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Age effect on striatal dopamine transporter binding in *de novo* Parkinson's disease: exploring the different contribution of caudate denervation and age at onset on cognitive deficits

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Introduction: Older age at onset and baseline caudate dopaminergic denervation are either reported risk factors for cognitive impairment in Parkinson's disease (PD). Moreover, they are also strictly interlaced, making it challenging to identify their differential contribution to cognitive outcomes.

Objective: To assess whether early cognitive performances in PD could be linked to an age-related decline in caudate dopamine transporter (DAT) availability and to capture the relative contribution of age at onset and baseline caudate binding to the development of longitudinal cognitive deficits.

Methods: We investigated the relationship between baseline dopaminergic striatal dysfunction (measured by using [123I]-FP-CIT SPECT), age at disease onset and neuropsychological performance of 126 drug-naïve PD patients, using the putaminal and caudate binding values of 77 healthy controls (HC) for a comparative exploration of age-dependent loss of DAT availability in normal aging. In addition, we explored whether age at onset and DAT binding value of caudate could be independent predictors of cognitive changes during a median follow-up of 7 years.

Results: [123I]-FP-CIT-SPECT binding values had significant negative correlation with age in both PD and HC, but in PD aging was associated with a steeper slope for the caudate than putamen (-4.0% and -3.7% per decade in PD vs -3.3% and -4.9% in HC). Older age at onset and lower caudate uptake were associated with either worse global cognitive function and performance in specific neuropsychological tests at baseline and demonstrated to be significant independent predictors of both MCI and dementia at follow-up.

Conclusions: Our findings confirm a different age effect on [123I]-FP-CIT binding in the striatal subregions of *de novo* PD patients. Notably, we found a less age-related attrition of dopamine neurons in the putamen than in the caudate [1] reflecting likely the superimposition of compensatory mechanisms and the increased predisposition of old onset PD patients to develop cognitive disturbances [2-3].

References:

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