

Indices of Motor Synergies as Early Biomarkers of Parkinsons Disease

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Research Abstract

ABSTRACT Parkinson's disease (PD) is a common neurological disorder caused by progressive loss of dopamine- producing neurons in the substantia nigra. One of the main problems in treating PD is the lack of early biomarkers that would provide crucial information for making practical decisions on treatment and prevention plans for individual patients. Our main goal is to demonstrate that indices of stability of motor actions (indices of synergies) can and should be used as theory-based, quantitative, and objective biomarkers of PD. Our recent studies using the framework of the uncontrolled manifold (UCM) hypothesis to quantify synergies have shown that PD patients demonstrate impaired synergies (low stability of action)

and impaired ability to adjust synergies in preparation to action (delayed and reduced anticipatory synergy adjustments, ASAs). In a few patients at stage-I (Hoehn-Yahr) of PD, changes in synergies and ASAs were seen during actions involving body parts without clinical signs of the disease. These results suggest that studying synergies may yield objective biomarkers that are able to detect and quantify impaired motor function in PD and may be sensitive to pre-motor-symptom stages of the disease. We plan to collect pilot data to support this hypothesis by studying a group of drug-naïve patients at stage-I (Hoehn-Yahr) of PD. Testing drug-naïve patients will allow disambiguating effects of PD from possible effects of long-term exposure to drugs on the non-symptomatic extremities. We also plan to determine the effects of dopamine replacement therapy on these indices. Our main specific hypotheses are: (1) Drug-naïve patients with PD stage-I will show reduced synergy indices and shorter, delayed ASAs as compared to healthy controls in both symptomatic and non-symptomatic hands/arms; and (2) These indices will be sensitive to dopamine-replacement drugs. Two specific aims will test the main hypotheses. Aim 1: To demonstrate and quantify changes in synergic control in symptomatic and asymptomatic extremities of newly diagnosed, drug-naïve HY stage-I PD patients. We will quantify indices of multi-finger synergies stabilizing total force and multi-joint synergies stabilizing hand trajectory in both upper extremities. We expect the synergy indices to be reduced similarly on both sides compared to controls. We also predict delayed and reduced ASAs in PD. Aim 2: To demonstrate and quantify the effectiveness of dopamine-replacement therapy in improving synergic control in PD patients. Studies described under Aim-1 will be repeated one hour after taking carbidopa/levodopa 25/100 regular, gold standard for dopaminergic replacement. We plan to show positive effects of the drug on the synergy indices across. If successful, these results will help us to optimize design of a longer prospective study that would test the prognostic value of changed multi-finger and multi-joint synergies by following prospectively a large group of early-stage PD patients over several years to explore how synergy indices predict the occurrence of clinical symptoms such as emergence of symptoms on the less-affected body side, postural instability, and freezing of gait tasks. We view the impaired synergies in the upper extremities as early reflections of a general disruption of the mechanisms of synergic control, which later leads to effects in other body parts including those involved in postural and locomotion tasks.

Further information available at:

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