# Scaling and Sequencing Motor Output in Humans: fMRI Study

https://neurodegenerationresearch.eu/survey/scaling-and-sequencing-motor-output-in-humans-fmri-study/

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**Country**

USA

**Title of project or programme**

Scaling and Sequencing Motor Output in Humans: fMRI Study

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NIH (NINDS)

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**The project/programme is most relevant to:**

Parkinson's disease & PD-related disorders

**Keywords**

Monoamine Oxidase B, Motor output, putamen, Functional Magnetic Resonance Imaging, Parkinson Disease

**Research Abstract**

PROJECT SUMMARY Parkinson’s disease (PD) is a progressive neurodegenerative syndrome that is characterized by the loss of dopaminergic cells in the substantia nigra and reduced

dopamine in the putamen. In PD, a major goal has been to develop therapies that modify disease progression. Unfortunately, despite dozens of clinical trials in PD over the past several decades, identifying a disease-modifying drug for PD has not been achieved. A major reason for this failure is because prior studies have relied upon subjective clinical ratings as outcome measures, and these ratings cannot quantify small differences in disease progression. Sensitive and objective markers of PD progression that directly relate to basal ganglia and cortical neuroanatomy are critically needed. Our group has successfully validated objective markers of disease progression using novel methods from diffusion magnetic resonance imaging (dMRI) and functional magnetic resonance imaging (fMRI). These novel disease progression biomarkers using dMRI and fMRI provide a critical step forward to evaluate disease- modifying therapies in PD. In this Renewal R01, we will build on these key observations by evaluating how the dMRI and fMRI biomarkers of progression respond to a monoamine oxidase type B (MAO-B) inhibitor. The rationale is that MAO-B inhibitors stop the breakdown of dopamine, and may allow the neurons in the nigrostriatal pathway to function more effectively for a longer period of time. We choose to evaluate a MAO-B inhibitor because it is a safe and FDA approved therapy for treating PD symptoms, numerous animal studies already suggest it has disease-modifying qualities, and MAO-B inhibitors have shown some initial promise as a potential disease-modifying therapy for PD. We will study how the MAO-B inhibitor affects biomarker progression using a prospective, placebo-controlled study design. Aim 1 studies a dMRI progression marker of the substantia nigra and Aim 2 studies a task-based fMRI progression marker of the putamen, primary motor cortex, and supplementary motor area. We will conduct a 12-month study in PD patients to test the hypothesis that the MAO-B inhibitor will slow the progression of free-water accumulation in the substantia nigra and slow the reduction of the blood oxygenation dependent signal in the putamen, primary motor cortex, and supplementary motor area. We will also assess a battery of secondary outcomes to monitor motor performance, cognitive status, and emotional status. The outcome and impact of this study will provide the first evaluation of MAO-B inhibitors at slowing the progression of the nigrostriatal pathway using advanced dMRI and fMRI methods in PD.

**Lay Summary**
PROJECT NARRATIVE Parkinson’s disease (PD) is a progressive neurodegenerative syndrome affecting close to 1.5 million Americans. The major unmet clinical need is to develop therapeutics that slow the progression of the disease. Sensitive and objective markers of PD progression that directly relate to basal ganglia and cortical neuroanatomy are critically needed for evaluating potential therapies. Our group has successfully validated objective markers of disease progression using novel methods from diffusion magnetic resonance imaging (dMRI) and functional magnetic resonance imaging (fMRI). The current project will conduct a 12-month study in PD patients to test the hypothesis that the MAO-B inhibitor will slow the progression of dMRI and fMRI progression markers in the basal ganglia and cortex.

**Further information available at:**

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Investments > €500k

**Member States:**
United States of America

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