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Exenatide treatment alleviated symptoms of depression in patients

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Non-motor symptoms of Parkinson's disease (PD), such as depression, apathy, cognitive impairment, sleep disorders, and sensory symptoms, can have a greater impact on health-related quality of life than motor deficits. In a post hoc analysis of the exenatide-PD trial results, investigators found that patients on exenatide treatment experienced improvements in severity of depression, independent of whether their motor function improved. They report their findings in the *Journal of Parkinson's Disease*.

GLP-1 receptor agonists are used to treat people with type 2 diabetes by stimulating the GLP-1 receptors in the pancreas, which triggers the release of insulin. GLP-1 receptors have been found in the brain and may also play a role to in the treatment of PD. In the exenatide-PD trial, a randomized, placebo-controlled clinical trial in patients with moderate-stage PD, the GLP-1 receptor agonist exenatide showed positive effects on the motor severity of the disease, which continued 12 weeks beyond the period of exenatide exposure.

"In the original analysis of the exenatide-PD trial, the primary outcome was a comparison in the motor severity of PD," explained Thomas Foltynie, Ph.D., MBBS, Sobell Department of Motor Neuroscience, UCL Institute of Neurology, and The National Hospital for Neurology and Neurosurgery, London, UK, who led the exenatide trial and is lead investigator of the current study. "Analysis of pre-defined secondary outcomes revealed no statistically significant differences between patients treated with exenatide in total non-motor symptom burden and

overall quality of life measures, including the Non Motor Symptoms Scale (NMSS). However, the response of individual non-motor symptoms to an intervention may vary."

The current research was a post hoc analysis of the trial data and aimed to identify whether in addition to improvement in motor function, there were any indications that exenatide affected specific non-motor symptoms of PD compared to placebo, rather than considering the non-motor symptoms severity scale as a whole.

Results indicated that all measures evaluating depression improved in patients who received exenatide. The proportion of patients reporting depressive symptoms in the placebo group increased from 17% at baseline to 25% at 48 weeks, while in the exenatide group, the proportion of patients reporting depressive symptoms reduced from 23% at baseline to 6% of patients at 48 weeks. Among the other post hoc comparisons of specific non-motor symptoms, self-reported apathy and cognition also improved with exenatide.

These results are of particular interest given the effects on mood appear to be independent from the previously reported beneficial effects on motor function. Furthermore, they are consistent with laboratory data indicating that exenatide has potential beneficial effects on mood in animal models.

"These data should be considered as hypothesis-generating rather than formal evidence to support an effect of exenatide on mood or cognition and should not be used to influence patient treatment decisions. Nevertheless, we will consider carefully how best to capture mood severity in planned future trials of exenatide in PD," commented Professor Foltynie.

"The study of potential benefits of anti-diabetic agents that might

modify disease progression in Parkinson's is a vibrant research area. Not only are we learning about what the effects of the drugs might be in patients, but emerging parallel work in laboratories is also beginning to unravel the underlying mechanisms of action of the drugs in the brain," added Patrik Brundin, MD, Ph.D., Associate Director of Research, Professor and Director of the Center for Neurodegenerative Science, Van Andel Research Institute, Grand Rapids, MI, and Co-Editor-in-Chief of the *Journal of Parkinson's Disease*.

More information: Dilan Athauda et al, What Effects Might Exenatide have on Non-Motor Symptoms in Parkinson's Disease: A Post Hoc Analysis, *Journal of Parkinson's Disease* (2018). DOI: 10.3233/JPD-181329

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