Odour Recognition Memory and Odour Identification in Normal Elderly and Alzheimer's Disease Patients

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Abstract

Background: Olfactory dysfunctions have been frequently observed in ageing, in various neurodegenerative conditions and in psychiatric disorders. Notably olfactory impairments that accompany or precede the early stage of Alzheimer's disease may be seen as first clinical biomarkers of the pathology and predictors of the it's progression.

Methods: The present study evaluated odour recognition memory and odour identification in two groups of 12 mild Alzheimer's disease patients (M age 64.4 years, range 61 - 77), 12 moderate Alzheimer's disease patients (M age 67.2 years, range, 62 - 69), 12 Elderly (Elderly 1 group, M age 65.3 years, range, 60 - 68) and 12 very Elderly (Elderly 2 group, age 75.3, years, range, 70 - 83) with the aim to test whether in the Alzheimer's disease individuals olfactory deficits do occur already at an early stage and increase in function of the disease severity and to examine the influence of ageing on the olfactory efficiency. We were also interested to test, beside the documented impairment in the identification of odours in neurodegenerative diseases and old people, the extent to which the less investigated odour memory was also impaired.

Results: Data analyses showed that moderate Alzheimer' disease patients performed significantly worse than Mild ones on both tasks and that a similar outcome was observed for the elderly (with the older group of Elderly performing worse than the younger).

Conclusions: The present results highlight the presence in Alzheimer's disease patients of early and progressive olfactory dysfunctions and the role of the two olfactory tasks as useful instruments to discriminate between patients characterized by different levels of severity; they also confirm the available data from the literature showing a decrease in olfactory performance in the elderly population beyond the age of 60 - 65 years.

Keywords: Olfactory Assessment; Odour Recognition Memory; Odour Identification; Aging; Alzheimer Disease

Background

Extensive data from the literature document the presence of olfactory dysfunctions in ageing [1-9] and in various neurodegenerative conditions (e.g., Alzheimer's, Multiple System Atrophy, Parkinson's, Korsakov's, Huntington's; [4,10,11]). In particular Alzheimer's disease, one the most common neurodegenerative disorder, is characterized by early neuro-pathological changes (i.e., neurofibrillary tangles and amyloid plaques deposition) in brain structures involved in olfactory elaboration as olfactory bulbs, piriform cortex, amygdala and enthorinal cortex [4,12-17] as well as at the level of the olfactory ephitelium whereas pathological tau-immunoreactive fibers have been isolated [18,19]. Later, as the disease progresses, pathological lesions spreads from limbic and peripheral areas to neo-cortical regions (e.g., orbito-frontal structures; [15,20,21]). The causes responsible for Alzheimer' disease are not yet clarified; however both heritable factors and environmental agents like viruses, toxins and airborne xenobiotics penetrating the brain via the olfactory mucosa have been associated with the disease [22-25]. The early pathological changes described above match early olfactory dysfunctions in several olfactory abilities, the latter representing therefore one of the first clinical signs of the disorder and predictors of the disorder's progression

[11,26,27]. These abilities can be organized on a continuum from the most sensorial to the most cognitive, namely: odour detection, intensity discrimination, quality discrimination, odour recognition, cued-identification and free (non-cued) identification [7], and appear to be linked each other by a hierarchical and parallel fashion [28]. The awareness of the general and specific cognitive abilities that olfactory tasks draw upon and the perceptual attributes they measure on the peripheral-central continuum is crucial to help researchers to know what they are actually evaluating (i.e., a sensorial or a more demanding cognitive process). Available studies on olfactory abilities in Alzheimer's disease patients have shown higher-order deficits in odour identification and discrimination [11,17,26, 29-32] as a frequent feature, while investigations on the most basic odour detection have provided less consistent results [4,26,27,29,31,33]. Odour detection ability has resulted preserved [27] and impaired [26, 34] and in the latter case at an early [26] or late stage of the disease [33]. Odour recognition memory still remain under-investigated, although few early researches have shown a decreased ability in Alzheimer's disease patients [35-38]. Current available most widespread olfactory test kit which dominate the field are largely based on the participants ability to identify, to discriminate and to detect odorant [39-41]; and this can in part account for the lack of reports on odour memory in Alzheimer's disease, despite the extant of both procedures to measure odour memory and olfactory memory tests [7,42-45].

In the current study, we wished to study olfactory identification and memory for odours in patients with mild and moderate probable Alzheimer disease and in two groups of healthy elderly belonging on average to two different age cohorts of 65 and 75 years old.

The aim of the study was threefold: (i) to examine whether in the Alzheimer's disease group olfactory deficits do occur already at an early stage and increase in function of the disease severity, (ii) to examine the role of ageing on the olfactory efficiency, (iii) to confirm the presence of the documented impairment in the identification of odours in Alzheimer' disease patients and elderly and to test the extent to which their odour memory quality is also impaired.

Methods

Participants

Four groups were recruited: 12 mild Alzheimer's disease patients aged on average 64.4 ± (SD) 3.9 years (range, 61-67 years); 12 moderate Alzheimer's disease patients aged on average 67.2 ± (SD) 4.2 years (range, 62 - 69 years); 12 Elderly (Elderly 1 group) aged on average 65.3 ± (SD) 4.3 years (range, 60 - 68 years) and 12 very Elderly (Elderly 2 group) aged on average 75.3 ± (SD) 5.1 years (range, 70 - 83 years). In all groups both sexes were equally represented. The patients were examined at the former geriatric rehabilitation clinic of the hospital of Crema (I) by well-trained M.D. clinicians. The level of dementia was evaluated by means of the Milan Overall Dementia Assessment test (MODA) an Italian widely used battery of test [46]. This battery of tests measures cognitive processes such as attention, learning, memory, language, reasoning, visual perception, and also motor autonomy and spatial and temporal orientation. On the basis of individual scores (the range of the overall MODA is 0 - 100), patients are assigned to one of the following levels of dementia: mild (60 - 85); moderate (40 - 59); severe (< 40). Performance within the range 86–100 is evaluated as normal. The two groups of patients scored respectively 70.1 and 50.1 and were therefore diagnosed as probably Mild and Moderate Alzheimer's disease patients. The two groups of Elderly participants were healthy adults living at home with no cognitive impairments as confirmed by the MODA test overall score. None of them reported an acute or chronic impairment in olfactory function prior to testing. They were also free from major medical illness, neurological or psychiatric disorder and history of major olfactory pathologies, nor made use of drugs which may affect olfactory function.

Exclusion criteria for all participants were relative to those conditions which may cause temporary or permanent alterations to the sense of smell (e.g., current allergic rhinitis, polyposis, viral infection, respiratory tract infections, nasal trauma, head injury), drug or alcohol abuse.

The healthy elderly and the Alzheimer's disease participants (or their caregivers, in the case of moderate Alzheimer's patients) provided informed consent before their participation in the study. The study was conducted in accordance with the Declaration of Helsinki for experimentation with human subjects.

Materials and Procedures

Participants were administered a cued odour identification and an odour recognition task of suprathreshold common odorants comparable for subjective intensities, as based upon previous lab comparisons. Some of the substances were drawn from household items (e.g., onion, coffee), while others were essential oils and essences (Kart laboratories, Lausanne, Switzerland). Ten odorants were used as target and 30 as distracters (see table 1). The odorants were solute in mineral oil, in distilled water or neat, and contained in test glasses (height about 15 cm) fitted with rubber lids connected to a cotton swab wrapped around the end of a stick. Test tubes were covered with white paper to prevent participants from having visual cues. The odorants were refreshed every 48 h which was considered sufficient to maintain a fairly constant subjective intensity.

On the recognition task, each trial comprised the administration of a target odorant and a recognition set of four odorants. Each participant was asked to smell for about 4 s. the target, which was chosen randomly from the set of 10. About 3 - 4 s. after that, the participant was administered, one at a time, four test glasses one of which contained the to be recognized target odorant. The stimuli added to the target for each recognition trial were randomly selected from the 30 associated distracters (see, table 1). Six-second inter-stimulus intervals between odorants administrations were adopted to avoid carry-over adaptation effects. Among trials a 20-25 s rest was provided. The identification task required the participant to smell for about 4 s an odorant which was selected randomly from the set of 10. During smelling the examiner read out loud four alternative verbal labels [47]. Each participant was required to identify the correct label for the odorant. During the administration of the two tasks participants were requested to keep their eyes closed. The distance between the stimulus and the subject's nose was constant (i.e. the odorants were kept about 2 cm in front of the nostrils of the participant). The experiment was performed in one well-ventilated and quite room. The order of tasks presentation was counterbalanced among participants. Their responses were scored for accuracy. The participants' scores ranged from 0 to 10. All the patients performed both tests without difficulty. Each test procedure lasted about 20 minutes per participant.

Number Targets	Distracters		
1. Almond (100% N)	Anchovy paste (100% N)	Honey (100% N)	Pine (70% MO)
2. Camphor (100% N)	Banana (100% N)	Jasmine (70% MO)	Rose (70% MO)
3. Coffee (100% N)	Boot grease (100% N)	Juniper (100% N)	Rum (100% N)
4. Garlic (80% DW)	Cheese (100% N)	Lavender (70% MO)	Sulphur (100% N)
5. Ink (100% N)	Chocolate (100% N)	Lemon (70% MO)	Strawberry (100% N)
6. Marsala Liquor (70% DW)	Cinnamon (70% MO)	Licorice (100% N)	Tar (100% N)
7. Orange (70% MO)	Clove (70% MO)	Mustard (75% DW)	Tobacco (100% N)
8. Petrol (70% DW)	Denatured alcohol (70% DW)	Onion (80% DW)	Vanilla (100% N)
9. Shoe Polish (100% N)	Dish washing liquid (100% N)	Oregano (100% N)	Vinegar (70% DW)
10. Tomato (100% N)	Fennel (100% N)	Paint (100% N)	Violet (100% N)

Table 1: Odorants used listed in alphabetic order and their respective concentration.

DW = Dilution in Distilled water; MO = Dilution in Mineral oil; N = Neat.

(Percentage indicated the quantity of odourant used)

Results

The mean (± SEM) number of correct recognition and identification scores for each group are showed in Figure 1. The gender of the participants was not considered as a variable in the following analyses, because it had no influence on the performance of the tests as ascertained by an (unreported) set of previous analyses.
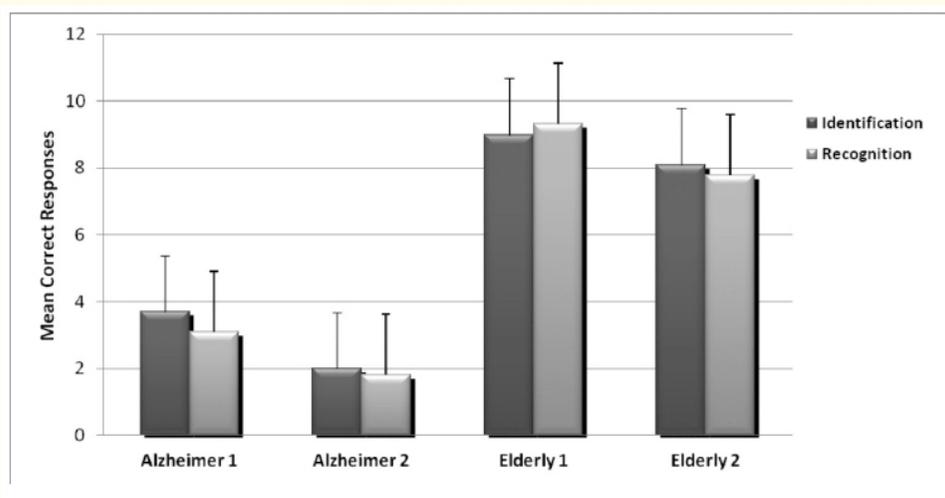

Figure 1: *Mean Number of correct responses for Alzheimer disease patients and healthy elderly as a function of odour identification and odour recognition tasks.*
(Legend: Alzheimer 1 = Mild Alzheimer's disease patients; Alzheimer 2 = Moderate Alzheimer's disease patients; Elderly 1 = Elderly aged on average 65.3 years; Elderly 2 = Very Elderly, aged on average 76.2 years. Error bars represent standard errors)

Results were analyzed by means of SPSS 21 statistical software for windows. The number of correct responses were analyzed by a two separate two-way mixed-design analysis of variance (ANOVA), the first on the Alzheimer's disease patients scores and the second on the healthy elderly scores. The rationale was to simplify the design as differences in performance between patients affected by a neurodegenerative disorder and healthy controls are well documented and obvious. Our aim here was to verify the extent to which odour identification and odour recognition memory deficits are present in the two groups of healthy elderly differing in age and how these deficits progress in the two groups of Alzheimer's disease patients according to the severity of their pathology.

The first analysis on Alzheimer's disease patients revealed a significant effect of the factor Group (Alzheimer 1 vs Alzheimer 2): [$F_{(1,22)} = 6.55$, $p = 0.013$] as well as the second analysis on the healthy elderly groups (Elderly 1 vs Elderly 2): [$F_{(1,22)} = 14.15$, $p = 0.01$]. The factor Tasks (Recognition vs Identification), did not reach a significant level in both analyses.

The mean scores (M) and standard errors (SE) for each group in function of the two tasks were as follows: Alzheimer's disease patients 1 (Recognition: M = 3.1, SE = 0.98; Identification: M = 3.7, SE = 1.4); Alzheimer's disease patients 2 (Recognition: M = 1.8, SE = 1.21; Identification: M = 2; SE = 1.26); Elderly 1 (Recognition: M = 9.33, SE = 0.88; Identification: M = 9, SE = 0.95); Elderly 2 (Recognition: M = 7.8, SE = 1.32; Identification: M = 8.1, SE = 1.64).

Discussion

The aim of the present study was to assess odour recognition memory and odour identification in two groups of mild and moderate probable Alzheimer's disease patients and in two groups of healthy elderly belonging to two different age cohorts.

Both the Alzheimer's disease patients and the very elderly (these aged on average 76.2 years), have clearly shown olfactory impairments in odour identification and in odour recognition memory tasks.

Relative to the Alzheimer' disease individuals our outcomes are consistent with the studies described in the introduction which have revealed reliable dementia-associated olfactory impairments in these patients, notably in the identification of odours. Such disorders appear to increase in function of the disease severity (with moderate Alzheimer's disease patients performing worse than mild ones) and occurs even at an early stage, thus representing one of the first markers of the disorder itself. Interestingly here, Alzheimer's disease individuals have exhibited marked deficits also in odour memory (a rather less investigated cognitive function). This in keeping with their early overt memory loss [48-51]. A similar picture is also distinctive of the Mild cognitive impairment disorder, which has been identified as a precursor stage of dementia [52,53] and whereas prominent olfactory dysfunctions have been isolated [26,30]. While early olfactory deficits in Alzheimer's individuals could be the consequence of early anatomical pathological injures to olfactory brain areas [4,27] the olfactory deficits observed in the elderly population are more likely the expression of physiological age-related changes. Consistently with the literature our data indicate indeed, a decrease in olfactory performance with increasing age beyond 60 - 65 years. Such impairments have been observed in odour identification [54-55] in odour threshold and discrimination [54] and in odour memory [7] and are likely due to peripheral factors [56] and to a reduction of efficiency in the brain areas where olfactory information are processed [5,7].

Conclusion

To conclude, our outcomes indicate also the great suitability of a recognition olfactory memory task together with an identification olfactory task as a reliable tool for the assessment of Alzheimer's disease at its early stage but also the olfactory efficiency in normal elderly.

Acknowledgments

Authors' Contributions

Conceived the experiment GMZ, IL; designed the experiment: GMZ. Performed the experiment: IM, GMZ. Supervision MODA test administration: SM; Analyzed the data: GMZ, Wrote the paper: GMZ. Final check: GMZ, SM.

Conflict of Interest Statement

No Financial interest or benefit arising from the applications of this research exist.

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