Neural correlates of impaired motor timing processing during speech production and hand movement in Parkinson’s disease

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Introduction

Background:
Parkinson’s disease (PD) is a neurodegenerative neurological disorder resulting from progressive cell death of dopaminergic neurons in the basal ganglia.2 A hallmark of PD is demonstrated by patients’ impairment in processing the temporal aspects of sensory stimuli for movement, which can have detrimental effects on their speech and limb motor function capability.3,4 Studies on the underlying neural bases of such motor timing impairment in PD have remained poorly understood. Evidence from previous studies suggests that the temporal aspects of externally presented sensory stimuli can modulate motor reaction time during tasks involving starting5 and stopping6 movement. These studies have indicated faster motor reaction time in response to temporally predictable vs. unpredictable sensory stimuli. This finding was discussed in the context of a predictive coding model in which an internal representation of timing is established to facilitate movement.

Objective:
The present study was a systematic investigation toward understanding the effects of PD on temporal processing mechanisms of movement in speech and hand motor systems. Our goal was to use objective measures of motor reaction time in response to external sensory stimuli with temporally predictable and unpredictable intervals to address the following questions:

1. How do the temporal aspects of sensory stimuli affect motor response reaction time during initiation and inhibition of speech and hand movement in PD patients?
2. Are the neurophysiological correlates of temporal processing modulations in response to predictable and unpredictable sensory stimuli in patients with PD?

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 relevant signal (SO) appeared on the screen and stop the cued movement when the circle disappeared (STOP signal). We designed two counterbalanced blocks within which the subjects performed the tasks in response to temporally predictable and unpredictable stimuli.

Results

Behavioral responses:
Results indicated slower reaction times in PD vs. control. Both groups showed faster responses for stopping vs. starting movement (Fig. 2).

There was no difference between PD and control in response to unpredictable stimuli. However, when stimulus timing was predictable, control subjects exhibited faster reaction times. No such effect was observed for PD patients (Fig. 3).

ERP responses:
Premotor ERPs were significantly diminished (p<0.05) for starting and stopping speech and hand movement in PD vs. control subjects (Fig. 4).

Discussion

Our novel approach led to the identification of the neural correlates of impaired motor timing processing during speech production and hand movement in patients with Parkinson’s disease. In the following paragraphs, we discuss the implications of these findings.

Patients with Parkinson’s disease have deficits in starting and stopping their speech and hand movement, as indicated by their slower motor reaction time in response to sensory stimuli compared with control individuals.

Our findings indicate that Parkinson’s disease is associated with an impairment of temporal predictive mechanisms that establish internal representations to facilitate motor function in response to predictable stimuli. This notion is supported by our data showing that when control subjects performed the speech and hand movement tasks, their motor reaction time was significantly improved in response to temporally predictable stimuli. However, patients with Parkinson’s disease did not exhibit such improvement in their motor performance when stimulus timing was predictable.

We propose that impaired motor timing processing in Parkinson’s disease is reflected by the attenuation of pre-motor components of ERP activities in speech and hand movements. This notion is corroborated by our data showing that the amplitude of pre-motor ERPs were significantly reduced before starting and stopping speech production and hand movement in PD patients compared with controls.

References


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Experimental task:
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 on the screen and were instructed to prepare to press a button or vocalize the sound /a/ after a circle (go/signal) appeared on the screen and stop it after it disappeared. In figure A, we indicate the predictable stimuli by the word “Predictable” and unpredicted stimuli by the word “Unpredictable.” The predictable block, the time interval (T1) was fixed at 1500 ms, whereas for the unpredictable block, the time interval (T2) was pseudo-random between 1500-2000 ms. ITI represents the interval at which was about 2.5 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 actiClamp amplifier (Brain Products GmbH, Germany) on a computer utilizing Py- corder software recorded the EEG signals at 1 kHz sampling rate after applying a four-pass anti-aliasing filter with 200 Hz cut-off frequency.

EEG analysis:
The EEGLAB toolbox (https://www.eeglab.org) was used to analyze EEG signals to extract event-related potentials (ERPs) time-locked to the onset of the speech and hand movement for temporally predictable and unpredictable stimuli. ERP 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, blink, muscle, and line noise artifacts. The signals were then segmented into baseline corrected epochs ranging from −300 to 500 ms at baseline (−300 to 200 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 ERPs and behavioral measures of speech and hand reaction time.

Methods

Subjects:
We recruited 15 right-handed non-demented PD patients (5 females, mean age: 66.4 ± 4 years) and 15 neurologically intact control (7 females, mean age: 63.9 ± 9 years). At the time of testing, PD patients had a mean disease onset of 41 years (std: 1.5) and all were clinically stable with mild-to-moderate motor impairments (UPDRS Part III mean score: 13.6, std: 3.6, range: 6–19). The mean upper lip hypokinesia was assessed at 5.5 (std: 9.93) 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) prescribed by their own neurologists. For each patient, Levodopa Equivalent Dose (LED) was obtained by adding the LED for each antiparkinson medication. Theoretically, LED of a medication can be defined as the level at which an 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.