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Dopamine Striatal binding and cognition in Parkinson's disease

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INTRODUCTION AND OBJECTIVES

Cognitive impairment and dementia are common during the course of Parkinson's disease (PD). Between 20 and 40% of PD patients presents with mild cognitive impairment (MCI) already in the early stage of the disease. The role of dopamine depletion in caudate and putamen in explaining the cognitive deficits is still not clear.

The aim of the study was to evaluate the correlation between striatal and cortical [1231]-FP-CIT and cognitive impairment in PD patients

METHODS

PD patients without dementia underwent dopamine transporter (DAT) single photon emission computed tomography (SPECT) and 123I-FP-CIT (DaTscan®, GE Healthcare). The striatal tracer uptake was evaluated using BRASS software (Hermes, Sweden). Whole-brain voxelwise analysis was performed using SPM12. PD-NC versus PD-MCI for both approaches (BRASS and whole-brain SPM) was performed using covariance analysis adjusted for age, sex, disease duration and presence of impulse control disorders. Moreover, each patient underwent an extensive neurological (including UPDRS-III) and neuropsychological evaluation allowing the level II definition of mild cognitive impairment (PD-MCI). Logistic regression analyses adjusted for age, gender and disease duration were performed in order to identify differences in binding between PD-NC and PD-MCI patients. Multiple regression analyses corrected for the same factors to test the correlation between performances in specific neuropsychological tests and striatal dopaminergic binding.



Figure 1 . Normal (A) and abnormal /(B) DATScan

RESULTS (1)

Sixty-seven PD patients without dementia (34 with mild cognitive impairment and 33 with normal cognition, PD-NC) entered the study (mean age 67.6 + 10.7 years, mean disease duration 5.1 + 4.2 years, mean UPDRS-III 14.8 + 7.7 points).

No differences in striatal binidng between PD-NC and PD-MCI were detected after adjusting for age, gender and disease duration.



RESULTS (2)

Right caudate binding significantly correlated with MMSE (p=0.04) and TMA scores (p=0.02). Right putamen binding positively correlated with verbal fluency (p=0.04).





SPM-analyses: Direct comparison of PD-MCI vs PD-NC showing the reduced DAT binding in left precuneus in PD-MCI (125 voxels, adjusted p=0.001, uncorrected) Montreal Neurological Institute of standardized space are shown below of each slices

RESULTS (3)

SPM-VBM analyses showed a significant reduction in binding of [123I]-FP-CIT in the left precuneus in PD-MCI vs PD with normal cognition

CONCLUSIONS

Our findings suggest that nigrostriatal and cortical dopaminergic deficits might contribute to reduction in global cognition and attentional/executive performances in PD patient's without dementia.

These findings need further validation in larger cohorts including patients with dementia and longitudinal evaluation.