

Evidence for improved speech production following levodopa medication in idiopathic Parkinson's disease

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This critical review examines current research evidence available concerning speech improvement, specifically considering intelligibility and speaking rate, following the use of levodopa in patients with Parkinson's disease. All studies in the present review employed a within-subject design to compare speech production during on and off medication conditions. Overall, research suggests improved intelligibility and little evidence for improved speaking rate. Due to subject selection and methodological concerns, further research is required to replicate and refine prior findings.

Idiopathic Parkinson's disease is a progressive neurological disease characterized primarily by the progressive death of dopaminergic neurons in the brain, mainly in the substantia nigra (Goberman, Coelho, & Robb, 2002). This loss of dopamine has many motor effects such as rigidity, akinesia (inability to initiate movement), bradykinesia (slowness of movement), and rest tremor (Thanyi et al., 2004). These motor deficits also involve speech production and often result in hypokinetic dysarthria. Hypokinetic dysarthria is characterized by a number of speech deficits including reduced intelligibility and changes in speech rate (Duffy, 2005; Pinto et al., 2004). Approximately 70% of patients with Parkinson's disease experience speech impairments (Miller et al., 2006; De Letter, Santens, & Van Borsel, 2005; Pinto et al., 2004).

Pharmaceutical treatment involving dopamine replacement therapy has been found to improve Parkinsonian motor symptoms such as akinesia, rigidity, and tremor. The efficacy of such therapy to treat axial symptoms such as speech has been found to be controversial (Klawans, 1986, as cited in Pinto et al., 2004; Adelman, Hoel, & Lassman, 1970; Rigoordsky & Morrison, 1970; Fetoni et al., 1997; Mawdsley & Gamsu, 1971; Nakano et al., 1973; De Letter, 2006; Anderson et al., 1999; Louis, Winfield, Fahn, & Ford, 2001).

Levodopa and its effects on speech production in Parkinson's disease patients has been investigated several times over the past 30 years, and mixed results have been reported (Adelman, Hoel, & Lassman, 1970; Rigoordsky & Morrison, 1970; Fetoni et al., 1997; Mawdsley & Gamsu, 1971; Nakano et al., 1973; De Letter, 2006; De Letter et al., 2005). Levodopa has been reported to improve articulation, voice quality, and pitch (De Letter, Santens, & Van Borsel, 2005; Thanyi et al., 2004; Rascol et al., 2003). Other studies have reported no improvement (Goberman & Blomgren, 2003; Wolfe, Garvin, Bacon, & Waldrop, 1975; Poluha, Teulings, &

Brookshire, 1998), or worsening of speech characteristics following taking levodopa (Anderson et al., 1999; Louis, Winfield, Fahn, & Ford, 2001). Methodological differences across studies may partially account for these inconsistencies.

It is important to be aware of the effects of levodopa on speech as this is the most commonly prescribed pharmaceutical treatment to treat symptoms of Parkinson's disease (De Letter, Santens, & Van Borsel, 2005; Thanyi et al., 2004; Rascol et al., 2003).

Objectives

The purpose of the present review of evidence is to critically evaluate the research available at present concerning the effects of levodopa on speech production in patients with Parkinson's disease. The present review will focus on two speech production parameters: intelligibility and rate, as these are two of the most frequently impaired and disabling speech parameters in individuals with Parkinson's disease. Methodological concerns will be addressed and recommendations will be provided.

Methods

Search Strategy

A search of the following computerized databases was conducted using the described search strategy: CINAHL ["Parkinson AND speech AND (levodopa OR l-dopa)"]; Medline ["Levodopa AND Parkinsons AND speech"]; PsycINFO ["(l-dopa OR levodopa) AND (Parkinson*) AND (intelligib*)"]; PubMed ["Levodopa AND Parkinson AND speech"]. The search strategies listed above were the final strategies applied as they yielded the most relevant results.

Selection Criteria

Research articles were included in the present critical review if they met the following inclusion criteria:

a) Discussed levodopa treatment for Parkinson's disease patients; b) outcome measure(s) included intelligibility and/or rate; c) study was published in English.

Data Collection

The literature search yielded nine articles that were identified and selected for critical review based on the above search criteria. Following a full-text reading of the articles, only six were retained based on relevant outcome measures. All studies retrieved employed a within-subject experimental design.

Results

The first study reviewed was by Adelman, Hoel, and Lassman (1970), who included twenty-five patients to investigate the effects of levodopa on speech intelligibility and other speech parameters. All patients read a passage and participated in various speech tasks. Audio tape recordings of their speech were taken four times: upon admission to the hospital, when patients stopped their conventional medication, six weeks after patients began levodopa treatment, and six months after patients began levodopa treatment. All samples were randomized and blindly rated. Selected samples, in addition, were also analyzed using instrumentation. Results were deemed 'preliminary' and indicated an improvement in speech intelligibility following levodopa. A few subjects showed no change while off and on medication.

The second study reviewed was conducted by De Letter, Santens, and Van Borsel (2005). Ten patients diagnosed with idiopathic Parkinson's disease participated in this study. Only the data from nine patients was analyzed. All participants were treated with levodopa combined with other various dopamine receptor agonists. All patients were examined on and off medication. Patients were examined when medications were stopped for 12 hours constituting the "off" condition, and one and a half hours following their morning medication, constituting the "on" condition. Word intelligibility was assessed using the Dutch version of the Yorkston and Beukelman Assessment of Intelligibility of Dysarthric Speech (AIDS). The Intelligibility test was also videotaped for the purposes of further analysis to be conducted by a panel of Speech-Language Pathologists. Results were analyzed using the Wilcoxon signed-ranks test. Significant differences were found in patients between on and off medication states, such that intelligibility was significantly improved when patients were on levodopa medication ($z=12.199, p=0.028$).

In the third study by De Letter, Santens, De Bodt, Boon, and Van Borsel (2006), twenty-five patients diagnosed with advanced stage idiopathic Parkinson's disease were included to investigate the effect of levodopa on speaking rate. All patients had been previously treated with levodopa. Patients with any psychiatric and/or cognitive impairment were not included in the study. Patients were examined both on and off medication. Patients read a standardised passage while being video-recorded. Rate was measured by counting syllables per minute. Results were analyzed using the Wilcoxon signed-ranks test. Overall, no significant difference was found for speaking rate when comparing the on and off levodopa conditions.

The fourth study reviewed was by Nakano, Zubick, and Tyler (1973), who examined eighteen patients with Parkinson's disease. In their study investigating the effects of levodopa on speech intelligibility, patients were provided a sequence of medication to which they were blind: levodopa, placebo, and procyclidine hydrochloride, and they served as their own controls. All drugs were visibly similar when they were presented to the patients. Patients were off all medication for 10 days prior to the presentation of each medication. Audio-recordings of speech were assessed using a multiple-choice intelligibility test. Results indicated that two patients showed improved speech intelligibility on the placebo drug, one patient improved both on levodopa and placebo, one patient did not improve on either drug, and 14 patients improved on levodopa only. Overall, levodopa was found to be superior to placebo & procyclidine ($X=3.12, p<0.01$) in improving speech intelligibility.

The fifth study by Rigrodsky and Morrison (1970) included twenty-one patients who ranged from mild to advanced Parkinson's disease. Duration of Parkinson's disease ranged from three years to 38 years. Participants were admitted to the hospital for four to eight weeks, and were assigned to a neurologist and a physician. Patients were initially given a placebo which was gradually replaced with daily doses of levodopa, three to four times each day. Speech recordings were conducted four times throughout levodopa therapy, twice at minimal dosage, and twice at maximal dosage. Speaking samples included oral reading of a paragraph and spontaneous speech. A 7-point rating scale was used to evaluate each speech sample for time factor in speaking, as well as other speech and voice parameters. Results were analyzed using t-tests. A significant difference was found only for time factor in speaking, indicating that patients showed improved rate, appropriateness of phrasing and pause time, fluency, and rhythm, when receiving the maximum

dose of levodopa compared to no levodopa ($t=2.69$, $p<.05$).

The final study reviewed included seventeen patients with idiopathic Parkinson's disease and was conducted by Wolfe, Garvin, Bacon, and Waldrop (1975), to investigate the effects of levodopa on speaking rate. Patients were new recipients of levodopa and were assessed while on and off medication (i.e., prior to beginning levodopa therapy, and while on the new drug)(using a 5-point rating scale). Raters were Speech-Language Pathologists. Patients read a speech passage both before and after the administration of levodopa. Results were analyzed using t-tests. No significant differences were found for speaking rate.

Discussion

Appraisal of Results

The reviewed literature suggests that levodopa treatment in patients with idiopathic Parkinson's disease can result in improved intelligibility. There was little evidence to suggest improved speaking rate as a result of levodopa therapy.

Subject Selection

One main concern with subject selection in the studies reviewed is procedures for participant recruitment and/or descriptions of participants were not reported (Adelman, Hoel, & Lassman, 1970; Nakano, Zubick, & Tyler, 1973; Wolfe et al., 1975). Some authors also didn't report the severity of Parkinson's disease in participants, and included participants of varying severity levels and stage of disease without controlling for this in the analysis of results (Adelman, Hoel, & Lassman, 1970; De Letter et al., 2005; Nakano, Zubick, & Tyler, 1973; Wolfe et al., 1975). Furthermore, Nakano, Zubick, and Tyler (1973) included one patient in their study who had received a prior thalamotomy. This could have interfered with the group results.

Methodology

All studies included in this review defined the purpose of the study, and randomized samples for raters to evaluate blindly, therefore controlling for bias and increasing validity.

However, none of the authors calculated the power of their sample, and as a result it is difficult to assess the adequacy of each sample size. Furthermore, with the exception of Wolfe (1975), none of the authors reported inter-rater reliability. As a result, it is difficult to assess the reliability of the ratings for each speech parameter.

Other issues that may compromise the results include poor descriptions of methods used to rate speech

samples (Adelman, Hoel, & Lassman, 1973), lack of control for the testing environment (Rigrodsky & Morrison, 1970), and lack of description of study procedures used (Adelman, Hoel, & Lassman, 1973). Considering the rating of speech samples, studies only used interval scaling procedures (Rigrodsky & Morrison, 1970; Wolfe et al., 1975). Interval scaling procedures have been found to have problems with construct validity when compared to other procedures such as direct magnitude estimation (Schiavetti, Metz, & Sitler, 1981). Interval rating scales can introduce bias in the results as the extreme points on the scale may not be chosen frequently.

In one study, authors also failed to use standard testing procedures for the AIDS test. The raters used both audio and visual tape recordings of speech samples instead of just audio recordings (De Letter, Santens, & Van Borsel, 2005). This may have affected the validity and reliability of the ratings.

Other concerns include not reporting the timing within the drug cycle when speech recordings were made (Rigrodsky & Morrison, 1970) and not accounting for patient fluctuations within the on and off conditions (Rigrodsky & Morrison, 1970; Wolfe et al., 1975). One study only used a single word version of the AIDS (De Letter, Santens, & Van Borsel, 2005). As a result, the findings are limited to levodopa improving intelligibility at the single word level and cannot be generalized to sentence material.

Authors also reported the presence of dyskinesias and dysfluencies, the latter which can reduce speech rate; however, they did not control for these. As a result, the lack of observable difference in rate following levodopa may be the result of these influences. The authors could have correlated dysfluencies with rate to check for this, or tested for a significant difference in dysfluencies across on and off conditions (De Letter, Santens, De Bodt, Boon, & Van Borsel, 2006).

In two studies, statistical significance of results was not reported (Adelman, Hoel, & Lassman, 1970; De Letter, Santens, De Bodt, Boon, & Van Borsel, 2006).

Recommendations

Considering the aforementioned subject selection and methodological concerns, it is recommended that further research be conducted with the following considerations:

- a) Large sample size, participant selection criteria and description of participants, detailed descriptions of procedures and assessment measures implemented, results of rater reliability data, criteria for statistical significance (i.e., p value), and statistical

- results to compare patients both on and off levodopa.
- b) Assessment of conversational speech samples in a less controlled environment. Is there a difference between reading task performance in a structured setting and conversation performance in a natural environment?
 - c) Comparison of articulation, speech intelligibility, and rate during on and off states of levodopa in patients at different stages of the disease. Does severity of disease influence the amount or lack of improvement?
 - d) Comparison of perceptual evaluations of speech parameters from professionals (i.e., Speech-Language Pathologists) and lay listeners (i.e., untrained listeners).
 - e) Correlation of overall motor function and motor-speech function during on and off levodopa states for articulation, intelligibility, and rate of speaking.
 - f) Longitudinal study design. As patients continue taking levodopa, do existing speech effects change with time? (i.e., after five years on the drug, are improvements still noticeable?)
 - g) Comparison of patients who have been taking levodopa for some time and those who are new to the drug.

The results of current research concerning the effects of levodopa on intelligibility and speaking rate, as well as other speech parameters, is important for Speech-Language Pathologists to be aware of for assessment and treatment purposes. When assessing patients who are taking levodopa, one should consider varying performance based on the levodopa cycle, and one should assess such patients at multiple times in the drug cycle to obtain an accurate representation of speaking performance. For treatment purposes, one must also anticipate varying performance and control for this in the assessment of treatment outcome.

Conclusion

Findings from these research studies suggest that there is evidence that levodopa improves intelligibility in patients with Parkinson's disease (Adelman, Hoel, & Lassman, 1970; DeLetter, Santens, & Van Borsel, 2005; Nakano, Zubick, & Tyler, 1973). Considering speaking rate, two of the three studies investigating rate did not find a significant effect of levodopa (DeLetter et al., 2006; Wolfe et al., 1975), while Rigrodsky and Morrison (1970) did find a significant effect of levodopa on

speaking rate. Methodological and subject selection concerns may have affected the reliability and/or validity of the research findings reviewed. Further research would be beneficial to replicate and refine prior research findings in this area.

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