Session P271 - Human Studies: Genetics and Diagnostics PD II

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P271.03 - First test of dopamine buffering capacity imaging as a disease severity biomarker in Parkinson disease

November 9, 2021, 9:30 AM - 10:30 AM | Virtual Only

Grant Support
The Michael J. Fox Foundation for Parkinson's Research (Grant ID: 13280)

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Disclosures
K.J. Black: E. Ownership Interest (stock, stock options, royalty, receipt of intellectual property rights/patent holder, excluding diversified mutual funds); QuanDyn.com. **J.M. Koller:** E. Ownership Interest (stock, stock options, royalty, receipt of intellectual property rights/patent holder, excluding diversified mutual funds); QuanDyn.com. **J.S. Perlmutter:** None.

Abstract
BACKGROUND: We tested whether a novel pharmacological fMRI approach, dopamine buffering capacity imaging, could quantify disease severity in Parkinson disease (PD). This approach measures how quickly the effect of a dose of levodopa (LD) appears and wears off, using not a clinical effect (which can change e.g. with motivation and fatigue), but LD's objective effect on rCBF (regional cerebral blood flow) in the midbrain and pons. This large rCBF response has been demonstrated repeatedly (e.g. 62-74% increase in DOI: 10.7717/peerj.1381/table-2), but previous studies all averaged over participants and averaged over before-*vs.* after-drug time points. The present study relies on a mathematical model that is well grounded in available information (DOI 10.3389/fneur.2020.00370), but requires measuring for the first time rCBF responses to levodopa over numerous brief time intervals and in individual participants.
METHODS: Details appear in the pre-registered study protocol (DOI 10.17605/OSF.IO/G7DFY). After 200 mg carbidopa by mouth, pCASL fMRI measured rCBF repeatedly for over an hour in 16 people with Parkinson disease, before and during an i.v. infusion of levodopa bioequivalent to about 80 mg by mouth. The effect site rate constant k_e was calculated for a pre-specified midbrain-pons region with a large LD-induced increase in rCBF.
RESULTS: On average, the midbrain region showed a plausible time course of response to LD, with mean rCBF beginning to increase near the end of the i.v. LD loading dose and persisting elevated throughout the 15-40 min. time period during which an increase was expected. However, some participants' time-rCBF curves showed little response, including the participant who appeared to have the best scan session (minimal head movement, no sleep). The hypothesized correlations of midbrain k_e with disease duration and severity (UPDRS III score and tapping speed in an overnight off state) showed the expected sign but none was significant.
DISCUSSION: This novel pharmacological fMRI method to quantify PD disease progression did not perform as expected in this sample using these methodological choices. Specifically, the midbrain region did not give in every subject the expected, pharmacologically sensible time course of increased activity after LD administration. We will discuss possible explanations and potential methodological improvements.