

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

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Introduction

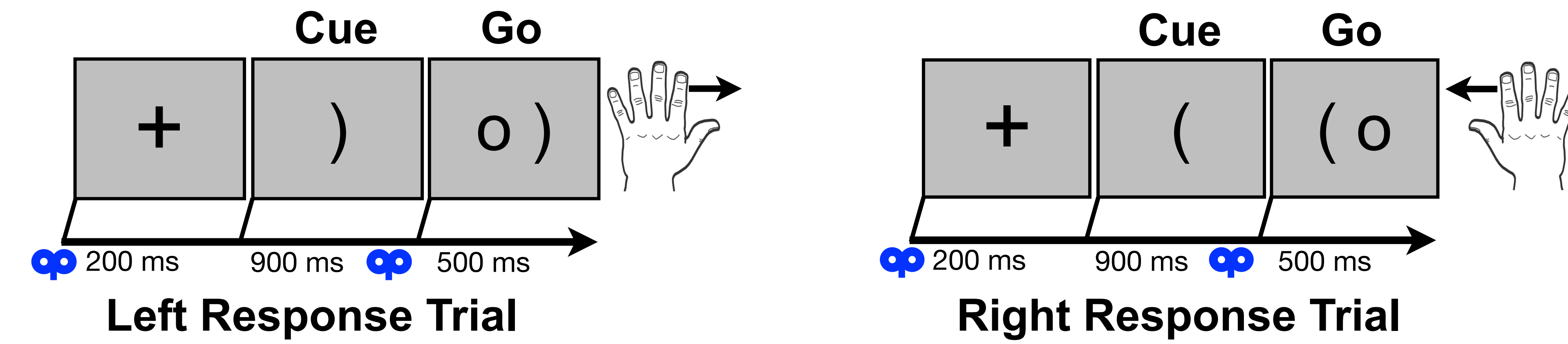
Corticospinal activity is inhibited during the preparation of responses. The source of this inhibition remains unclear. Although some evidence implicates frontal cortical regions¹, the basal ganglia may also contribute given the association of this subcortical structure with motor inhibition².

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

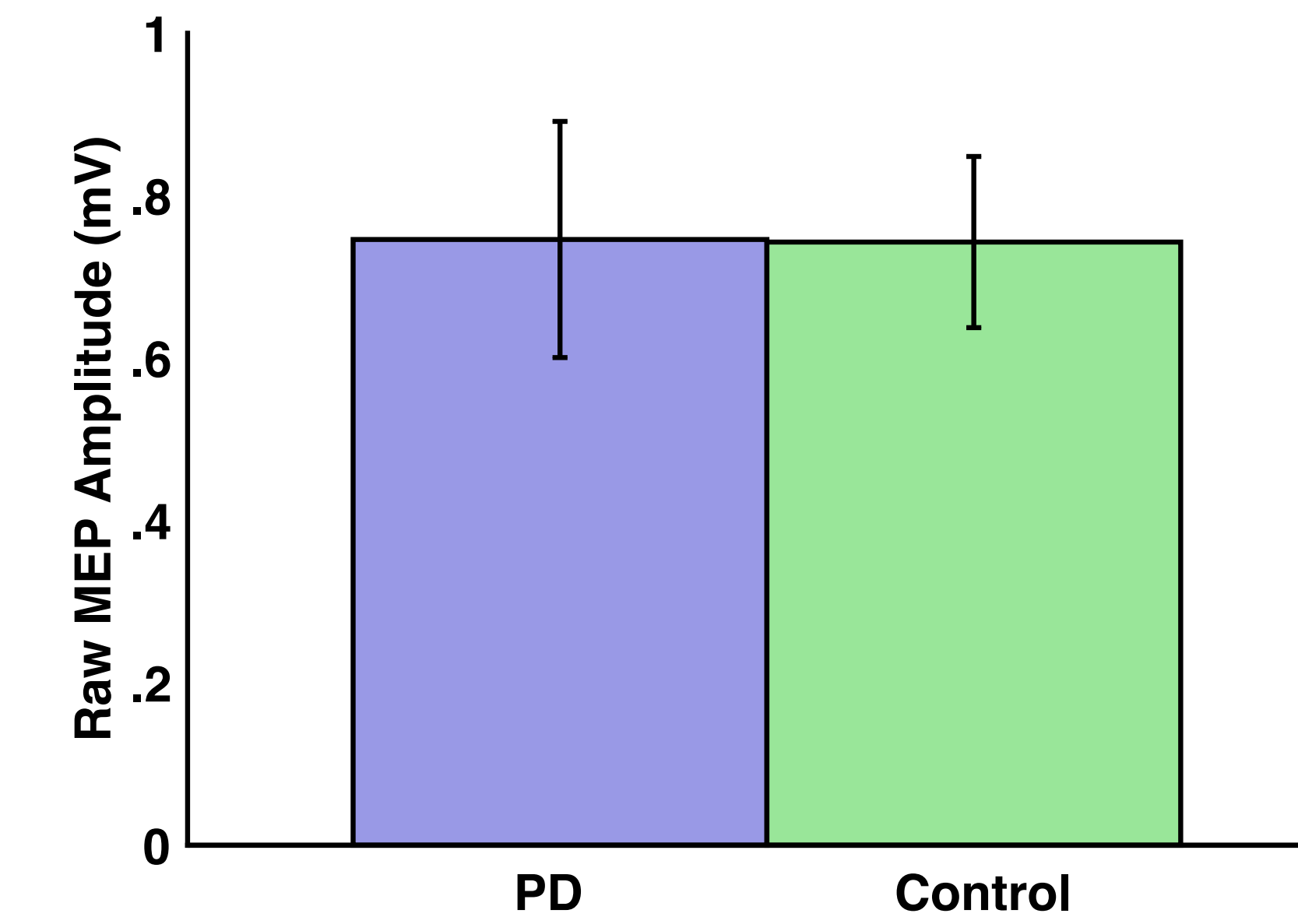
- Cue indicated whether to prepare a left or right index finger response.
- Go stimulus signaled execution of prepared response.
- Electromyography (EMG) recorded from the left and right first dorsal interosseus muscle.
- TMS administered at baseline or 800 ms into the 900 ms preparatory delay.



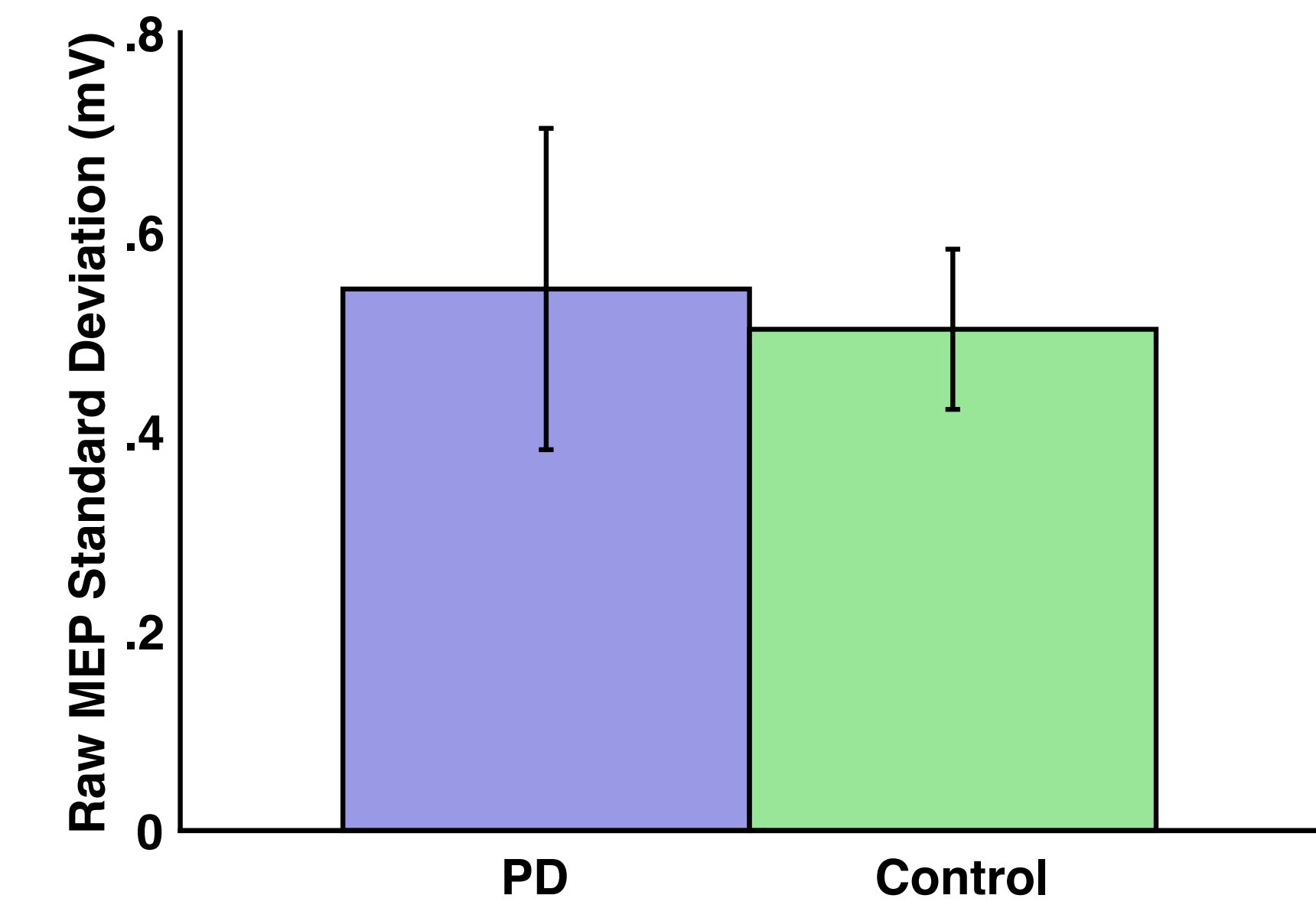
Preparatory Inhibition was operationalized as reductions in MEP amplitudes measured 800 ms after preparatory Cue onset, relative to baseline MEP amplitudes. EMG onset time was used to assess response initiation time relative to the Go stimulus.

Baseline Excitability

MEP Amplitudes



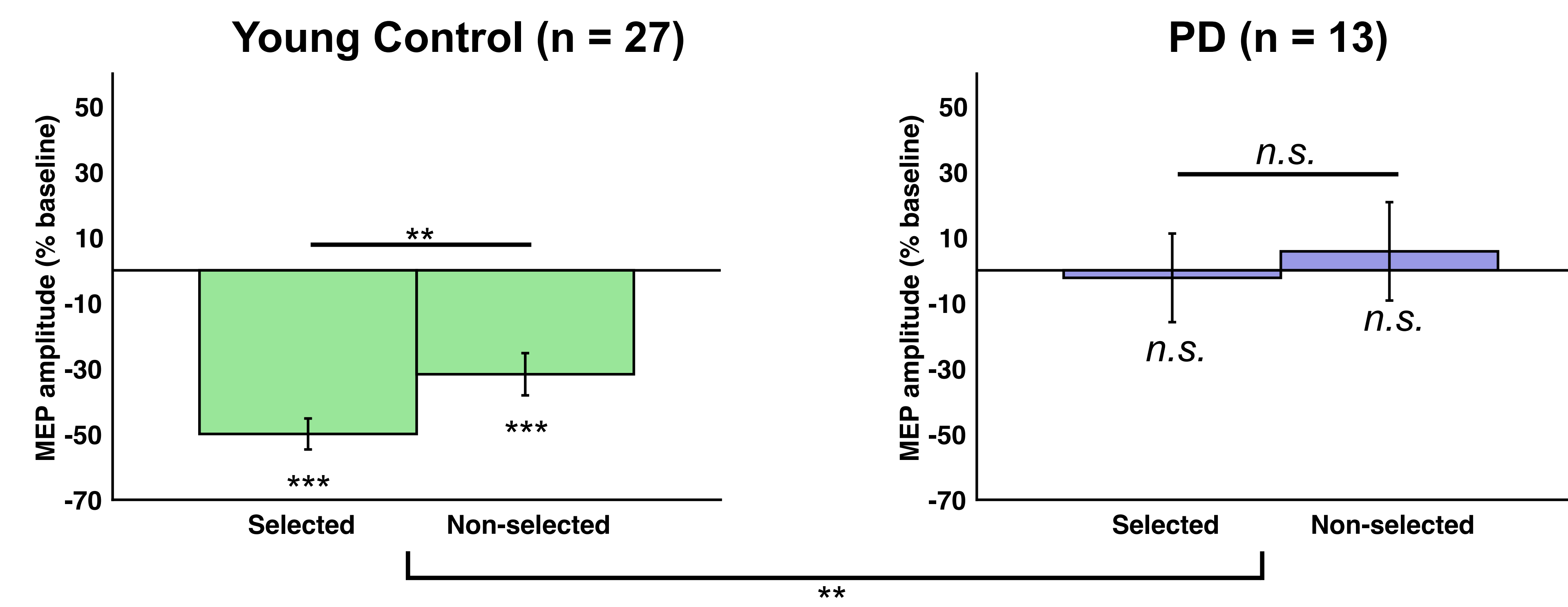
MEP Variability



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

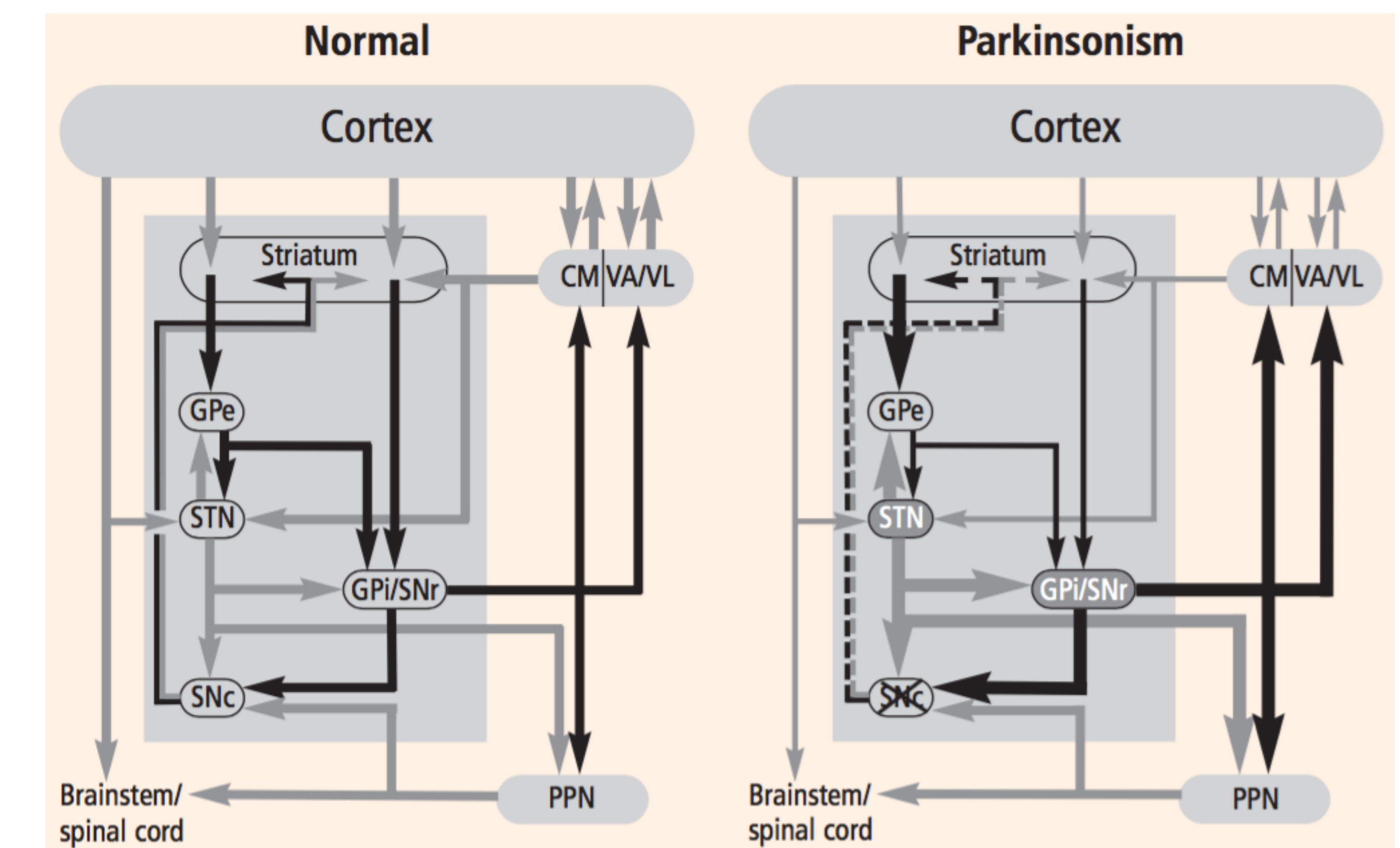
Preparatory Inhibition is Absent in PD



Healthy young controls exhibited marked inhibition during the preparation of responses with either hand and showed greater inhibition in the selected than the non-selected hand. This pattern is consistent with that observed in previous studies.

In contrast, Parkinson's patients exhibited no evidence of preparatory inhibition and were significantly different from the controls.

Role of Basal Ganglia in Preparatory Inhibition



(Vitek, 2008)

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.

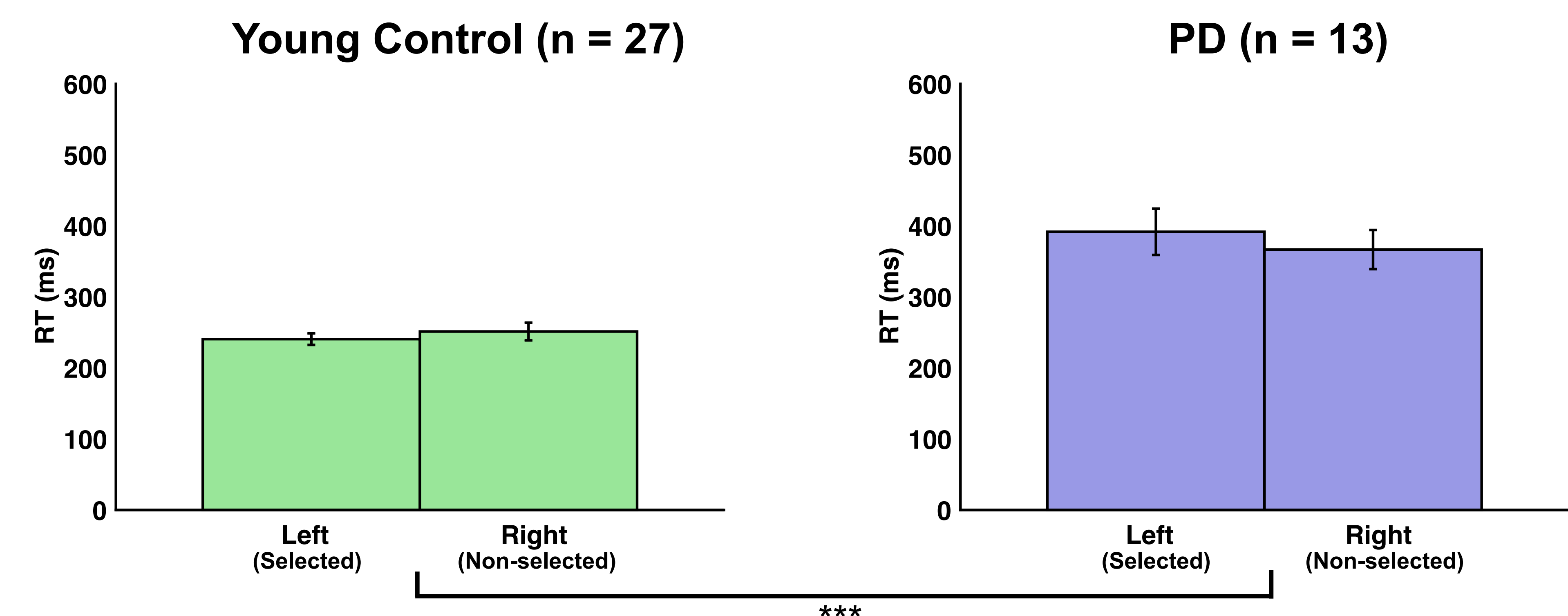
Discussion

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.

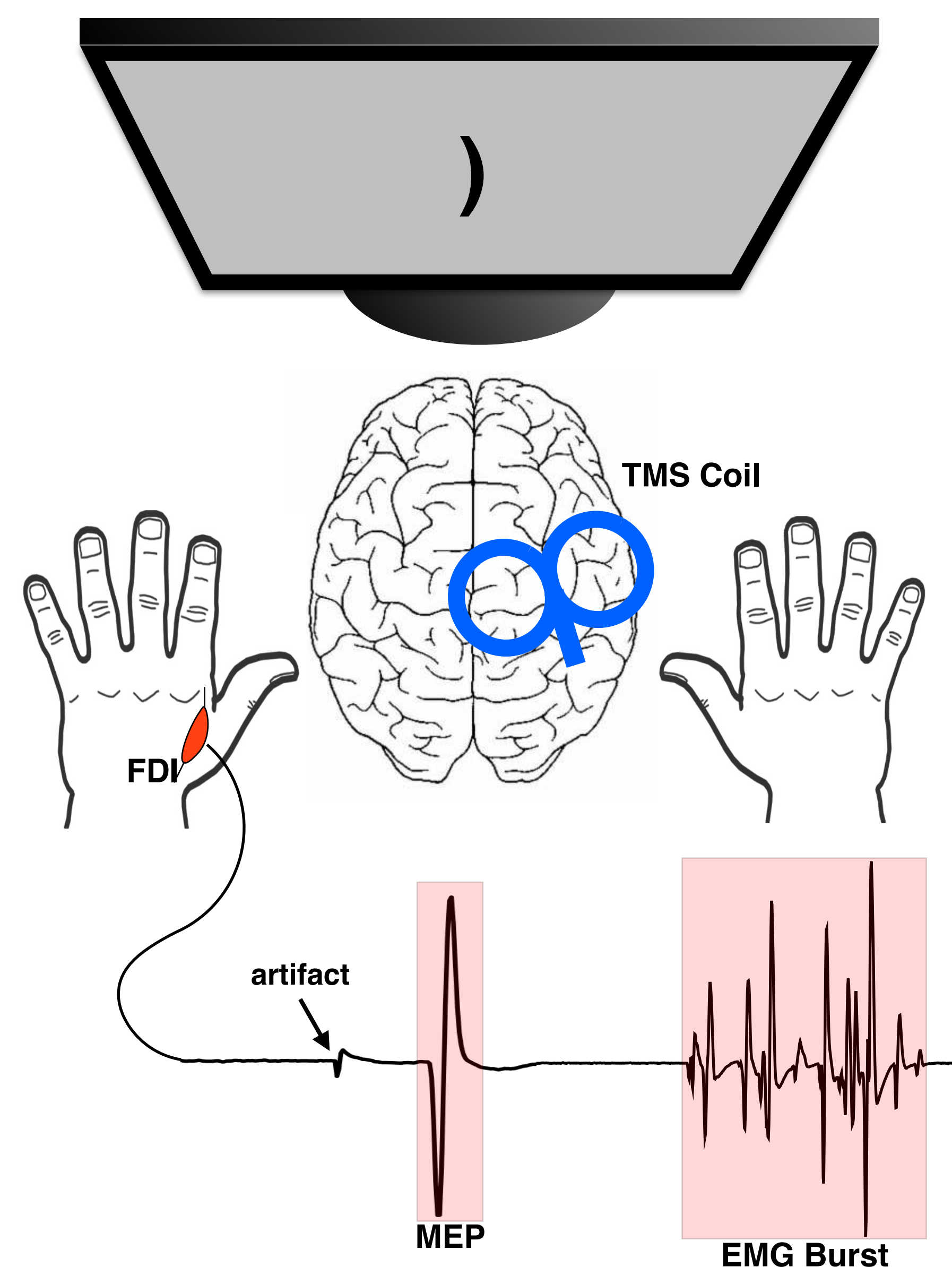
Accordingly, a loss of preparatory inhibition in PD may reflect either an inability to suppress motor noise or tonic excessive motor inhibition that restricts the range of excitability. Either scenario could constrain signal-to-noise within the motor system and impede action preparation.

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.

EMG RT is Slower in PD



Healthy young controls had significantly faster EMG onset times than Parkinson's patients. This may be an effect of aging, which will be tested with a group of age-matched controls.



Transcranial magnetic stimulation (TMS) over right motor cortex was used to elicit motor evoked potentials (MEPs) from the left first dorsal interosseus (FDI) muscle during task performance.

To examine whether preparatory inhibition is abnormal in Parkinson's disease we tested:

- 13 idiopathic Parkinson's disease patients (63.5 ± 1.7 y.o., 7 female), on medication (UPDRS 11.5 ± 0.9), RMT 40.2 ± 2.4%

- 27 young adult healthy males (21.6 ± 0.4 y.o.), RMT 44 ± 1.3 %

- Future testing will include age and education matched controls