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.

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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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Objective: Autonomic dysfunction is an important non-motor symptom of Parkinson's disease (PD), with point prevalence estimates of approximately 50-70%. Common presentations include cardiovascular dysregulation, gastrointestinal dysfunction, impaired thermoregulation, and sexual dysfunction. In the present study, we sought to examine whether autonomic symptoms would predict trajectories of change in depression and anxiety over a 5-year period in newly diagnosed individuals with PD. Given that alterations in autonomic nervous system functioning (e.g., reduced heart rate variability, lower autonomic arousal) are frequently observed in individuals who have anxiety and depression, as well as the negative influence these symptoms can have on quality of life/functioning, we predicted that greater autonomic symptoms would be related to increased mood symptoms over time.
Participants and Methods: Participants included 414 individuals from the Parkinson's Progression Markers Initiative, a prospective study of newly diagnosed and untreated individuals with PD. The PD participants (mean age=61.6+9.7, mean education=15.6+3.0, 92.5% non-Hispanic White) were followed annually for up to five years. Self-reported autonomic symptoms were measured using the Scales for Outcomes in Parkinson's Disease–Autonomic Dysfunction (SCOPA–AUT), which consists of a total score and 6 subdomain scores (gastrointestinal, urinary, cardiovascular, thermoregulatory, pupillomotor, sexual). Mood measures included the Geriatric Depression Scale (GDS) and State-Trait Anxiety Inventory (STAI). Motor severity was assessed using the Unified Parkinson's Disease Rating Scale (UPDRS) Part III. Bootstrapped linear regressions were performed to evaluate the relationship between autonomic symptoms (subdomains) and mood using data from the last visit (year 5). For longitudinal analyses, bootstrapped multilevel modeling was used to examine a) changes in SCOPA–AUT total over time (unconditional growth model only) and b) the relationship between mood and SCOPA–AUT total score over time, controlling for age/sex and motor severity.
Results: Autonomic symptoms explained 28.2% of the total variance in trait anxiety, with unique predictors of gastrointestinal (β=.266, p<.001) and thermoregulatory (β=.202, p=.004) symptoms. For depression, autonomic symptoms explained 27.9% of the total variance, with unique predictors of gastrointestinal (β=.225, p=.012), thermoregulatory (β=.178, p=.013), and cardiovascular (β=.154, p=.012) symptoms. There was a gradual linear increase in total autonomic symptoms over time (b=0.86, p<.001). Greater total autonomic symptoms were associated with higher average trait anxiety (b=0.54, p<.001), slightly greater increase in trait anxiety over time (b=0.04, p<.05), and occasion-to-occasion fluctuations in trait anxiety (b=0.24, p<.001). Similarly, increased total autonomic symptoms were associated with higher average depressive symptoms (b=0.14, p<.001), minimally greater increase in depressive symptoms over time (b=0.01, p<.05), and occasion-to-occasion fluctuations in depressive symptoms (b=0.08, p<.001). Motor severity did not explain individual differences or trajectories of change in depression or trait anxiety.
Conclusions: Autonomic symptoms, particularly gastrointestinal, cardiovascular, and thermoregulatory dysfunction, were related to increased mood symptoms in PD patients and predicted increases in depression/anxiety over time. Our findings do not distinguish between two theoretical possibilities – whether autonomic symptoms lead to depression/anxiety versus involvement of co-occurring neural systems underlying both. Regardless, our study highlights the importance of treating autonomic dysfunction in early PD, and future work should incorporate additional measures of autonomic dysfunction (e.g., physiological probes).

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Keyword 1: Parkinson's disease
Keyword 2: depression
Keyword 3: anxiety
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4 An Update: Greater Apathy Associated with Selective Serotonin Reuptake Inhibitor Use in Parkinson's Disease

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