Olfactory Dysfunction in Parkinson’s Disease

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Olfactory dysfunction is well-recognized in early stage Parkinson’s disease (PD) patients, although the underlying mechanisms have not been investigated in either animal PD models or PD patients [1-3]. It has been proposed that in early stages of neurotoxin-generated animal PD models, the decrease in olfactory function precedes the appearance of motor symptoms. In fact, intranasal administration of the dopaminergic toxin 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine generates an early etiology of PD (olfactory and memory deficits, reduced dopamine concentration in many brain areas) without motor symptoms [4]. It should be noted that loss of dopamine neurons also precedes the appearance of motor symptoms. Therefore, olfactory symptoms might represent a more precise temporal correlation to the loss of dopaminergic signaling due to vulnerability of this neuronal pathway [5] (Fig. 1). However, anatomical changes have yet to be correlated to behavioral symptoms in PD patients. Now, a study by Scherfler et al. has employed neuroimaging techniques (diffusion tensor imaging, transcranial sonography and positron emission tomography) to examine the microstructural and functional changes of the dopaminergic system in PD patients, in combination with behavioral tests in these individuals [6]. Their findings demonstrate a correlation between olfactory tract microstructural degradation and progression of putaminal dopaminergic dysfunction.

![Fig. (1).](image)

During Parkinson’s disease progression, the dopamine neuronal loss correlated to olfactory function loss, which precedes the appearance of clear motor symptoms.

Scherfler et al. recruited 16 PD patients at different clinical stages, with confirmed decreased olfactory function (discrimination, detection threshold and identification). Dopaminergic terminal functions in caudate and putamen were examined via 6-[18F]levodopa positron emission tomography. The PD patients demonstrated decreased dopa uptake in both regions, while changes in the putamen also correlated to the increase in diffusivity of olfactory tract (an index of increased extracellular fluids) as well as a decrease in odor identification ability [6], suggesting that the odor function loss progresses alongside the degeneration of dopaminergic connections.

Previous studies suggested that some aspects of olfactory function (e.g. detection and identification) are not progressive across different stages of PD [7, 8], mainly based on motor symptoms. The study by Scherfler et al. proves that putaminal dopamine transporter binding is more accurate and predictive for olfactory function decrease in PD patients. Since the olfaction decrease precedes motor symptoms, it is possible that in many PD patients olfaction is already severely decreased at the time of diagnosis. It will therefore be interesting to examine if the putaminal dopaminergic terminal functional decrease can act as a prognosis marker for PD development in aged patients.

In addition, diffusion tensor imaging-detected microstructural degeneration can be used to document early degeneration of the olfactory system, including the bulb and tract, even before detectable olfaction loss. This might facilitate early diagnosis of PD and other neurodegenerative diseases across the vulnerable population.

At present, neurological evaluation of PD stages (Hoehn-Yahr (H-Y) staging system) mainly relies on motor symptoms, and much less on mental, behavioral and other non-motor symptoms (such as olfaction loss). The combined assessment of symptoms at all stages is, however, difficult for each neurologist. The present study opens the possibility to evaluate PD...
progression from other aspects by performing functional and ultrastructural neuroimaging on the patient. It is expected that in the future neuroimaging, neurophysiological and neurological assessments will offer a combined staging system for all PD patients.

REFERENCES


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