is estimated that approximately 60-80% of individuals with IPD will experience dysarthria (De Letter et al., 2005).

Individuals with IPD are commonly treated with pharmaceuticals, such as Levodopa (L-dopa), a dopamine-based medication that replaces dopamine no longer present in individuals with IPD. Dopamine agonists can also be used to enhance dopamine receptors in the brain (Spencer, Morgan, & Blond, 2009). Pharmaceutical treatment for IPD has shown to have remarkable effects on motor control deficits, however little is known about its effects on speech (Cahill et al., 1998; De Letter et al., 2007a; De Letter, Santens & Van Borsel, 2005; Leanderson, Meyerson, & Persson, 1971; Nakano, Zubrick, & Tyler, 1973; Spencer, Morgan, & Blond, 2009; De Letter et al., 2007b).

Several studies over the past 40 years have investigated the effects of L-dopa therapy on speech and results have varied. Many studies have found that L-dopa improves speech intelligibility, pitch, loudness, dysfluency and articulation (Adelman, Hoel & Lassman, 1970; Cahill et al., 1998; De Letter et al., 2007a; De Letter, Santens & Van Borsel, 2005; Leanderson, Meyerson, & Persson, 1971; Nakano, Zubrick, & Tyler, 1973; Louis et al., 2001; Anderson, et al., 1999), while other studies have failed to show consistent improvements in speech (De Letter et, al., 2007a; Ho, Bradshaw & Iansek, 2008; Goberman & Blomgren, 2003; De Letter et al., 2007b; Gallena, Smith, Zeffiro & Ludlow, 2001).

Objectives

The primary objective of this paper is to critically evaluate the literature pertaining to the effects of L-dopa on speech, specifically intelligibility and articulation. The secondary objective is to provide evidence-based practice recommendations and clinical implications for the field of speech-language pathology.

Methods

Search Strategy

Computerized databases including SCOPUS, Medline and PubMed were searched using the following search strategy: [("Parkinson's Disease" OR Parkinsons)] AND [(l-dopa OR levodopa)] AND [(speech OR intelligibility OR articulation)]. Reference lists from articles retrieved were examined for further articles that would contribute to this critical review.

Selection Criteria

Articles were included in this critical review if they were published in English, provided information pertaining to L-dopa treatment in IPD, and focused on intelligibility and/or articulation speech parameters. There were no limits set on the dates of articles published or geographical location of research participants. Studies that did not include IPD patients, L-dopa treatment, or the aforementioned speech parameters were excluded from this review.

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Data Collection

Results of the literature search yielded seven research studies; however, only six articles were used as they were most congruent with the selection criteria above. Study designs include: non-randomized within-groups pre-posttest (5) and randomized within-groups pre-posttest (1).

Results

Nakano, Zubrick & Tyler (1973), investigated whether speech intelligibility and labial movement improved with L-dopa treatment. Eighteen IPD patients participated in this randomized double blind study, all with no previous history of taking L-dopa. Participants were provided with a sequence of medications including placebo, procyclidine or L-dopa. Participants were blind to the treatment options and served as their own controls. All three medications were identical in size, shape and colour and thus appeared visibly similar to the patients. Each patient received no medication for the first ten days and underwent standardized testing of intelligibility using an unnamed multiple-choice subtest. These tests were repeated on the final day of administration of L-dopa medication. The patients as well as 10 naïve listeners judged audio recordings of the pre- and post-measure of intelligibility. Results indicated that two patients displayed improved speech intelligibility with the placebo, one patient improved on both L-dopa and placebo, one patient did not improve on either drug and 14 patients improved on L-dopa only. Overall, group findings suggest a significant improvement in speech intelligibility as a result of L-dopa therapy compared to placebo and procyclidine ($X=3.12$; $0.05<p<0.10$).

To investigate the patients labial movements and articulatory function post L-dopa treatment, needle electrode tracings of facial musculature activity and coordination during speech tasks were employed. A blinded speech-language pathologist analyzed the facial muscle activity during performance on several oral exercises (smile, labial eversions, counting and repeating phonemes and dipthongs). Only twelve of the eighteen patients participated and results indicated that all but one had improvement of labial movement and articulation with L-dopa therapy. More specifically, it was noted that L-dopa improves the articulatory pattern for increased speech intelligibility by allowing patients to initiate labial movement more frequently, have increased symmetry and speed of their lips, and enhance labial motility at the corners and lower portion of the mouth.

De Letter, Santens & Van Borsel (2005) investigated the effects of L-dopa on speech intelligibility in ten patients with IPD. The participants were all treated with L-dopa medication in combination with dopamine receptor agonists and amantadine. Only nine participants were analyzed. All participants were examined in both 'on' and 'off' states in the morning to avoid fatigue. L-dopa therapy was discontinued for approximately 12 hours to induce a practical 'off' condition. The patients' word intelligibility was assessed using the Dutch version on the word subtest of the Yorkston and Beukelman Assessment of Intelligibility of Dysarthric speech (AIDS). The entire procedure was repeated one hour later after dopaminergic medication was administered. This time period is referred to as the 'on' state. A panel of five speech-language pathologists were shown the video-recorded assessment of intelligibility and asked to transcribe each of the 50 words in each condition from the AIDS. Results were analyzed using Wilcoxon's signed-rank test and indicated significant improvement of single word intelligibility during the 'on' state compared to the 'off' state ($Z=-2.199$; $p=0.028$).

A follow-up study of De Letter, Santens & Van Borsel's (2005) findings was conducted by De Letter et al., (2007a) to investigate the effects of L-dopa medication on measures of intelligibility and respiration. For the purpose of this critical review, only methods and results pertaining to speech intelligibility will be discussed. Twenty-five "probable" IPD patients were evaluated using the word subtest of the AIDS in both 'on' and 'off' conditions. Three speech-language pathologists analyzed the speech samples via video-recordings. The data were analyzed using Wilcoxon's signed-rank test and reliability between the four raters was calculated using intraclass correlation of kappa. Similar to results discussed in De Letter, Santens & Van Borsel's article, the authors discovered a significant increase in intelligibility at the single word level during the 'on' state of L-dopa therapy ($M= 72.92$; $p=0.002$).

De Letter et al., (2007b) looked at the relationship between prosodic characteristics including, pitch, loudness and speech rate with comprehensibility following L-dopa administration. Ten individuals diagnosed with advanced IPD participated in the study. All patients were seen by a psychiatrist to exclude significant cognitive impairment and were examined in both 'on' and 'off' conditions. L-dopa medication was discontinued for at least twelve hours to simulate the 'off' condition. Each patient was required to read a 182 syllable standardized passage from the Dutch version of *The North Wind and the Sun*, International Phonetic Association. Patients were given the opportunity to read the passage once before starting the recording to become familiar with the semantic context. One hour after administration of L-dopa, the reading task was

repeated. Four speech-language pathologists evaluated the video-recorded tapes. Each recording was presented once and 'off' and 'on' samples were presented auditorily in a randomized manner. The panel was instructed to rate the speech sample according to its variation in pitch, loudness, reading rate and comprehensibility. These aspects were scored using a ten-point scale with severely abnormal on the left end and normal on the right end of the scale. Statistical analyses were performed using a non-parametric test for paired groups between the 'off' and 'on' states. Again, reliability between the four raters was calculated using intraclass correlation of kappa. In accordance with previously mentioned articles, results revealed a significant improvement in comprehensibility during the 'on' state of L-dopa treatment (X=0.1; p=<0.5).

Leanderson, Meyerson & Persson (1971) conducted an electromyography (EMG) study to examine the articulatory function of the labial musculature before and after L-dopa therapy. Seven individuals with IPD participated in this study. EMG activity was recorded from the labial musculature while the patients produced different vowel-consonant-vowel utterances. The muscles investigated included the orbiculares oris superior and inferior (lip rounding/closing muscles) and the levator and depressor labii (lip-opening/spreading muscles). Results indicated that six of the patients subjectively reported improvements in speech post L-dopa therapy. In two of the patients, improvements were corresponded by a normalization of the articulatory pattern from the EMG. One patient developed perioral hyperkinesias and thus evaluation of recordings was impossible. EMG traces showed that before medication there was an increased tonic activity in the muscles that presented as a high intensity background noise making articulatory movements hard to identify. Once medication had been administered, the background muscular activity both between and during utterances was reduced. Thus, articulation of speech was more easily identifiable.

Cahill et al., (1998) investigated labial movement disruption and measured interlabial pressure. Sixteen patients with mild-moderate IPD, all receiving stable doses of L-dopa participated in the study. A baseline measure of lip function was obtained in the 'off' condition for both speech and non-speech tasks. A bite block was used to help stabilize the jaw and ensure pressure being generated was a result of lip function only. Non-speech tasks included: maximum lip pressure, maximum sustained lip pressure, fine lip pressure, and maximum rate of repetitive lip pressure. Speech tasks included: repetition of phrases "I can say pa," and "I can say poppy." Each task was repeated three times and the best attempt was analyzed. The tasks were completed again and interlabial pressures recorded at 0.5, 1.5 and 3.0 hours after L-dopa administration. Results were analyzed using a series of one-way repeated-measures Analysis of Variance (ANOVA). Outcomes indicated an increase in lip function following L-dopa therapy, which as a result had a positive effect on articulation. Findings showed improvement for maximum lip pressure ($F=3.70$; $p<.05$), maximum sustained lip pressure ($F=3.68$, $p<.05$) and fine lip pressure control ($F=7.85$, $p<.05$) following L-dopa therapy. However, variability most closely related to speech production and articulation did not change significantly. More specifically, there was no significant improvement in maximum lip pressures ($F=1.82$, $p<.05$), Maximum rate of repetitive lip pressure- rate ($F=.30$, $p<.05$), maximum rate of repetitive lip pressure-pressure ($F=.90$, $p<.05$), pressure of initial "p" in production of "pa" ($F=1.00$, $p<.05$) and pressure of initial "p" in production of "poppy" ($F=.52$, $p<.05$).

Discussion

Appraisal of Results

Based on the reviewed articles, there appears to be suggestive evidence that intelligibility and articulatory function are improved with the administration of levodopa medication in IPD patients.

Subject Selection

There were several concerns noted with respect to subject selection among the articles reviewed. It was apparent that several of the studies failed to report how their participants were recruited (Cahill et al., 1998; De Letter et al., 2007; De Letter, Santens & Van Borsel, 2005; Leanderson, Meyerson, & Persson, 1971; Nakano, Zubrick, & Tyler, 1973; De Letter et al., 2007). Moreover, in some studies, participants were composed of varying severity levels or stages (Leanderson, Meyerson, & Persson, 1971; Cahill, et al., 1998), while in other studies, the authors failed to provide the severity level or stage of their participants (Nakano, Zubrick, & Tyler 1973; De Letter, 2005). Not controlling for this could have an impact on the results.

In two of the studies reviewed, the authors included participants with advanced IPD only (De Letter et at al., 2007a; De Letter et al., 2005). This could limit the generalization of the results to the entire IPD population. Likewise, the distribution of female to male participants among the studies was similar, however in some cases, minimal information regarding specific characteristics (e.g., education, socio-economic status, language spoken) was provided. This could have influenced the possibility for drawing conclusions on the IPD population as a whole (Leanderson, Meyerson, & Persson, 1971; Nakano, Zubrick, & Tyler, 1973).

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Nakano, Zubrick & Tyler (1973), as well as Leanderson, Meyerson & Persson (1971) included participants who have undergone bilateral or unilateral thalamotomies prior to the study. It is possible that such surgeries can interfere with overall findings and conclusions. Additionally, both studies were conducted on participants that were first time users of L-dopa medication. As a result, findings are not generalizable to IPD patients that are regular, on-going L-dopa users. Lastly, De Letter et al. (2007b) included twenty-five participants with "probable" IPD. Such wording leads one to question the validity of IPD disorder in subjects recruited.

Methodologies

Although most studies reviewed reported significant improvement of intelligibility and articulation post L-dopa therapy, methodological concerns limit confidence in some of the findings. The sample size amongst the articles reviewed varied from seven to twenty-five participants. Studies failed to provide a power analysis, making it difficult to analyze the sufficiency of each sample size.

Four out of six articles reviewed, required rater judgments to be made (Nakano, Zubrick, & Tyler, 1973; De Letter et al., 2007a; De Letter et al., 2007b; De Letter, Santens, & Van Borsel, 2005). All samples were randomized for raters, increasing validity and reducing bias, however, with the exception of Nakano, Zubrick, & Tyler (1973), it was uncertain whether raters were blinded to the medication status of the participants. Furthermore, of these four articles, only two (De letter et al., 2007a; De Letter et al., 2007b) included inter-rater reliability computations. As a result, the reliability of rater judgments is a concern.

Poor descriptions of methods used (Leanderson, Meyerson, & Persson, 1971; Nakano, Zubrick, & Tyler, 1973) and insufficient tasks performed (Cahill et al., 1998; Leanderson, Meyerson, & Persson, 1971) by participants may also affect the reliability and validity of findings. Other factors that can lead to questionable results include articulatory measures that are not completed by all participants (Nakano, Zubrick, & Tyler, 1973), failure to report timing within drug cycle when speech recordings were made (Leanderson, Meyerson, & Persson, 1971), and failure to report how long after baseline the L-dopa was administered (Leanderson, Meyerson, & Persson, 1971).

It was also noted that the studies were conducted in a manner that introduced the possibility for a practice effect or familiarity with speech tasks. More specifically, the participants were always tested in the 'off' state followed by the 'on' state (Nakano, Zubrick, & Tyler, 1973; De Letter et al., 2007a; De Letter et al., 2007b; Cahill et al., 1998; De Letter, Santens, & Van Borsel, 2005). Three studies investigated intelligibility using only one-word intelligibility tests (De Letter, Santens, & Van Borsel, 2005; De Letter et al., 2007a; Nakano, Zubrick, & Tyler, 1973), and as a result, findings are limited to one-word intelligibility and may not generalize to longer forms of connected speech. One study (De Letter, Santens, & Van Borsel, 2005) failed to comply with the AIDS test manual as an auditory visual mode was used to present speech recordings. Although this mode was more representative of a natural environment and provided greater ecological validity, it violated standard testing procedure and could affect the reliability and validity of findings.

In Leanderson, Meyerson, & Persson, 1971, EMG procedures were used to investigate articulatory function post L-dopa therapy. It is possible that an abnormal lip EMG may not correspond to or predict abnormal speech production. Thus the EMG method may lack ecological validity in the assessment of speech articulation. It is suggested that other instrumental measures, such as acoustic measures of speech may be a more appropriate measure of articulation, as they have been found to correlate with listener perception and intelligibility.

Level of Evidence

In addition to analyzing the methodology to determine the validity and reliability of the articles, the study design should be considered as well. The level of evidence provided by each study is more or less similar in nature. All studies utilized a within-groups design, with only one (Nakano, Zubrick, & Tyler, 1973) being a randomized control trial. The nature of the study designs used in this critical review represents a level one (randomized control trial) and level two (non-randomized, within-groups control trial) quality of evidence. This suggests that the findings reported are deemed compelling.

Recommendations

Further research is needed to validate, and refine previous research findings. Future recommendations include:

a) Include comprehensive descriptions of methods used, larger sample size and comparison of the nature and severity of participants with IPD and L-dopa.
b) Include assessments of connected speech to better represent natural, conversational speech.

c) Compare naïve listener versus speech-language pathologist judgments during patient testing.
d) Compare patients taking L-dopa overtime with first time users. Is speech intelligibility and articulation altered depending on length of L-dopa use?
e) Explore in greater detail the relationship between intelligibility and variability of other speech parameters.
f) Determine if motor symptom severity is correlated with speech symptom severity.
g) Evaluate the relationship between specific motor symptoms in different parts of the speech system in IPD and their respective influence on individual speech characteristics and overall intelligibility.
h) Include acoustical measures in the instrumental evaluations of speech articulations.
i) Determine the point in the drug cycle when speech is optimum.
j) Determine the length of benefit to speech.

Clinical Implications

The results analyzed suggest that speech intelligibility and articulatory function are improved with levodopa medication in IPD patients. Such evidence has important clinical implications for speech-language pathologists (SLPs). Understanding L-dopa's effects on speech will help SLPs in providing a more comprehensive assessment and superior treatment for their clients. For instance, if L-dopa has a positive effect on speech, SLPs must then be cognizant of their client's medication cycles to assure their assessment and/or therapy is administered when the client's speech performance is at its greatest. Similarly, understanding the precise effects of L-dopa on articulation and speech intelligibility will allow SLPs to design treatment approaches tailored specifically to their client's needs.

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