Detection of preclinical Parkinson's disease: the olfactory approach

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Objectives: In Parkinsons disease (PD), a substantial loss of dopaminergic neurons occurs prior to the appearance of clinical parkinsonism. Identifying patients in this preclinical period is of major importance in the development of effective neuroprotective treatment strategies. Olfactory dysfunction is an early and common finding in PD patients that appears to precede the development of (clinical) motor signs. The aim of our ongoing longitudinal study is to determine whether otherwise unexplained hyposmia is associated with an increased risk of developing PD.
Methods: A cohort of 361 asymptomatic relatives of subjects with PD, in whom other causes of olfactory dysfunction were excluded, was recruited. Baseline performance on a combination of olfactory processing tasks (detection, identification and discrimination) was used to select groups of hyposmic (10% worst performing) and normosmic (10% best performing) individuals for clinical follow-up and sequential [123I]Î²-CIT SPECT scanning to assess nigrostriatal dopaminergic function at baseline and two years from baseline. A validated mail questionnaire, sensitive to the presence of parkinsonism, was used in the follow-up of the remaining 283 relatives.
Results: Two years from baseline, 10% of the individuals with idiopathic hyposmia, who also had strongly reduced [123I]Î²-CIT binding at baseline, had developed clinical PD as opposed to none of the other relatives in the cohort. In the remaining non-parkinsonian hyposmic relatives, the average rate of decline in dopamine transporter binding was significantly higher than in the normosmic relatives.
Conclusion: These results indicate that idiopathic olfactory dysfunction in first-degree relatives of PD patients is associated with an increased risk of developing PD of at least 10%. Considering the accelerated rate of loss of [123I]Î²-CIT binding in the group of asymptomatic hyposmic relatives, extended follow-up of the cohort may reveal this risk to be even higher.
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