Corticospinal inhibition during response preparation is abnormal in Parkinson’s disease

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Introduction

Corticospinal activity is inhibited during the preparation of responses. The source of this inhibition remains unclear. Although some evidence implicates frontal cortical regions, the basal ganglia may also contribute given the association of this subcortical structure with motor inhibition.

To explore this question, we tested patients with Parkinson’s disease, which affects the basal ganglia and offsets the excitation-inhibition balance of the motor system. We hypothesized that preparatory inhibition depends either directly or indirectly on the basal ganglia and would be abnormal in Parkinson’s disease.

Task Design

- Cue indicated whether to prepare a left or right index finger response.
- Go stimulus signaled execution of prepared response.
- Electromyography (EMG) recorded from the left and right first dorsal interosseous muscle.
- TMS administered at baseline or 800 ms into the 900 ms preparatory delay.

Preparatory Inhibition was operationalized as reductions in MEP amplitudes measured 800 ms after preparatory Cue onset, relative to baseline MEP amplitudes. EMG onset time was used to assess response initiation time relative to the Go stimulus.

Baseline Excitability

Resting motor excitability was similar between the two groups (all p’s > 0.34) in terms of:
- resting motor threshold (RMT)
- task baseline MEP amplitudes
- within-subject standard deviation of baseline MEP amplitudes

Role of Basal Ganglia in Preparatory Inhibition

The progressive loss of dopaminergic nigro-striatal projections in PD disrupts the excitation/inhibition balance throughout the motor system.

Current models suggest this imbalance produces excessive inhibition of thalamic motor nuclei that project to cortical motor regions. Excessive tonic thalamic inhibition may reduce the overall bandwidth of motor excitability.

Discussion

One theory speculates that preparatory inhibition facilitates action selection and initiation by suppressing motor noise to increase the overall signal-to-noise ratio within the motor system.

Accordingly, a loss of preparatory inhibition in PD may reflect either an inability to suppress motor noise or tonic excessive motor inhibition that restricts the range of excitability. Either scenario could constrain signal-to-noise within the motor system and impede action preparation.

Alternatively, the absence of preparatory inhibition in PD may reflect a failure to utilize the cues to properly prepare responses. Future experiments will measure both cued and uncued response times to address this concern.

References