



## Smell function in patients with Parkinson's disease can be expected to deteriorate over time

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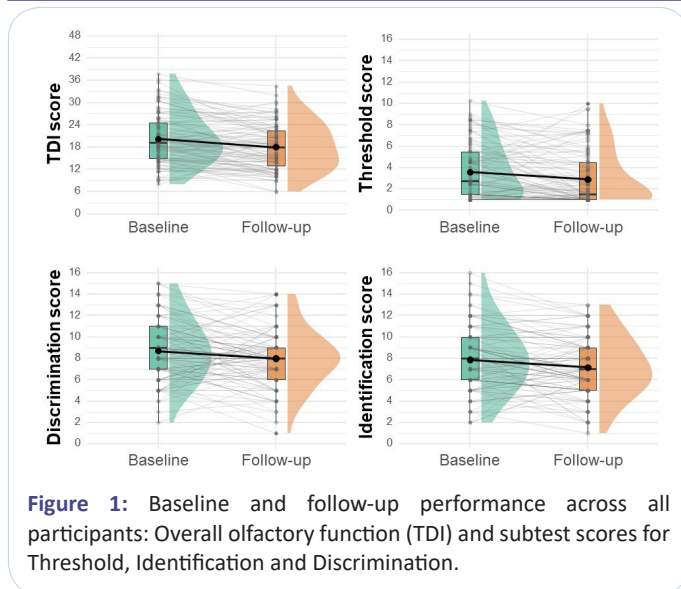
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### Short communication

Olfactory dysfunction is one of the leading prodromal symptoms of Parkinson's Disease (PD) [1], and has been investigated extensively in the past. However, hyposmia is generally considered a binary trait in manifest PD and less attention has been paid to the quantitative evolution of hyposmia after the clinical diagnosis of PD. It remains unclear whether the course of the disease will result in absent or undirected changes, as previously assumed. The few studies conducted to date have focused on odor identification or have only included a small number of cases. The aim of this study is to fill these gaps by tracking changes not only in odor identification, but also in odor threshold and discrimination. By longitudinally assessing patients after PD diagnosis based on standardized clinical criteria, we investigated changes in olfactory function over time.

One hundred and five PD patients (67 men, 38 women; mean  $\pm$  SD age: 66.4 $\pm$ 9.25 yrs; mean  $\pm$  SD disease duration; 7.32 $\pm$ 6.05 yrs; median H&Y stage: 2.2, median UPDRS score: 18.2) participated in the study. Forty-eight patients suffered from akinetic-rigid subtype, 24 presented with tremor-dominant type and 33 patients with a mixed phenotype. Olfactory function was assessed using the "Sniff in` Sticks" test kit [2] which involves tests for odor Threshold (T), odor discrimination (D), and odor identification (I) at the time of their first presentation to the Movement Disorders Clinic and after 4.0 $\pm$ 3.21 yrs (mean  $\pm$  SD).

Olfactory function expressed as comprehensive TDI score was significantly different between baseline and follow-up testing ( $t=4.54$ ,  $p<0.001$ ). With regard to individual subtests of olfactory function, odor threshold ( $t=3.04$ ,  $p=0.003$ ) as well as odor discrimination ( $t=2.48$ ,  $p=0.015$ ) and odor identification ( $t=2.88$ ,  $p=0.005$ ) decreased significantly compared to the baseline examination (Figure 1).



A tertile analysis was performed to assess the progression of the different baseline olfactory abilities (mean±SD: TDI:20.0±6.69; norm osmic: n=13, hyposmia: n=58, anosmia: n=34). Participants in the highest tertile demonstrated a significant decline in both TDI and all three subtests ( $p < 0.001$ ). No significant change in the TDI score was observed in the lowest tertile ( $p = 0.916$ ). The middle tertile showed a statistically significant change in overall TDI score ( $p = 0.018$ ), but component-specific analyses revealed no significant differences in threshold, discrimination, or identification within this tertile ( $p > 0.05$  for all).

No significant correlations emerged between the TDI score change, age ( $r = -0.03$ ,  $p = 0.73$ ), duration of disease ( $r = -0.06$ ,  $p = 0.55$ ), the H&Y score ( $r = -0.05$ ,  $p = 0.63$ ), and the UPDRS ( $r = 0.07$ ,  $p = 0.56$ ). There was no difference between the individual PD subtypes in terms of further deterioration of the sense of smell ( $p = 0.81$ ).

Our results indicate that comprehensive olfactory function and individual olfactory subscores decrease significantly in PD as the disease progresses. The extent of decline does not appear to depend on PD subtype, age, duration of illness, or motor impairment. The most pronounced loss of smell was observed in patients who initially have a relatively intact sense of smell, consistent with a floor effect for the tertile with most impairment at baseline. Our results complement previous results [3-5] by showing that in PD a progressive loss can be observed in overall olfactory performance and also in all of its components, olfactory threshold, discrimination, and identification. Our results clearly demonstrate that most PD patients (including those who are initially normosmic and mildly hyposmic) can be expected to experience a significant olfactory deterioration over the course of the disease. Because olfactory function is unaffected by dopaminergic medication, quantitative measurements of olfaction could potentially report the effects of disease-modifying therapies in PD.

## Declarations

**Ethics approval and consent to participate:** Before participation, written informed consent was given by all participants. The study was conducted according to the ethical standards laid down in the 1964 Declaration of Helsinki and approved by the local ethics committee of the Technical University of Dresden.

**Competing interests:** The authors have no relevant financial or nonfinancial interests to disclose.

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**Authors' contributions:** AV analyzed and interpreted the data, and was a major contributor in writing the manuscript. AH and TH conceptualized and designed the study. AH, TH, and BF acquired, analyzed and interpreted the study data. All authors read and approved the final manuscript.

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