Altered Sensorimotor Transformations for Balance In Parkinson’s Disease

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Introduction

Long latency automatic postural responses to balance perturbations are often abnormal in Parkinson’s disease (PD) and may cause impaired balance and falls.

- Antagonist and agonist muscles during long latency postural responses are often coactivated in PD (Carpenter et al. 2004; Dimitrova et al. 2004; St George et al. 2012), which may increase rigidity and decrease stability. However, pathologic changes underlying abnormal postural responses are poorly understood, limiting our ability to develop improved therapies.

We have developed a mechanistic model of the sensorimotor feedback transformation underlying the magnitude and timing of muscle activation during postural responses: the sensorimotor response model (SRM).

- We demonstrated that in behaving cats (Lockhart and Ting 2007) and in young healthy individuals (Safavinya and Ting 2012; Welch and Ting 2009), postural responses are created through multisensory estimates of the motion of the body center of mass (CoM) to activate muscles in an optimal tradeoff between postural error and control effort.

Here, we applied the SRM to investigate whether and how PD modifies the sensorimotor transformation during postural responses.

- We compared postural responses to forward perturbations of the CoM in two female patients: advanced PD (age, 75 y; Hoehn & Yahr stage 3; UPDRS-III score 43; daily falls, OFF medications), and mild PD (4 y; H & Y 1.5; UPDRS-III 24, no previous falls, OFF medications) with postural responses from healthy older (female, 70 y) and healthy young (female, 19 y) participants.

We hypothesize that pathologic changes in PD cause impaired inhibition of competing sensorimotor feedback motor programs during postural responses.

- Mink has hypothesized that the basal ganglia provide “focused facilitation and surround inhibition of motor mechanisms in thalamocortical and brainstem circuits” which is compromised in PD (Mink 2003).

- We predicted that in PD, antagonist muscles would be activated with increased magnitude, reflected in increased SRM parameter magnitudes, and in advanced PD, antagonists and agonists are also activated with abnormal timing, including shortened bursts of initial activity, reflected in increased values of SRM parameter $k_p$.

Results and Discussion

Perturbations probe automatic postural responses

- 3 backward perturbations (peak displacement: 7.5 cm displacement; 15 cm/s velocity; 0.1 g acceleration) within unpredictable multidirectional block
- Surface EMG recorded at 1,080 Hz from 16 leg and trunk muscles (Basmajian and Blumenstein 1980) and synchronized with kinematics and kinetics.
- EMG processed as in previous studies (hi-pass, 35 Hz, de-mean, rectify, low-pass, 40 Hz; bidirectional Butterworth filtering used in all cases to remove phase artifacts).
- Average EMG in medial gastrocnemius (MGAS) and tibialis anterior (TA) analyzed.

The SRM describes the mapping from postural error to EMG

- We quantified average EMG responses with delayed feedback of CoM motion.
- We minimized average absolute error between recorded and reconstructed EMG signals (Matlab, fmincon.m).
- In these initial analyses, initial guesses and boundary values were set manually, and transient encoding “clipping” was incorporated as necessary by manually setting feedback signals to zero after initial response windows (Welch and Ting 2009).

Individuals with PD in the OFF medication state demonstrated elevated antagonist activity, quantified as increased destabilizing antagonist SRM gains

- Overall, delayed sensorimotor feedback of CoM motion was sufficient to reproduce recorded muscle activity with high precision in all participants (variance accounted for = 0.87±0.09).
- SRM parameters also accounted for abnormal co-contraction between agonist and antagonist muscles in PD. While healthy individuals maintained balance primarily via agonist muscle activation (Figure: A,B), co-contraction in PD patients (Figure: C,D) was quantified by elevated antagonist SRM parameters (P<0.001; z-test) but no statistically-significant changes in agonist SRM parameters (P>0.26).

More advanced PD was associated with increased sensitivity to higher-order terms of CoM motion in both antagonists and agonists

- Advanced PD was associated with shortened initial bursts of muscle activity (Figure: A vs. D, black bars), which was quantified with elevated values of SRM parameters $k_l$ and $k_a$ (P<0.001; z=4.7 z-test vs. other participants), suggesting that higher-order derivatives of CoM motion contribute substantially to muscle responses in advanced PD, but not controls or mild PD.

Conclusions

- These results provide preliminary evidence that PD may alter sensorimotor balance control via impaired descending inhibition to favor higher-order terms of CoM motion. Because deep brain stimulation of globus pallidus or subthalamic nucleus can improve automatic postural responses – although via poorly understood pathways (St George et al. 2012) – future mechanistic models of these pathways may allow us to develop refined therapeutic strategies.

- Improved mechanistic models may also enable clinicians to prospectively identify individuals at increased fall risk who could then be referred for rehabilitation (Ashburn et al. 2007; Canning et al. 2013; Hackney and Earhart 2010; 2009; Mansfield et al. 2010; Proctor et al. 2005; Smania et al. 2010) or other therapeutic strategies to mitigate the fall risk (Kim et al. 2013).

References

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