Categories: Neuroimaging
Keyword 1: apolipoprotein E
Keyword 2: cerebral blood flow
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Paper Session 03: Parkinson's disease related topics

9:00 - 10:30am
Thursday, 2nd February, 2023
Pacific Ballroom E

Moderated by: Cady Block

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1 Basal Forebrain Free Water Fraction is Associated with Cortical Cholinergic Levels in Idiopathic Parkinson's Disease

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Objective: Cognitive dysfunction is a common non-motor symptom of Parkinson's disease (PD). Cognitive decline in PD is likely associated with dysfunction in the cholinergic system, which is affected by synuclein pathology early in the disease course. Recent studies have shown an association between reduced integrity of the basal forebrain (BF), which provides cholinergic innervation to most of cortex, and diminished cognitive functioning in PD. Specifically, those with PD and reduced cholinergic innervation also have higher rates of cognitive impairment. However, no study has directly investigated the relationship between basal forebrain integrity and cortical cholinergic levels. In the present study, we examined this relationship through measures of basal forebrain microstructural integrity and cholinergic nerve terminal density in cortical and subcortical gray matter.

Participants and Methods: Participants included 92 non-demented individuals with idiopathic PD (M:F=64:28; Age=67.0±7.1 yrs) who underwent structural MRI, diffusion MRI, and [18F] fluoroethoxybenzovesamicol (FEOBV) cholinergic PET imaging. We used a basal forebrain and region of interest defined by AssemblyNet, which uses ensembles of pretrained convolutional neural networks to create a full brain segmentation. Bilateral putamen from this atlas was also included as a control region. We measured microstructural integrity using free water fraction (FWF), a diffusion MRI-derived metric of extracellular water that associates with cellular density and neuroinflammation. For PET data, we computed the distribution volume ratio (DVR) by regions as defined by FreeSurfer. A factor analysis of DVR in all 88 FreeSurfer ROIs resulted in seven clusters of ROIs covering 1) widespread bilateral cortical regions (PC1); 2) subcortical and limbic regions (PC2); 3) bilateral cingulate regions (PC3); 4) left frontal regions (PC4); 5) right frontal and temporal regions (PC5); 6) cerebellum (PC6); and 7) bilateral entorhinal cortex and left temporal cortex (PC7). We performed seven separate regression analyses per ROI (controlling for age and disease duration) to evaluate the association between BF FWF and cholinergic levels in these regions. To determine if these ROIs showed unique associations with BF FWF, we then entered ROIs with a significant association with BF FWF as independent variables in a stepwise regression with forward selection with BF FWF as the dependent variable.
Results: BF FWF was significantly and negatively associated with cholinergic levels in PC1 ($\Delta R2=.042$, $\beta=-0.208$, $p=.04$), PC3 ($\Delta R2=.044$, $\beta=-0.206$, $p=.03$), PC4 ($\Delta R2=.056$, $\beta=-0.239$, $p=.02$), and PC7 ($\beta=-0.215$, $p=.04$). BF FWF trended towards a negative association with cholinergic levels in PC5 ($\Delta R2=.045$, $\beta=-0.168$, $p=.09$) and PC6 ($\beta=-0.188$, $p=.09$). Putamen FWF did not significantly associate with any of the ROIs. In the follow-up stepwise regression, only PC4 contributed significantly to the overall model ($\Delta R2=.061$, $\beta=-0.261$, $p=.02$).
Conclusions: Basal forebrain FWF was inversely related to cholinergic levels in regions that are directly innervated by the basal forebrain (e.g., cingulate cortex, left frontal cortex, and bilateral entorhinal cortex). Future research should directly investigate the relationship between basal forebrain integrity, cortical cholinergic levels, and cognition.

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Separating the basal forebrain into specific nuclei would also be beneficial, as different nuclei may have differing associations with specific hemispheric cholinergic pathways and cognition.

Categories: Movement and Movement Disorders
Keyword 1: Parkinson's disease
Keyword 2: neuroimaging: structural
Keyword 3: neurotransmitter systems
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2 A Randomized, Double-blinded, Placebo-controlled Trial of Liraglutide in Patients with Parkinson's Disease: Neuropsychological Outcomes

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Objective: Parkinson's disease (PD) is associated with metabolic disorders such as insulin resistance. Pharmacological intervention used to treat insulin resistance, like GLP-1 agonists, may have auspicious results in the treatment for PD. The objective of this clinical trial was to assess the therapeutic effect of liraglutide on non-motor symptoms, such as, but not limited to, cognitive function and emotional well-being, and quality of life for individuals with PD.
Participants and Methods: In a single-center, randomized, double-blind, placebo-controlled trial, PD patients self-administered liraglutide injections once-daily (1.2 or 1.8 mg, as tolerated) or placebo in a 2:1 study design for 52 weeks after titration. Primary outcomes included adjusted difference in the OFF-state Movement Disorders Society Unified PD Rating Scale (MDS-UPDRS) part III, non-motor symptom scale (NMSS) and Mattis Dementia Rating Scale (MDRS-2). Secondary outcomes included quality of life scores (Parkinson Disease Questionnaire, PDQ-39) and other neuropsychological tests, including Delis-Kaplan Executive Function System (DKEFS), Geriatric Depression Scale (GDS), and Parkinson's Anxiety Scale (PAS) scores.
Results: Sixty-three subjects were enrolled and randomized to liraglutide (n=42) or placebo (n=21). Mean age in years was 63.5 (9.8) and 64.2 (6.4) for liraglutide and placebo cohorts, respectively (p=0.78), and mean age at symptom onset was 58.9 (10.5) and 59.3 (7.5) for liraglutide and placebo cohorts, respectively (p=0.86). At 54 weeks, NMSS scores had improved by 6.6 points in the liraglutide group and worsened by 6.5 points in the placebo group, a 13.1 point adjusted mean difference (p<0.05). Further analysis showed all nine NMSS sub-domain changes favoring the liraglutide group, with one (attention/memory) reaching statistical significance (p<0.05). Secondary outcome analyses revealed a significant improvement of PDQ-39 (p<0.001) and Parkinson's Anxiety Scale - Avoidance Behavior scores (p<0.05) in the treatment group. MDRS-2 sub-scores did not further differentiate study groups, while DKEFS letter fluency scores favored placebo group (p<0.05).
Conclusions: Treatment with liraglutide improved self-reported non-motor symptoms of PD, activities of daily living, and quality of life. These results validate similar outcomes reported with other GLP-1 agonists implicating consideration for novel treatment opportunities for individuals with PD. Notably, the absence of significant performance-based cognitive changes over the duration of the trial for the participants in this study has several plausible explanations given participant-related baseline demographic and clinical factors. Implications for neuropsychologists will be discussed.

Categories: Movement and Movement Disorders
Keyword 1: Parkinson's disease
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3 The Relationship Between Depression, Anxiety, and Autonomic Dysfunction in de novo Parkinson's Disease Patients Over Time

Adrianna M. Ratajska, Francesca V. Lopez, Lauren E. Kenney, Katie Rodriguez, Rachel Schade, Joshua Gertler, Dawn Bowers

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