Molecular imaging of impulse control disorders in Parkinson's disease

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Main text

Impulse control disorders (ICDs) affect approximately one-seventh of patients with Parkinson's disease (PD) [1]. Common ICDs include gambling disorder, hypersexuality, compulsive shopping and binge eating. These disorders have been strongly linked to dopamine replacement therapy and, especially gambling disorder (GD), share many clinical features with substance addictions [1, 2]. However, not all patients develop ICDs with dopamine replacement therapy, but the reasons for this and the neurobiological mechanisms underlying ICDs are still relatively poorly understood.

In this issue of European Journal of Nuclear Medicine and Molecular imaging, Dr. Navalpotro-Gomez and colleagues report a study investigating striatal dopamine transporter (DAT) availability and its association with cortical glucose metabolism [3]. The authors investigated 16 PD patients with ICDs (PD-ICDs) and 16 PD patients without ICDs (PD-noICDs) using DAT single-photon emission computed tomography and ^{18}F-FDG positron emission tomography (PET) (only PD-ICDs). They report that PD-ICDs had reduced DAT binding in the ventral striatum, which is further associated with lower glucose metabolism in several cortical regions, including the motor cortex, anterior cingulate cortex, right anterior prefrontal cortex, bilateral entorhinal cortex and subgenual area.

With some exceptions, previous molecular imaging studies in PD-ICDs have focused on the brain dopamine system because of the link with dopaminergic treatment and the central role of dopamine in reward processing and addiction disorders in general [4]. The present findings add to the cumulative and fairly consistent data showing reduced DAT binding in the ventral striatum in the PD-ICDs compared to PD-noICDs [5-10]. There is also evidence of lower dopamine D2 and D3 receptor binding in PD-ICDs, although these findings are not entirely consistent across studies [11-16].

As pointed out by the authors, reduced mesolimbic DAT binding has been reported to predate ICDs, indicating that it may be a predisposing factor for the development of these disorders [10]. However, the interpretation of altered DAT binding is not straightforward because DAT binding may not correlate with dopaminergic neuron counts in PD [17, 18]. Given that striatal dopamine synthesis capacity in PD-ICDs is not reduced when compared to matched PD-noICDs [19], the reduction in DAT binding is likely to reflect changes in DAT expression rather than reduced dopamine function. In fact, reduced DAT in combination with normal dopamine synthesis capacity would result in *increased* synaptic dopamine levels, consistent with findings in individuals with non-PD gambling disorder [20-23]. Accordingly, increased dopamine release has been reported in PD-ICDs in response to a gambling task or reward-related cues [11, 12, 15]. However, it is important to note that there are also some recent data showing a negative correlation between ventral striatal dopamine synthesis capacity and ICD severity, indicating that the relationship between dopamine function and the neurobiological mechanisms of PD-related ICDs is likely to be more complex than simply too much dopamine [24, 25].

Navalpotro-Gomez et al. reported a positive correlation between striatal DAT binding and ^{18}F-FDG uptake in multiple cortical brain regions in the PD-ICD group. As the authors acknowledge, these findings did not survive correction for multiple comparisons and should be interpreted with caution, as use of uncorrected thresholds has been shown to result in inflated type I error rates [26]. The PD-noICD group was not studied with ^{18}F-FDG PET, preventing a direct comparison between the PD-ICDs and PD-noICDs. One previous ^{18}F-FDG PET study investigated regional brain glucose metabolism in PD-ICDs [27]. In this study, the authors measured resting ^{18}F-FDG PET uptake in 18 PD-ICDs and 18 PD-noICDs and found decreased glucose metabolism in the right middle and inferior temporal gyri in PD-ICDs, showing little overlap with the current results by Navalpotro-Gomez et al. and warranting further studies to characterize the full meaning of these findings.

PD-ICDs are a heterogeneous group of patients considering that they all have an underlying neurodegenerative disorder (PD) with different disease stages, symptoms and treatments, and ICDs (type and number of ICDs). This is likely to result in increased variance in the data. Thus, it is not surprising that there is some heterogeneity in the published findings. We are happy to see active research in this field and hope to see further studies verifying and building on these findings to be better able to characterize the neurobiology of PD-related ICDs.

Compliance with Ethical Standards

Conflict of Interest: Dr Majuri has received a speaker honorarium from Boehringer Ingelheim. Dr Joutsa has received a grant from the Orion research foundation, and taken part in sponsored academic meetings/seminars.

Ethical approval: This article does not contain any studies with human participants or animals performed by any of the authors.

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