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Olfactory dysfunction in behavioral variant frontotemporal dementia

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ABSTRACT

Objective: Several neurodegenerative disorders show olfactory dysfunction. In patients with frontotemporal dementia (FTD), olfactory impairment is probably due to the involvement of the temporal and orbitofrontal lobes. We hypothesized that due to the disrupted areas in FTD, there would be an impairment in smell identification, differentiation and association. Moreover, we hypothesized that there would be a correlation between the severity of FTD and the severity of odor dysfunction.
Methods: In the current study, we compared odor identification, discrimination and association of nine patients with behavioral variant FTD with eleven healthy controls using the Brief Smell Identification Test and the Odor Perception and Semantics Battery.
Results: The results showed significant differences in the odor association test, but not in the identification or discrimination test. There was no correlation between disease severity and the performance in the odor tests.
Conclusion: We showed impairment of odor association that is most likely due to disruption of specific associative areas involved in olfactory processing. Specifically, we propose that the impairment may well be due to disrupted areas in the temporal lobe and amygdala.

1. Introduction

Though olfactory function is a primal sense in animals and humans, it seems to be an underestimated topic in medical practice. Specifically, the olfactory functions are rarely investigated and patients are often unaware of their olfactory problems [1]. Olfactory dysfunction significantly influences quality of life, nutrition, the enjoyment of food, as well as everyday safety [2]. In general, three aspects of olfaction are defined: olfactory threshold, identification and discrimination. The threshold as a measure of the lowest concentration of odorant that will activate the olfactory receptor cells, is likely to be influenced by the most peripheral part of the olfactory system. Identification and discrimination are respectively the ability to identify odorants and the ability to differentiate odorants. These two aspects are partly cognitive tasks influenced by the central olfactory system.

The anatomy of the olfactory system is complex and mostly localized in the temporal regions of the brain. The bipolar smell receptors consist of a small area of neuroepithelial cells forming the olfactory mucosa. These receptors form the nervi olfactorii that cross the cribiform plate of the ethmoid bone into the ipsilateral olfactory bulb [3].

Caudal to the olfactory bulbs groups of cells are located that form the anterior olfactory nucleus. From the anterior olfactory nucleus fibers of the lateral striae run caudally to the medial and cortical nuclei of the amygdaloid complex and the prepiriform area. The latter represents the primary olfactory cortex, which in humans occupies a restricted area on the anterior end of the parahippocampal gyrus and uncus, and is important in identifying and differentiating odors. Thus olfactory impulses reach the cerebral cortex without a relay through the thalamus. From the prepiriform cortex, fibers project both to the neighboring entorhinal cortex in the medial temporal lobe, including fibers to the hippocampus for odor memory, and to the medial dorsal nucleus of the thalamus. The thalamus is connected with the orbitofrontal cortex, which is probably important for the conscious perception of odor and odor differences. The amygdala, important in the affective components of odor as well as odor memory, connects with the hypothalamus, responsible for autonomic reactions like increased salivation in response to smelling tasty food [4].

Several studies have described patterns of olfactory dysfunction in neurodegenerative disorders such as Alzheimer disease (AD) and Parkinson disease (PD) [5–8]. Olfactory dysfunction has been shown in frontotemporal dementia (FTD) as well [9,10]. FTD is a

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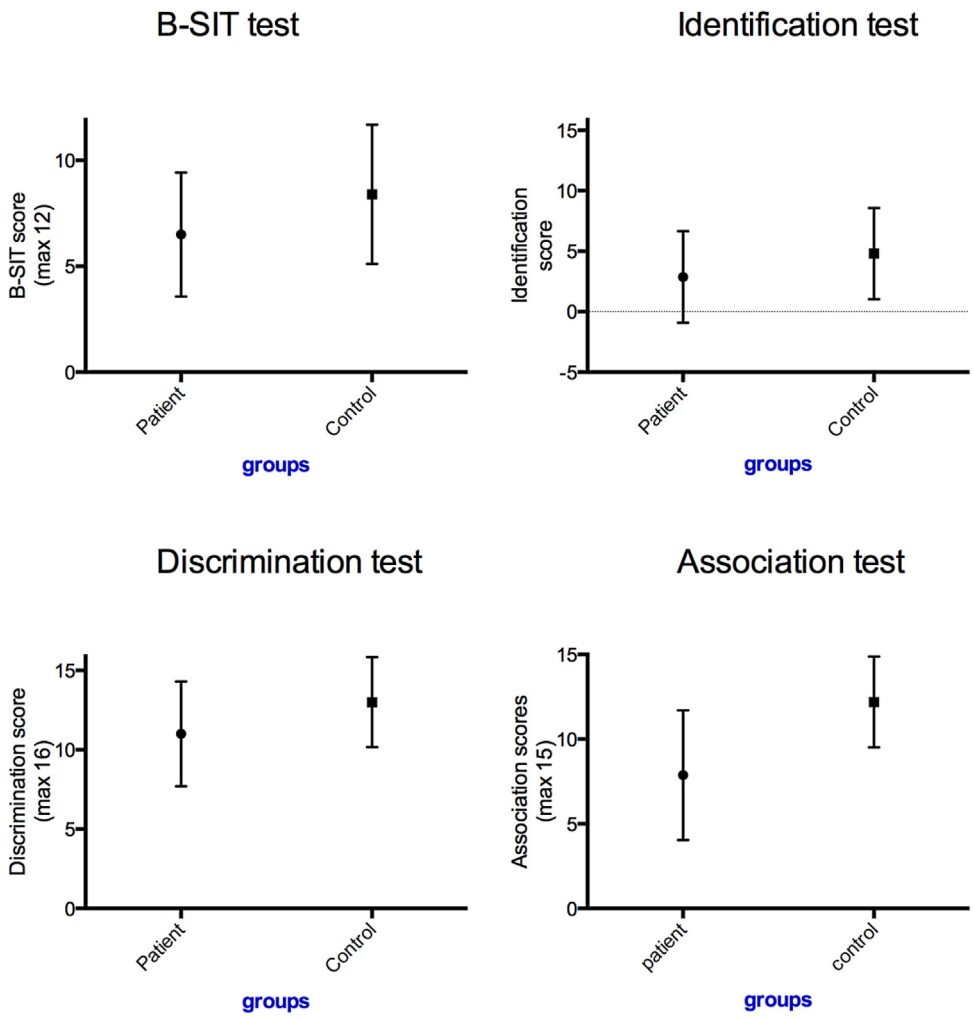

Fig. 1. The performance of the groups on the four odor test (mean and standard deviation). The B-SIT, the identification test and the discrimination test showed no statistical difference between the two groups. The odor association test showed a difference between the groups ($p = .014$).

neuropathologically and clinically heterogeneous disorder characterized by bilateral frontal and anterior temporal lobe degeneration [11]. The behavioral variant (bv-FTD) is characterized by striking personality changes such as apathy, breakdown in social conduct and abulia. Patients develop social disinhibition and impulsivity and most patients seem unaware of their deficits [11,12]. Luzzi et al [9] describe a small study in which they compared the olfactory functioning in patients with AD, semantic dementia variant of FTD, bv-FTD and corticobasal degeneration. They found severely impaired odor identification in patients with semantic dementia, which is most likely due to their loss of semantic knowledge, whereas in patients with the bv-FTD the deficits were mild and could not be related to semantic deficits [9]. Impaired odor identification was found by McLaughlin and Westervelt as well, the olfactory deficits being similar in magnitude to those in AD [10]. Olfactory dysfunction was correlated with volume loss of the right midfrontal gyrus in bv-FTD patients [13].

Given the involvement of the temporal and orbitofrontal lobes in odor processing, we hypothesized that due to the disrupted areas in bv-FTD, there would be impairment in smell identification, differentiation and association. Also, we hypothesized that there would be a correlation between the severity of bv-FTD and the severity of odor dysfunction. Therefore, in the present study we assessed olfactory function using four olfactory tests in nine patients with bv-FTD and in eleven healthy controls. Neuropsychological tests were performed to study the correlation between olfactory function and disease severity. So far no study assessed olfaction in bv-FTD using such a comprehensive procedure involving odor identification, discrimination and association.

2. Material and methods

2.1. Participants

The patient cohort comprised nine bv-FTD patients (eight males and one female) from our own hospital FTD database. Diagnoses were made based on the criteria by Neary et al. [14]. Two neurologists reviewed patient records independently before patients were selected for the study. Patients were included if both neurologists marked the patient as bv-FTD. Exclusion criteria were either significant central neurological history or surgery in the olfactory area. Patient's smoking habits and usage of nasal spray were recorded for future reference but were no reason for exclusion.

Controls were healthy volunteers of the same age range as our patient population. Exclusion criteria included a significant central neurological history, psychiatric disorder, nasal surgery or usage of medication that could affect cognitive function. Smoking and usage of nasal spray were recorded for future reference, but were no reason for exclusion.

All participants gave informed consent to the study. The study was approved by the local Ethics Committee.