Instability of Syllable Repetition in Parkinson’s disease: Influence of levodopa and DBS


Background of the Study

Patients with Parkinson’s disease (PD) often develop alterations of speech rate that inhibit their ability to communicate effectively, which may worsen quality of life. Although altered speech rate is frequently attributed to hypokinesia (weakness or loss of movement) of the speech organs, newer studies suggest that it may actually stem from an underlying impairment of vocal pace performance (speed in voice production) in PD. This is because patients with altered speech rate show:

- An unusual acceleration and instability of vocal pace during speech that cannot be explained by inadequate (or poor) movement of the speech organs
- Little or no improvement with the most common therapies for hypokinesia in PD, including:
  - Levodopa or other dopamine-based medications that reduce PD motor symptoms
  - *Subthalamic nucleus deep brain stimulation (STN-DBS)*, or surgical therapy that electrically stimulates the STN region of the brain to reduce PD motor symptoms.

As a result, newer studies have attributed altered speech rate in PD to an underlying dysfunction of the brain’s basal ganglia, a network of brain structures that, when damaged, may impair patients’ ability to maintain a speech motor program (the mental commands that coordinate speech-related movements). However, since a person’s speech can be broken down into simpler units and speech sounds, the origin of altered speech rate may be clarified or better understood by examining patterns of syllable repetition in patients with PD and the influence of levodopa and STN-DBS.

Accordingly, researchers of the Ruhr University of Bochum in Germany conducted a recent study to examine syllable repetition “ON” and “OFF” levodopa or STN-DBS in 36 Parkinson’s patients in order to determine whether altered speech rate stems from an underlying impairment of vocal pace performance or hypokinesia of the speech organs. The study found that patterns of syllable repetition in patients with PD were similar to more complex alterations of speech rate and showed higher-than-normal pace instability that was not influenced by levodopa but was worsened by STN-DBS therapy. Overall, these findings support that altered speech rate may actually stem from an inability to maintain a speech motor program in PD due to a dysfunction of the basal ganglia.
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Purpose of Study
The purpose of the study was to test whether there is an underlying impairment of vocal pace performance in PD by evaluating syllable repetition in patients with PD and the influence of levodopa and STN-DBS therapy. To do so, researchers compared vocal pace performance “ON” vs. “OFF” levodopa or STN-DBS in 36 patients with PD and tested the following hypotheses:

- If vocal pace performance improves when patients are “ON” levodopa or “ON” STN-DBS, then instability of syllable repetition is most likely caused by hypokinesia of the speech organs.
- If vocal pace performance does not improve “ON” levodopa or “ON” STN-DBS, then instability of syllable repetition may represent an inability to maintain a speech motor program in PD and might hint to the dysfunction of the basal ganglia.

Patients & Study Participants
During the study, researchers analyzed three groups of study participants recruited from the Ruhr University of Bochum’s Department of Neurology. These study participants included:

- A group of 30 control subjects, or healthy study participants who do not have PD
- A total of 36 Parkinson’s patients, including a:
  - Medical treatment group: 22 patients who were regularly treated with levodopa medication
  - STN-DBS group: 14 patients who underwent surgery for STN-DBS and were regularly treated with DBS therapy.

Some general characteristics of participants in each study group are:

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Control Group</th>
<th>Medical Treatment Group</th>
<th>STN-DBS Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (Male/Female):</td>
<td>15M/15F</td>
<td>9M/13F</td>
<td>9M/5F</td>
</tr>
<tr>
<td>Average age:</td>
<td>66 years old</td>
<td>64 years old</td>
<td>66 years old</td>
</tr>
<tr>
<td>Average duration of PD:</td>
<td>N/A</td>
<td>4 years</td>
<td>12 years</td>
</tr>
</tbody>
</table>

Study Methods
In order to evaluate whether or not there is an underlying impairment of vocal pace performance in Parkinson’s disease, researchers used the following methods:

- Firstly, researchers assessed syllable repetition in a normal, healthy population by asking each control group participant to repeat the syllable /pa/ 25 times in a “comfortable” steady pace without speeding up or slowing down.
Afterwards, researchers performed the same speech test “ON” and “OFF” therapy for each PD patient in the medical treatment group and the STN-DBS group. To do so, researchers used the procedure below:

- **Medical treatment group:** To evaluate the influence of levodopa on syllable repetition in PD, researchers tested each patient after withholding levodopa medication (“OFF” therapy) and after administering 200mg of levodopa (“ON” therapy)
- **STN-DBS group:** Then, to evaluate the influence of STN-DBS on syllable repetition in PD, researchers tested each patient during ongoing stimulation (“ON” therapy) and after stopping stimulation for 30 minutes (“OFF” therapy)

Next, researchers assessed vocal pace performance by measuring stability of pace in each group using the coefficient of variation (COV), or the percentage of change in the average amount of time it takes to complete one syllable repetition and start the next

Lastly, researchers tested both study hypotheses (previously mentioned) by comparing the average COV in each study group and analyzing the changes in COV measured “ON” vs. “OFF” therapy in the medical treatment group and the STN-DBS group.

**Study Results**

In regards to whether or not there is an underlying impairment of vocal pace performance in PD, the study data supports the hypothesis that alterations of speech rate are not caused by a dopamine-related disorder (i.e. hypokinesia), but rather by an underlying dysfunction of the basal ganglia and inability to maintain a speech motor program in PD. This suggestion was based on a comparison of the average COV of syllable repetition tests in each study group (i.e. control, medical treatment, and STN-DBS) and an analysis of the change in COV measured “ON” vs. “OFF” levodopa or STN-DBS therapy in the medical treatment group and STN-DBS group.

According to the average COV measurements, COV was significantly higher in both the “ON” and “OFF” states of each PD group than in the control group. As compared with the healthy control group, which had a 1.08% COV on the syllable repetition test, researchers found that:

- Patients in the medical treatment group had a 2.0% COV “OFF” levodopa therapy and a 1.91% COV “ON” levodopa therapy
- Patients in the STN-DBS group had a 2.22% COV “OFF” STN-DBS therapy and a 2.9% COV “ON” STN-DBS therapy.

Altogether, this study data suggests that patients with PD had significant difficulties maintaining a steady vocal pace on the syllable repetition tests, regardless of their therapeutic state. Moreover, the data indicates that there was no significant difference between COV in the “ON” and “OFF”
state in the medical treatment group, whereas COV was significantly higher in the “ON” state than in the “OFF” state in the STN-DBS group. This suggests that vocal pace performance in PD was not influenced by dopamine-based therapy (i.e. levodopa) but was further deteriorated by STN stimulation.

**Study Discussion & Implications**

Overall, the study found that patterns of syllable repetition in patients with PD show similarities to more complex speech rate alterations and support the hypothesis of an underlying impairment of vocal pace performance in Parkinson’s disease. This is evident by:

- The inability of PD patients to keep a steady vocal pace during syllable repetition tests in the “ON” and “OFF” states
- The ineffectiveness of levodopa on vocal pace stability during syllable repetition tests in patients with PD
- The worsening effect of STN stimulation on vocal pace stability during syllable repetition tests in patients with PD.

As a result, researchers suggest that altered speech rate may represent a non-dopamine-related disorder of PD and might hint to a dysfunction of the basal ganglia that inhibits patients’ ability to maintain a speech motor program and, thus, impairs vocal pace performance in PD. Researchers therefore recommend that dopamine-based medications or STN-DBS therapy be avoided when treating patients with severe speech rate alterations, since these therapies do not improve or may even deteriorate the networks of the brain that control vocal pace performance in PD.