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# Association between olfactory loss and cognitive deficits in Parkinson's disease

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ABSTRACT

*Objective:* The aim of this study was to compare the cognitive deficits and olfaction in PD patients.
*Patients and Methods:* In all, 42 PD patients and 38 controls were selected. All the individuals in both groups underwent cognitive assessment with the SCOPA-Cog neuropsychological battery and Mini-Mental State Examination (MMSE) and olfactory assessment with the Sniffin' Sticks Screening 12 Test. Parkinson's disease dementia (PDD) was diagnosed using the International Parkinson and Movement Disorder Society (MDS) criteria.
*Results:* The prevalence of olfactory dysfunction in PD patients was 95.24% (40/42). There was no statistically significant difference in olfaction when compared to patients with PDD and PD without cognitive deficits (5.12 ± 3.25 vs. 6.71 ± 2.63, p = 0.115). Attention [r = 0.35, 95% CI = (0.05–0.59), $p$ = 0.01] was the only cognitive domain correlated with olfactory loss in PD patients. There was a higher correlation among the scores of cognitive and olfactory assessments in controls, r = 0.40 (95% CI = [0.09–0.64], $p$ = 0.007), with MMSE.
*Conclusion:* The olfactory deficits prevalence in PD patients was significantly high. There may be a correlation between frontal lobe dysfunction and olfactory deficit.

## 1. Introduction

Parkinson's disease(PD) has long been considered a purely motor disease. However, in recent decades various sensory abnormalities have been identified as a result of more effective diagnosis and improved treatment strategies [1]. In the case of smell, which appears to be the sense that is involved the earliest, the dysfunction prevalence can reach 90% [2].

The new functional and neuropathological studies, showing the involvement of extranigral pathways changed drastically the initital description of DP pathology [3]. Lewy bodies are found throughout the nervous system and affect even the peripheral nervous system; a search began for nonmotor clinical findings and pathophysiological responses in PD, particularly dysautonomias, olfactory dysfunctions and sleep disorders [4,5]. Hyposmia in PD, for example, does not fluctuate during ON and OFF periods of levodopa treatment [6], indicating that this dysfunction may not be entirely related to dopaminergic dysfunction or the degenerative process responsible for motor signs. There is evidence that the cholinergic pathways degeneration in the archicortex is the main factor determining impaired odor identification [7].

The first olfactory deficits description in PD was published almost 40 years ago [8], and five years later this sign was described as a "motor signs precursor" [9]. Ross et al. [10], following up 2263 seniors, showed in post mortem analyses that individuals with olfactory deficits were at greater risk of developing symptomatic PD and Lewy bodies in the CNS. In the' 80 s, studies showed that odor detection threshold, discrimination and identification, three of the characteristics used to assess olfaction, were abnormal in PD [11,12].

Baba et al. [13] found possible associations between olfactory dysfunction and the developing dementia risk in PD. They also showed that more severe hyposmia can be a dementia predictor [13]. This finding has been confirmed by other more recent studies [14–16], which indicate a higher 3.1 risk of patients with hyposmia develop cognitive deficits in 10 years [16]. In addition, olfactory deficits can act as cortical atrophy markers during the initial and moderate stages of PD, indicating a pathological process that appears to be present in parallel

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with the neuronal death that affects the dopaminergic nigrostriatal pathways [17].

The aim of this study was to compare cognitive deficits and olfaction in PD patients.

## 2. Patient and methods

Forty-two patients who had been seen at the Campos Gerais Regional University Hospital (HURCG) Neurology Service and INOVARE Serviços de Saúde Ltda. and agreed to take part in the study were selected in accordance with the Parkinson's Disease Society Brain Bank diagnostic criteria [18]. All the participants signed a voluntary informed-consent form. The exclusion criteria, which were intended to exclude patients whose signs and symptoms made it impossible to perform a cognitive assessment or apply the proposed tests, were as follows: (a) advanced-stage PD with severe motor or sensory impairment; (b) severe psychotic symptoms and (c) another dementia not associated with PD (d) patients who had cognitive changes started at least one year before motor symptoms (possible dementia with Lewy bodies) [19]. The State University of Ponta Grossa (UEPG) Research Ethics Committee (COEP) approved the study (reference no. 631.285 F A).

All the patients were assessed during the ON phase of levodopa therapy, preferably two hours after the medication had been administered. A team trained in movement disorders carried out clinical assessment. A semi-structured questionnaire was applied to collect epidemiologic data and data about disease progression and previous and current treatment. The Hoehn and Yahr Scale [20] and Unified Parkinson's Disease Rating Scale III (UPDRS-III) [21] were used to classify patients according to their motor symptoms.

After the diagnosis confirmation, the patients' cognition was assessed. All the patients were assessed during the best period of the ON phase. Patients using acetylcholinesterase inhibitors were assessed while the medication was still exerting an effect. Cognition was assessed with the Scales for Outcomes in Parkinson's Disease-Cognition (SCOPA-Cog) [22] instrument; a score of more than 22 out of a possible maximum of 43 was considered to indicate an absent dementia. The Mini-Mental State Examination (MMSE) [23] was also used, and a score of more than 26 out of a possible maximum of 30 was considered to indicate an absence of dementia. Parkinson's disease dementia (PDD) was diagnosed using the International Parkinson and Movement Disorder Society (MDS) criteria [19].

For the control group, 38 individuals without a PD diagnosis were selected. Controls were paired with the PD patients by age, years of schooling and gender.

Olfaction was assessed with the Sniffin' Sticks Screening 12 Test [24]. In this test, patients are given 12 sticks that release an odor and asked to name the smell of each stick by choosing one of four options. After the individual had smelt all the sticks, the level of olfaction was classified based on the number of correct answers. The following classification was used for the results of the analysis: 0–5 = anosmia; 6–10 = hyposmia and 11–12 = normal olfaction (possible scores: 0–12).

The normality assumption was confirmed with the Shapiro-Wilk test for all the groups. Statistical differences among the means of the groups were determined using the one-tailed Student's *t*-test. Correlations were measured using the Pearson correlation coefficients. Results are given as mean ± standard deviation or as an odds ratio (OR) and a 95 % confidence interval (CI) [OR (95 %CI)]. Differences were considered statistically significant when $p < 0.05$. All the statistical analysis was performed with Statistic for Windows (ver. 99) and Microsoft Office Excel 2010.

## 3. Results

In all, 42 PD patients and 38 controls were assessed for cognition and olfaction. PD patients achieved lower scores in the cognitive assessment with SCOPA-Cog and MMSE and the olfactory assessment with the Sniffin' Sticks Screening 12 Test than the control group (Table 1).

**Table 1**
Comparison of the two groups by age, gender, years of schooling and the results of cognitive tests.

| | Parkinson's disease | Control group | *p* |
|---|---|---|---|
| N | 42 (100%) | 38 (100%) | |
| Gender | | | 0.4982 |
| Male | 26 (61.90%) | 20 (52.63%) | |
| Female | 16 (38.10%) | 18 (47.36%) | |
| Age | 70.67 ± 10.67 | 69.21 ± 6.46 | 0.4682 |
| Years of schooling | 7.14 ± 5.84 | 7.16 ± 4.67 | 0.9886 |
| Smoking | 26 (61.90%) | 24 (63.16%) | 1 |
| SCOPA-Cog | 13.26 ± 7.22 | 19.79 ± 6.56 | < 0.0001 |
| MMSE | 23.05 ± 3.75 | 27.37 ± 2.89 | < 0.0001 |
| Sniffin' Sticks Test | 5.26 ± 3.25 | 8.61 ± 2.58 | < 0.0001 |

The olfactory dysfunction prevalence in PD patients was 95.24% (40/42). Of the 42 patients with PD, 34 (81%) were diagnosed with dementia (PDD) on the MDS criteria for dementia. PDD patients had fewer years of schooling (6.44 ± 4.40 vs. 10.13 ± 5.46, p = 0.04831) than PD patients without.

There was no correlation between Sniffin 'Sticks Screening 12 Test and patient age (r = −0.12, p = 0.445), both in patients with PPD (r = −0.127, p = 0.474) and without PPD (r = −0.138, p = 0.781). Among the controls, there was a discrete correlation between older age and olfactory worsening (r = −0.364, p = 0.02). Regarding the time of disease, there was no correlation with olfactory scores in patients with PD (r = −0.279, p = 0.073), however in the small subgroup without PPD there was a correlation of better olfactory scores and more years of disease (r = 0.97, p < 0.0001). There was a slight correlation between female gender and olfactory changes (r= −0.378, p = 0.013) in PD patients, which was not significant in the group without PPD (r = 0.25, p = 0.58) and was moderate in the PPD group (r= −0.482, p = 0.003). This correlation with the female gender was not showed among the controls (r = −0.105, p = 0.51).

There was a higher correlation among the scores of cognitive and olfactory (Sniffin' Sticks Screening 12 Test) assessments in controls, r = 0.40 (95% CI = [0.09 – 0.64], *p* = 0.007) with MMSE and r = 0.46 (95% CI = [0.16 – 0.68], *p* = 0.001) with SCOPA-Cog. The same was not observed in patients with PD, r = 0.26 (95% CI = [−0.04–0.52], p = 0.05) with MMSE and r = 0.20 (95% CI = [−0.11–0.47], *p* = 0.20) with SCOPA-Cog.

The correlation among the scores in the different areas of the SCOPA-Cog neuropsychological battery and scores in the olfactory test for control group were positive for almost all, the exception was executive functions. For patients with PD, there was only a positive correlation in the areas of the SCOPA-Cog that assessed the attention (Table 2).

## 4. Discussion

The olfactory dysfunction prevalence in PD patients in this study was 95.24%, a significantly high prevalence that agrees with values reported by Doty et al. [2] (90%) and Boesveldt et al. [25] (73%). Olfactory ability was lower in the PD patients than in the controls. There also was a large percentage of individuals with dementia (80.95%) among the PD patients. These individuals had significantly fewer years of schooling than patients without dementia, a finding previously reported in individuals with a clinical picture of dementia, such as Alzheimer's and PD patients [26]. The high proportion of patients with PDD compared with other studies [12,27] can be partly explained by the fact that the study was carried out in a reference center for PD treatment, where patients had longer disease duration (9.05 ± 8.94 years on average) and more complications.