

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.

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3 The Relationship Between Depression, Anxiety, and Autonomic Dysfunction in de novo Parkinson's Disease Patients Over Time

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