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Olfactory dysfunction in cerebellar ataxia and multiple system atrophy

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Abstract *Background* Olfactory dysfunction has been reported in Parkinson's (PD) and Alzheimer's disease (AD). *Objective* We studied olfactory function in eight patients with multiple system atrophy of cerebellar type (MSA-C), eleven patients with sporadic cerebellar ataxia of unknown etiology and thirteen controls matched for age and gender. Subjects received tests for n-butanol odor thresholds, odor identification, and odor discrimination. *Results* Olfactory thresholds were abnormally high in 16 % of the patients. Odor discrimination and odor identification were impaired in 44 % and 74 % of the patients, respectively. There was no significant difference in olfactory function between patients with sporadic ataxia of unknown etiology and MSA-C patients. *Conclusions* The present data suggest that olfactory dysfunction is common to various neurodegenerative disorders and not specifically restricted to PD or AD. Cerebellar dysfunction affected suprathreshold olfactory function more severely than odor thresholds. Thus cerebellar lesions may affect the processing of odor-related information to a higher degree than the transport of odorants to the receptor through sniffing.

Key words sporadic cerebellar ataxia · multiple system atrophy · olfactory dysfunction

Introduction

Olfactory dysfunction has been reported in different neurodegenerative disorders including Parkinson's disease (PD), Alzheimer's dementia (AD) and Guamanian amyotrophic lateral sclerosis (ALS) [2]. In addition, olfactory activation is a consistent finding in studies using functional magnetic resonance imaging [11, 14]. Recent work by Sobel and colleagues suggests that the cerebellum plays a role in the processing of olfactory information and in the coordination of sniffing [12]. The aim of the present study was to evaluate the frequency of olfactory dysfunction in neurodegenerative disorders of the cerebellum. To this end, olfactory function was assessed in patients with multiple system atrophy of cerebellar type (MSA-C) and patients with sporadic ataxia of unknown etiology.

Methods

We studied 8 patients who fulfilled the diagnostic criteria for probable MSA (4 men, 4 women; mean age 59.8 ± 9.1 years, mean duration of disease 4.5 ± 1.2 years) with predominant cerebellar symptoms and 11 patients who were diagnosed with late onset sporadic ataxia of unknown etiology (6 men, 5 women; mean age 58.7 ± 13.2 years, mean duration of disease 6.9 ± 5.3 years [3]. Thirteen volunteers without a history of any neurological disease served as controls (8 men, 5 women; mean age 53.9 ± 8.8 years); patients and controls were matched for age ($t = 1.40$, $p = 0.17$) and sex ($\chi^2 = 0.249$, $p = 0.62$). All participants underwent thorough neurological examinations at the Department of Neurology at the University of Bonn by one of us (MA). Symptomatic and genetic causes of ataxia were carefully ex-

JON 1248

cluded in all patients [1]. All patients had cerebellar atrophy on routine MRI. Severity of cerebellar ataxia was rated on a scale ranging from zero (absent) to five (most severe) [6].

Olfactory function was investigated using the validated "Sniffin' Sticks" test kit which is comprised of 3 tests of olfactory function, namely tests for n-butanol odor threshold (testing by means of a single staircase), odor discrimination (16 pairs of odorants, triple forced choice), and odor identification (16 common odorants, forced choice from 4 verbal items per test odorant) [5, 7]. Olfactory function of each patient and control was compared with age-related normative data which had been obtained in a study involving over 1000 subjects [7]. All patients gave informed consent to participate in the study.

Statistical analysis was performed using SPSS 10.0 (SPSS Inc., Chicago, IL, USA). Frequencies were analysed using the χ^2 test. Parametric group comparisons were made using analyses of variance (MANOVA, repeated measures design; adjustment of degrees of freedom according to Greenhouse-Geisser); post-hoc testing was based on t-tests. The alpha-level was set at 0.05.

Results

Olfactory function was impaired in patients with cerebellar dysfunction (Fig. 1). While olfactory thresholds were increased in 3 out of 19 patients (16 %) and in 1 out of 13 controls (8 %; $\chi^2 = 0.46$, $p = 0.50$), odor discrimination was impaired in 8 out of 18 patients (44 %) and in 3 out of 13 controls (23 %; $\chi^2 = 3.27$, $p = 0.071$). Odor identification was impaired in 14 out of 19 patients (74 %) and in 5 out of 13 controls (38 %; $\chi^2 = 3.97$, $p = 0.046$). Accordingly, mean scores for the 3 different tests were consistently lower in patients than in controls. This is reflected in the results from the group comparison including all 3 tests (factor "group": $F[1,29] = 3.80$, $p = 0.061$). Post-hoc testing revealed that this was significant for odor discrimination ($t = 2.32$, $p = 0.03$); results for odor identification closely missed the criterion for significance ($t = 1.94$, $p = 0.06$). No difference was seen for odor thresholds ($t = 1.32$, $p = 0.20$).

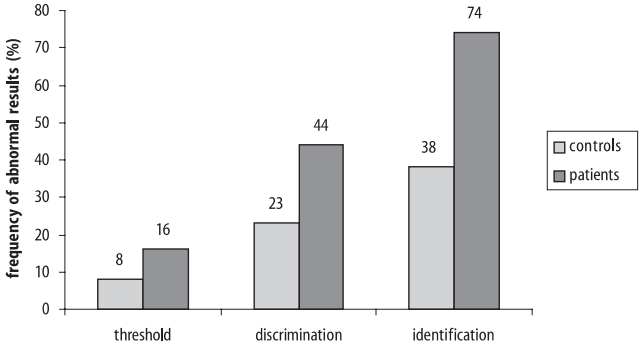

Fig. 1 Frequency of abnormal results for controls (n = 13) and patients with cerebellar ataxia (n = 19) for odor thresholds, odor discrimination, and odor identification

There was no significant difference in olfactory function between patients with sporadic ataxia of unknown etiology and MSA-C patients ($t < 0.71$, $p > 0.48$). Finally, there was no significant correlation between olfactory function and duration or severity of cerebellar disease ($p > 0.05$).

Discussion

The present data indicate that olfactory dysfunction is present in patients with cerebellar dysfunction. Work by Sobel and colleagues [12] indicates that the latero-posterior cerebellum is activated through odorants in the absence of any motor activities including sniffing. Sniffing-induced activation was found primarily in centro-anterior regions of the cerebellum. It was hypothesized that the cerebellum is important in terms of a feedback mechanism which might monitor the sensory input, i. e. odor concentration and modulates the motor output, i. e. sniff volume. While decreased abilities to sniff have been shown to contribute to the olfactory deficit in PD, it is interesting to note that cerebellar lesions affected suprathreshold olfactory tasks more severely than odor thresholds [13]. Given that threshold tasks reflect peripheral olfactory function rather than central-nervous processing of odor information (odor identification and discrimination), it may be hypothesized, that cerebellar lesions affect the processing of odor-related information to a higher degree than the transport of odorants to the receptor [4]. This cerebellar function in acquisition and processing of olfactory information may also play a role in other neurodegenerative diseases which affect the cerebellum, e. g. multiple sclerosis or Alzheimer's disease [8].

An argument against the role of cerebellar lesions in the perception of smells may be that, by definition, MSA is a disorder affecting multiple areas of the CNS. Indeed glial cytoplasmic inclusions are found throughout the brain and MSA-C patients may develop parkinsonian signs later in the disease process [10]. However, patients with sporadic ataxia of unknown etiology displayed an almost pure cerebellar syndrome and, albeit not significantly, tended to perform worse than MSA patients in odor discrimination and identification. Furthermore, patients with probable MSA of parkinsonian type were recently shown to have similar, although significantly less pronounced olfactory deficits than PD patients [9].

In conclusion, the present findings suggest that cerebellar dysfunction affects the processing of suprathreshold olfactory information.

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