What comes first in Parkinson's disease symptomatology? Olfactory dysfunction as an early clinical sign *Hummel T* 

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Olfactory loss is common in Parkinson's disease (PD). While a decreased sniff volume seems to add to this, electrophysiological recordings in response to passive stimulation established presence of olfactory impairment. This deficit is so reliable that it can be used as PD marker. In other words: If a patient with normal olfactory function presents with PD symptoms the diagnosis should be re-investigated. The olfactory deficit does not seem to be related to the degeneration of dopaminergic neurons. It appears to be non-responsive to dopaminergic drugs. Except for differences in olfactory function between patients with moderate and fulminant PD this deficit seems to be unrelated to stage/duration, when odor identification and odor thresholds are investigated. However, more recent studies using odor discrimination, and studies based on olfactory eventrelated potentials indicate that dysfunction is related to the progression of PD symptoms. The poor correlation between olfactory function and degree of PD seems to be based on the fact that olfactory dysfunction is already in an advanced stage when PD is first diagnosed. This indicates that olfactory loss starts before development of motor symptoms which typically leads to the clinical diagnosis of PD. Thus, the disease may already have started some 4-6 years before the diagnosis of PD is made. Recent data indicate that olfactory dysfunction may be among markers to indicate whether relatives of PD patients are at risk to develop PD. In addition, own studies indicate that transcranial sonography seems to be helpful in identifying patients potentially at risk to develop PD. While longitudinal follow-up studies are needed to estimate the reliability of these measures in terms of detection of people at risk to develop PD, presently available data seem to indicate that olfactory dysfunction is an early clinical sign which actually precedes the clinical signs related to the motor system.

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