Neural correlates of impaired speech and hand motor timing processing in Parkinson's disease

Karim Johari and Roozbeh Behroozmand
Speech Neuroscience Lab , Department of Communication Disorders, University of South Carolina

Introduction

Background:

Parkinson's disease (PD) is a neurological disorder associated with the degeneration of dopaminergic neurons in the basal ganglia primarily affecting the motor system. Studies have shown that patients with PD exhibit slower responses during a wide range of motor reaction time tasks [1-2], which is accounted for by their abnormal temporal processing during the planning phase of movement compared to neurologically intact control subjects [3-4]. In addition, PD patients show deficits in tasks involving temporal judgment and generate shorter timing intervals in self-paced tapping tasks[4].

The previous findings support the notion that temporal processing mechanisms of movement are compromised in PD due to dysfunctional fronto-striatal circuits. Electrophysiological studies have found desynchronization of neural activities within the Beta band (15-30 Hz) as a neural signature of impaired temporal processing in PD during the planning phase of limb movement [5]. However, our understanding about how PD may affect motor timing processing during speech remains relatively unclear.

Objectives :

In the present study, we conducted a systematic investigation to examine the neural and behavioral correlates of motor timing deficit during the planning phase of speech and hand movement in mild to moderate non-demented PD patients compared with neurologically intact healthy matched control subjects.

Methods

Subjects:

We recruited 15 right-handed non-demented PD patients (5 females, mean age: 66.4 yrs) and 15 neurologically intact control (7 females, mean age: 63.9 yrs). At the time of testing, PD patients had a mean disease onset of 4.1 years (std: 1.5) and all were clinically stable with mild-to-moderate motor impairments (UPDRS Part III mean score 13.56, std: 3.6, range: 6–19). The mean upper limb hypokinesia was assessed at 5.5 (std: 1.93) in PD based on finger tapping and rapid alternating hand movement items in Part III of the UPDRS battery . Patients were tested on-medication with individually tailored dosages of dopaminergic medication (e.g., Levodopa) prescriped by their own neurologists. For each patient, Levodopa Equivalent Dose (LED) was obtained by adding the LED for each anti-parkinson medication. Theoretically, LED of a medication can be defined as the level at which the equivalent improvement in motor symptoms would be observed as for 100 mg immediate Levodopa release. PD patients and control subjects had no history of psychiatric disorder, vision or hearing impairments.

Methods

Experimental task:

The experiment consisted of two random-order tasks of speech production and hand movement. Subjects prepared to perform one of the motor tasks following the onset of a relevant visual cue on the screen (**Fig. 1**). During each task, subjects were instructed to prepare for the cued movement and start vocalizing the speech vowel /a/ or pressing a button after a circle (GO signal) appeared on the screen. We designed two counterbalanced blocks within which the subjects performed the tasks in response to temporally predictable and unpredictable visual stimuli.

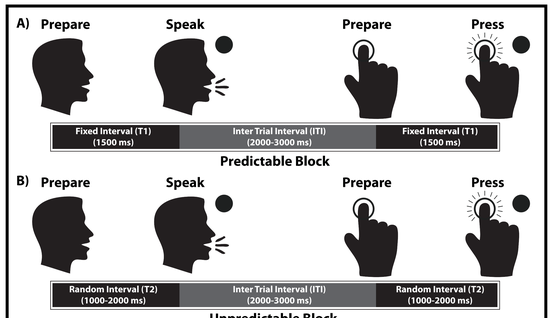

Figure 1. Experimental design of the motor reaction time task for A) temporally predictable and B) unpredictable blocks. In each block, subjects were presented with a task-relevant visual cue (hand or speech) and were instructed to prepare to press a button or vocalize the vowel /a/ after a circle (go signal) appeared on the screen. In this figure, T indicates the time interval between "Preparation" and "Go" in either button press or vocalization task. For the predictable block, the time interval (T1) was fixed at 1500 ms, whereas for the unpredictable block, the time interval (T2) was randomized between 1000-2000 ms. ITI represents the inter-trial-interval which was about 2-3 seconds for both predictable and unpredictable conditions.

EEG recording:

The EEG signals were recorded from 64 electrodes using the BrainVision active electrode system (Brain Products GmbH, Germany) placed on a standard cap with standard 10-20 montage. A BrainVision actiCHamp amplifier (Brain Products GmbH, Germany) on a computer utilizing Pycorder software recorded the EEG signals at 1 kHz sampling rate after applying a low-pass anti-aliasing filter with 200 Hz cut-off frequency.

EEG analysis:

The EEGLAB toolbox (https://sccn.ucsd.edu/eeglab) was used to analyze EEG signals to extract event-related potentials (ERPs) time-locked to the onset of speech and hand movement for temporally predictable and unpredictable stimuli. EEG signals were first filtered offline using a band-pass filter (1-30 Hz, –24 dB/oct) and then an ICA was applied to remove eye movement, blinks, muscle, and line noise artefacts. The signals were then segmented into baseline corrected epochs ranging from –500 to 500 ms (baseline at -500 to -400 ms). Extracted epochs were then averaged across all trials to obtain ERPs for each condition, separately.

Statistical analysis:

For each modality, mixed-model ANOVAs were implemented to examine the effects of group (PD vs. control), stimulus timing, and task on Global field power of ERPs and behavioral measures of speech and hand motor.

Results

Behavioral responses:

Results revealed that PD Patients were slower than control subjects for both speech and hand movement regradless of stimulus timing.

ERP responses:

The topographical distribution maps of ERP activities are illustrated for PD vs. Controls during predictable and unpredictable conditions for speech production (**Fig. 2A**) and hand movement (**Fig. 2C**).
The global field power analysis revealed that premotor neural activities over the frontal and parietal areas were significantly attenuated in PDs vs. control for speech production (**Fig. 2B**) and hand movement (**Fig. 2D**) regardless stimulus timing.

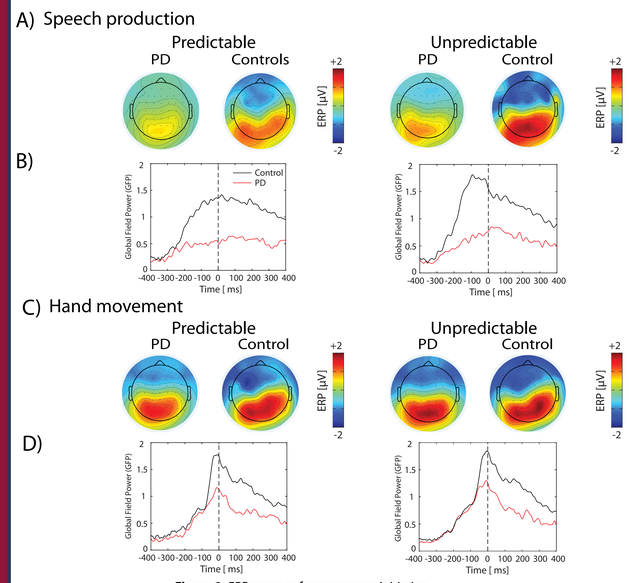

Figure 2. ERP reponse for movement initiation.

ERP source analysis:

ERP source estimation analysis revealed that the premotor neural activities were significantly stronger in controls vs. PD patients in areas within the right inferior frontal gyrus (r-IFG) during speech production (**Fig. 3A**), and within the right precentral gyrus cortical motor areas for hand movement (**Fig. 3B**) regardless of stimulus timing.

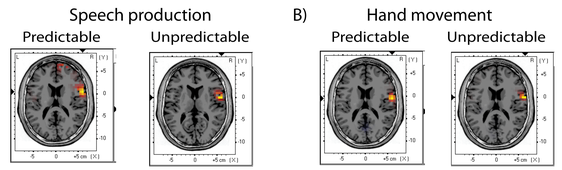

Figure 3. The Source estimation plots for Control vs. PD durin speech (A) and hand movement (B) for both predictable and unpredictable conditions.

Results

Correlation analysis:

The correlation analysis showed that the increase in the magnitude of global field power prior to onset of movement onset was associated with faster reaction times in PD patients regardless stimulus timing and response modality (**Fig. 4A**), whereas control subjects did not show such significant correlation (**Fig. 4B**).

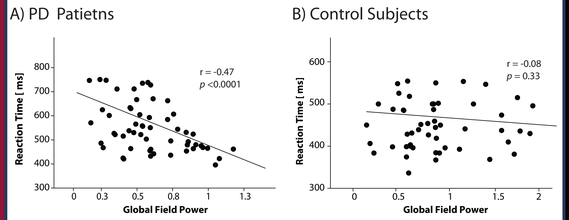

Figure 4. Correlation between GFP and reaction times.

Discussion

PD patients were significantly slower than control subjects for initiating speech production and hand movement regardless of stimulus timing.

Our findings showed that pre-movement ERPs activities were diminished in PD patients compared with healthy control subjects. In addition, correlation results showed that the increase in the pre-movement ERPs was associated with faster motor reaction time in PD, but not control subjects.

Source estimation findings linked the motor timing deficits in PD to the decrease in neural activities within the right inferior frontal gyrus (r-IFG) for speech and the right precentral gyri for hand movement.

Based on these findings, we propose that pathological attenuation of pre-movement ERPs within the right inferior frontal and precentral gyri areas is a neural biomarkers of impaired motor timing processing in PD during speech production and hand movement.

References

[1] Bloxham CA, Mindel TA, Frith CD. Initiation and execution of predictable and unpredictable movements in parkinson's disease. Brain 1984;107:371.
[2] Stelmach GE, Worringham CJ, Strand EA. Movement Preparation in Parkinson ' S Disease. Brain 1986;109:1179–94.
[3] O'Boyle DJ, Freeman JS, Cody FWJ. The accuracy and precision of timing of self-paced, repetitive movements in subjects with Parkinson's disease. Brain 1996;119:51–70.
[4] Pastor MA, Artieda J, Jahanshahi M, Obeso JA. Time estimation and reproduction is abnormal in parkinson's disease. Brain 1992;115:211.
[5] Kühn AA, Williams D, Kupsch A, Limousin P, Hariz M, Schneider GH, et al. Event-related beta desynchronization in human subthalamic nucleus correlates with motor performance. Brain 2004;127:735–46.