Mutant G2019S-LRRK2 induces neurovascular abnormalities in mice

Wanli Smith[1], Bo Ning[1], Chunming Gu[2,3,4], and Jun Hua[3,4]

1. Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA
2. Department of Biomedical Engineering, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA
3. Department of Radiology, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA
4. F.M. Kirby Research Center for Functional Brain Imaging, Kennedy Krieger Institute, Baltimore, Maryland, USA

ABSTRACT

Parkinson's disease (PD) is the second most common neurodegenerative disease and the most common movement disorder characterized by motor impairments resulting from midbrain dopamine (DA) neuron loss. Mutations in LRRK2 cause genetic PD and contribute to sporadic PD. We recently generated the human LRRK2 G2019S transgenic mouse model that displays PD-like movement impairment. Here, we used LRRK2-G2019S transgenic mouse model to investigate abnormalities in arteriolar cerebral blood volume (CBVa) in various brain regions using the inflow-based vascular-space-occupancy (iVASO) MRI technique. CBVa was measured in the substantia nigra (SN), olfactory cortex and prefrontal cortex. Compared to non-transgenic mice, G2019S-LRRK2 mice at 9 months of age showed decreased CBVa in the SN, but increased CBVa in olfactory and prefrontal cortex in both male and female groups, whereas WT-LRRK2 mice showed no change in CBVa in the SN (male and female), the olfactory (female) and prefrontal (female) cortex, but a slight increase in CBVa in the olfactory and prefrontal cortex in the male group only. Alterations in the blood volume of small arteries and arterioles (CBVa) were detected in the G2019S-LRRK2 mouse model of PD. The opposite changes in CBVa in the SN and the cortex indicate that PD pathology may have differential effects in different brain regions. Our results suggest the potential value of CBVa as a marker for clinical PD studies.

Sponsored By: NIH RO1000000

Presenter Name and contact information:
Wanli W. Smith, MD., Ph.D.
Department of Psychiatry and Behavioral Sciences, Neurobiology Division, Johns Hopkins University School of Medicine, Baltimore, MD 21287
Phone: 410-6146268; Fax: 410-614-0013;
Email:wsmith60@jhmi.edu