Freezing of gait

Freezing of gait (FOG) is a rare but disabling symptom in Wilson's disease (WD), typically appearing in advanced stages or in patients with significant basal ganglia involvement. While visual cueing has been widely studied in Parkinson's disease (PD), its application in WD remains anecdotal and understudied.

Treatment

see Freezing of gait treatment. Freezing of gait (FOG) is a devastating axial motor symptom in Parkinson's disease (PD) leading to falls, institutionalization, and even death. The response of FOG to dopaminergic medication and deep brain stimulation (DBS) is complex, variable, and yet to be optimized. Fundamental gaps in the knowledge of the underlying neurobiomechanical mechanisms of FOG render this symptom one of the unsolved challenges in the treatment of PD. Subcortical neural mechanisms of gait impairment and FOG in PD are largely unknown due to the challenge of accessing deep brain circuitry and measuring neural signals in real-time in freely-moving subjects. Additionally, there is a lack of gait tasks that reliably elicit FOG. Since FOG is episodic, we hypothesized that dynamic features of subthalamic (STN) beta oscillations, or beta bursts, may contribute to the Freezer phenotype in PD during gait tasks that elicit FOG. We also investigated whether STN DBS at 60 Hz or 140 Hz affected beta burst dynamics and gait impairment differently in Freezers and Non-Freezers. Synchronized STN local field potentials, from an implanted, sensing neurostimulator (Activa® PC + S, Medtronic, Inc.), and gait kinematics were recorded in 12 PD subjects, off-medication during forward walking and stepping-in-place tasks under the following randomly presented conditions: NO, 60 Hz, and 140 Hz DBS. Prolonged movement band beta burst durations differentiated Freezers from Non-Freezers, were a pathological neural feature of FOG and were shortened during DBS which improved gait. Normal gait parameters, accompanied by shorter bursts in Non-Freezers, were unchanged during DBS. The difference between the mean burst duration between hemispheres (STNs) of all individuals strongly correlated with the difference in stride time between their legs but there was no correlation between mean burst duration of each STN and stride time of the contralateral leg, suggesting an interaction between hemispheres influences gait. These results suggest that prolonged STN beta burst durations measured during gait is an important biomarker for FOG and that STN DBS modulated long not short burst durations, thereby acting to restore physiological sensorimotor information processing, while improving gait [1)].

Freezing of gait is a poorly understood symptom of Parkinson's disease, and can severely disrupt the locomotion of affected patients. However, bicycling ability remains surprisingly unaffected in most patients suffering from freezing suggesting functional differences in the motor network.

Storzer et al. present the first local field potential recordings directly comparing bicycling and walking in Parkinson's disease patients with subthalamic nucleus deep brain stimulation. Low (13-22 Hz) and high (23-35 Hz) beta power changes were analyzed in 22 subthalamic nuclei from 13 Parkinson's disease patients (57.5 +/- 5.9 years, four female). The study group consisted of five patients with and eight patients without freezing of gait.

In patients without freezing of gait, both bicycling and walking led to a suppression of subthalamic beta power (13-35 Hz), and this suppression was stronger for bicycling. Freezers showed a similar

pattern in general. Superimposed on this pattern, however, we observed a movement-induced, narrowband power increase around 18 Hz, which was evident even in the absence of freezing.

These results indicate that bicycling facilitates overall suppression of beta power. Furthermore, movement leads to exaggerated synchronization in the low beta band specifically within the basal ganglia of patients susceptible to freezing. Abnormal ~18 Hz oscillations are implicated in the pathophysiology of freezing of gait, and suppressing them may form a key strategy in developing potential therapies. [2)].

Stimulation-induced hypokinetic gait disorders with freezing of gait (FOG) have been reported as adverse effects of deep brain stimulation (DBS) of the globus pallidus internus (GPi) in patients with dystonia.

Wolf et al., prospectively performed computerized gait analysis in ten consecutive patients (mean age 57.8+/-14.3 years) with segmental dystonia but without involvement of lower trunk or legs who were treated with bilateral GPi DBS. Using pressure sensitive insoles, several parameters were measured preoperatively (pre-OP) and at a median of 7 months postoperatively.

The mean step length significantly decreased from 60.0+/-6.9cm pre-OP to 54.3+/-6.4cm with GPi DBS ($p<0.01$). Due to only small changes of walking distance and gait velocity, the cadence correspondingly increased from 105.6+/-9.2 steps/min to 111.3+/-11.4 steps/min ($p<0.05$). More importantly, the variance of several gait parameters significantly decreased postoperatively.

In patients with segmental dystonia, chronic DBS of the posteroventral lateral GPi is associated with only mild hypokinesia of gait, but with a relevant decrease in gait variability. Given other recently reported hypokinetic effects of GPi DBS for dystonia and recent results of electrophysiological coherence studies, these findings support the hypothesis of a general alteration of neuronal activity in striato-pallido-thalamo-cortical motor pathways following chronic stimulation of the posteroventral lateral GPi [3)].

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