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Olfactory Deficits in Normal Aging and Alzheimer's Disease in the Polish Elderly Population

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Abstract

Alzheimer's disease (AD) is the most frequent cause of dementia. For this reason, a simple, reliable, and inexpensive method of early AD detection is urgently required. The location of neuropathological changes in AD patients indicates the potential diagnostic utility of olfactory tests. The purpose of this study was to compare odor identification performance among Polish subjects and to define the correlation between olfactory deficits and cognitive impairment. Olfactory identification performance was established in AD patients, and young and elderly healthy subjects using the Pocket Smell Test. AD Assessment Scale, the cognitive subscale, was used to evaluate cognitive functioning in the elderly participants. Compared with young subjects, the elderly individuals exhibited a diminished capacity to identify odors. AD patients also identified significantly fewer odors than healthy participants of the same age. In both the AD patients and the elderly control group, odor identification ability correlated with performance in cognitive tests. It may be concluded that deficits in olfactory identification occur in AD and may be valuable as an indicator of this condition.

Keywords: Alzheimer's disease; Olfaction; Cognitive enhancement

Introduction

With advances in medicine that promote longevity and economic progression, the number of elderly persons and their contribution to the world's population is rapidly escalating. Currently in Poland, it is estimated that 840,000 people are over the age of 80, whereas 330 are over 100 years old. It has been estimated that by the year 2020 there will be over 9.5 million people over the age of 60, which corresponds to 25.6% of the Polish population (Gabryelewicz, 2004). It is a well-established correlation that the frequency of dementia increases in an aging population. In most countries like Poland, Alzheimer's disease (AD) is the most frequent cause of dementia. For this reason, a simple, reliable, and low-cost method to detect AD in its early stages is urgently required.

The neuropathology of AD is characterized by neural loss, the deposition of neurofibrillary tangles, and amyloid plaques in the brain (Attems & Jellinger, 2006). Anatomically, the neurodegeneration in AD is not homogeneous but is distributed most prominently in the medial temporal lobe structures and certain association areas of the neocortex (Brun & Gustafson, 1976; Pearson, Esiri, Hiorns, Wilcock, & Powell, 1985). These changes are associated with the decline in cognitive functions such as memory, language, and attention. It is also well documented that patients with AD exhibit olfactory deficits that markedly exceed those seen in normal aging (Doty, 2003; Moberg et al., 1997). Numerous structural and functional studies have reported both peripheral and central abnormalities in different parts of the olfactory system in patients with AD, including the olfactory epithelium (Talamo et al., 1989), olfactory bulb (Thomann et al., 2009), entorhinal cortex, and hippocampus

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(Mesholam, Moberg, Mahr, & Doty, 1998). Following observations that AD patients exhibit olfactory deficits in detection sensitivity, discrimination, identification, and memory (Djordjevic, Jones-Gotman, De Sousa, & Chertkow, 2008; Doty, 2003; Mesholam et al., 1998; Murphy, 1999), it has been proposed that olfactory dysfunction could be used as an early marker for AD and that inclusion of a criterion for olfactory decline may improve the detection of early AD (Albers, Tabert, & Devanand, 2006; Morgan, Nordin, & Murphy, 1995; Serby, Larson, & Kalkstein, 1991; Tabert et al., 2006). Moreover, olfactory deficits seen early in the course of this disease appear to be correlated with the decline in cognitive functions. Gray, Staples, Murren, Dhariwal, and Bentham (2001) documented a strong association between the UPSIT (40-item olfactory test) score and the degree of cognitive impairment as measured by the CAMCOG. Royall, Chiodo, Polk, & Jaramillo (2002) reported similar results following an examination of olfaction (UPSIT) and cognitive functioning (Mini-Mental State Examination [MMSE], EXI25) in almost 200 residents within a continuing care retirement community. Furthermore, in a few reported studies, impairment of olfactory function was linked with changes in the activity of brain regions implicated in olfactory information processing and memory (Kareken et al., 2001). For example, Buchsbaum and coworkers (1991) demonstrated impaired performance in an olfactory memory task in patients with AD relative to control subjects, and they found that the patient group had lower metabolic activity in the area of the brain implicated in olfactory information processing and memory. Taken together, the available data suggest that odor identification tasks require not only an intact olfactory function, but also higher order cognitive or memory processing. However, Westervelt, Carvalho, and Duff (2007) pointed out that olfaction impairment is not universal in patients with AD. They suggested that odor identification deficits might indicate a clinical subtype of the disease. In their study, AD patients with such deficits were more likely to be men, less likely to have a family history of dementia and had poorer visuospatial functioning than AD patients without olfaction impairment.

Normal aging results in decreasing sensory and cognitive functions. In particular, olfactory deficits are commonly found in older people and contribute to a decreased quality of life, due to taste disturbance and loss of pleasure connected with eating, as a result leading to changes in weight and difficulty in avoiding health risks such as spoiled food or leaking natural gas (Larsson, Nilsson, Olofsson, & Nordin, 2004). In accordance with this notion, many studies have shown selective deficits in odor identification in the elderly population. Elderly subjects present poorer odor identification (Doty et al., 1984; Murphy et al., 2002), recognition memory (Murphy, Nordin, & Acosta, 1997), as well as odor recall (Murphy et al., 1997). In response to these data, Cerf-Ducastel and Murphy (2003) investigated the cortical substrate of olfactory deficits related to aging with functional magnetic resonance imaging. They employed a retronasal olfactory stimulation protocol using flavored aqueous solutions administered orally to test subjects. In young subjects, the main activation was found in the piriform/amygdala region, orbitofrontal cortex, and in other areas including the insula and cerebellum. Similar areas were activated in elderly subjects, but the degree of activation was significantly lower in regions receiving primary olfactory projections (piriform cortex, entorhinal cortex, and amygdala). It was proposed that dysfunction and/or degeneration in areas critical for olfactory processing could be a major cause of olfactory deficits in older people.

To date, no studies have examined impairment of the sense of smell in the Polish geriatric population. However, research conducted on elderly subjects in the USA (Cerf-Ducastel & Murphy, 2003), and also in Norway (Kjelvik, Sando, Aasly, Engedal, & White, 2007) and China (Chan, Tam, Murphy, Chiu, & Lam, 2002), indicates the reliability of smell identification tests as a useful additional screening tool in the diagnosis of AD. All such reports highlight the need for further studies in this field. In this study, olfactory and cognitive performance were assessed in AD, elderly and young Polish individuals. The aim was to examine the correlation between the ability to identify odors and the following factors: age, gender, and level of cognitive functioning of the participants, the nature of the odors presented, and the conditions under which the tests were conducted.

Methods

Subjects

AD participants were identified retrospectively and included outpatients from the geriatric sector of the psychiatric clinic at the Medical University in Lodz. AD group comprised 30 patients (15 women and 15 men) of over 60 years of age who met the criteria of the International Classification of Diseases, Tenth Edition, and the National Institute of Neurological and Communicative Disorders and Stroke-AD and Related Disorders Association (NINCDS–ADRDA) for probable AD. These subjects scored between 23 and 15 on the MMSE (Folstein, Folstein, & McHugh, 1975). The second group (elderly controls, ECs) consisted of 30 subjects (15 women and 15 men) of the same age as those in the first group, who did not exhibit signs of cognitive decline (MMSE >27). These participants were recruited from senior citizen in the same geographic area (Lodz). The third group (young controls, YCs) was composed of young adults (15 women and 15 men) of between the ages of 19 and 35. YCs were recruited by advertisement. Participants in all examined groups were matched by educational level, in order to avoid potential influence of education on ability to identify odors (Table 1).

Table 1. Demographic data for control and experimental groups (means and standard deviation)

Group	*N*	Age (years)	Education (years)	MMSE	ADAS-cog (total scores)
Young controls	30	26.20 (4.97)	11.50 (3.60)	30 (0.00)	—
Elderly controls	30	72.33 (6.29)	11.33 (3.63)	28.97 (1.09)	10.43 (3.05)
AD patients	30	72.27 (6.09)	11.30 (3.58)	18.87 (2.95)	27.53 (9.20)

Notes: AD = Alzheimer's disease; MMSE = Mini-Mental State Examination; ADAS-cog = Alzheimer's Disease Assessment Scale, the cognitive subscale.

Exclusion Criteria

Potential participants were excluded if they presented a history of neurologic disease (e.g., epilepsy, brain tumor, Parkinson's disease), head injury, local respiratory tract factors such as active rhinitis or sinusitis (allergic or infectious), active asthma, or a history of nasal polyps or surgery. Current smokers and psychoactive substance abusers were excluded. Subjects were also not included if they had been diagnosed with a serious psychiatric disease (e.g., schizophrenia, bipolar disorder, or depression) or they were currently taking antidepressants, neuroleptics, antihistamines, or anticholinergics. The study was approved by the ethical board at the Medical University in Lodz (approval no. RNN/344/07/KB). Informed consent was obtained from all participants.

Procedures

Cognitive Evaluation

All participants over 60 years of age (EC and AD groups) were evaluated by a clinical interview and cognitive tests. To evaluate cognitive status, all subjects performed the Polish version of the AD Assessment Scale, the cognitive subscale (ADAS-cog), and the MMSE test.

Assessment of Olfactory Performance

The original version of the Pocket Smell Test (PST), a three-item (apple, natural gas, rose), four-choice, scratch-and-sniff, forced choice odor identification test, was administered to both nostrils in all subjects. The odor stimuli are embedded in microcapsules that are fixed on strips of paper. Each strip was scratched in turn to release the odor and this was immediately sniffed by the subject, who then chose one of four alternative odors, even if no smell was perceived. Smell identification scores were then calculated by totaling the number of correct responses. In any particular testing session, participants could score from zero (no correct answers) to 3 points (all answers correct). The experiment included two sessions. The first session, known as "absolute identification" session, was an experimental and nonstandard method of performing the PST, introduced by the authors of this paper. In this session, each subject was presented three odors and asked to name them without any suggestion from the examiner. If the subject named the odor correctly, the second session was not performed for that odorant. Where the subject answered incorrectly or had no response, a second session followed where the examiner presented the same odorant once again, but in a standard way called "forced choice". In the second session utilizing "forced choice", the three odors were again presented to the subject in the standard manner. This time, the odor presentation was accompanied by a written list of four possible responses. To minimize the cognitive demands of the test, it was administered by an examiner, who scratched the sense strip and read the choices aloud. The subjects could view the list of written answers while the examiner read the choices. They then identified the odorant by selecting the name from the provided responses.

Individuals were given an unlimited time in which to respond in both sessions.

Results

Demographic Information

Demographic characteristics of the participants are shown in Table 1. Mean age was different among the three groups; however, the observed differences were between the YC and EC, and the YC and AD groups ($p < .001$ for each comparison). The difference in the mean ages of the AD and EC groups was not statistically significant. There was no significant difference in years of education between groups.

Performance in Cognitive Tests

Analyzes conducted on the results of the MMSE and ADAS-cog tests indicated that the AD group differed significantly from the other groups in all cognitive measures. There was a group effect for the MMSE test (Kruskal–Wallis $\chi^2 = 73.86$, $p < .001$, in which the AD group had lower scores; Table 1). Series of nonparametric Man–Whitney *U* comparisons of performance in the MMSE test by the three groups (AD, EC, and YC) revealed significant differences between the AD group and the control groups ($p < .001$ for each comparison). A significant difference in MMSE scores was also found between the EC and YC groups ($p < .001$). There was also a significant group effect for the ADAS-cog test ($z = -6.38$, $p < .001$), with the AD group having higher total scores. Significant differences were also found for all subscales of the ADAS-cog test ($p < .001$ for each subscale).

Performance in the Olfactory Test

The responses of subjects to consecutive items in the PST were scored correct or incorrect. The distribution of PST scores is presented in Table 2. To evaluate any potential group differences in the olfactory test (PST), separate analyzes were performed for the two sessions: "absolute identification" and "forced choice." Since the gender effect or its interaction with group was not significant in any of these analyzes, the two genders were considered together within each group. In the case of the "absolute identification" session, the Kurskall–Wallis test indicated a significant group effect ($\chi^2 = 53.56$, $p < .001$), with significant differences between all groups ($p < .001$). In the "forced choice" session, there was a significant group effect ($\chi^2 = 44.33$, $p < .001$). Series of the Mann–Whitney *U*-tests revealed all pairwise comparisons including AD group to be significant, that is, all groups were significantly different ($p < .001$ for each comparison), yet there was only a tendency between EC and YC groups ($p = .066$; Figure 1).

Comparing the results of both sessions, performance in the second "forced choice" session was significantly better than in the first "absolute identification" session for the AD and EC groups ($p < .001$ for each group) as well as for the YC group ($p < .005$).

Additional nonparametric comparison was used to evaluate the statistical significance of the odor type identification (apple, natural gas, and rose). The Mann–Whitney *U*-test showed a clear deficit of the olfactory identification function in AD patients compared with EC for apple ($z = -3.027$; $p < .005$), gas ($z = -3.911$; $p < .001$), and rose ($z = -3.125$; $p < .005$) in "forced choice" session and apple ($z = -2.896$; $p < .005$), gas ($z = -4.414$; $p < .001$), and rose ($z = -3.860$; $p < .001$) in "absolute identification" session. The significant differences were found also between the AD and YC groups for apple ($z = -4.053$; $p < .001$), gas ($z = -4.632$; $p < .001$), and rose ($z = -3.843$; $p < .001$) in "forced choice" session and for apple ($z = -5.132$; $p < .001$), gas ($z = -6.433$; $p < .001$), and rose ($z = -5.313$; $p < .001$) in "absolute identification" session. The comparison of EC and YC groups showed the significant differences for apple ($z = -2.557$; $p < .05$), gas ($z = -2.748$; $p < .01$), and rose ($z = -1.994$; $p < .05$) only in "absolute identification" session.

The Friedman test showed that overall, subjects were better able to identify rose than other odors ($\chi^2 = 7.167$, $p < .05$) in "absolute identification" session. The significant differences were found between rose and apple odors ($p < .05$).

In general, the performance of the AD patient group in the olfactory test was poorer than that of the EC and YC groups. Impaired performance of the olfactory test was particularly reflected in reduced performance in the first "absolute identification" sessions. The rose odor was recognized better than the other odors in this session.

To evaluate the diagnostic capability of the PST ("absolute identification" and "forced choice" sessions), a receiver operating characteristic curve analysis was additionally computed for EC and AD patients. Table 3 lists the sensitivity, specificity,

Table 2. Distribution of scores for PST

	Young controls	Elderly controls	AD patients
PST "absolute identification" score (total correct out of 3)			
0	0	2	16
1	0	6	9
2	6	10	5
3	24	12	0
PST "forced choice" score (total correct out of 3)			
0	0	0	5
1	0	2	10
2	1	5	10
3	29	23	5

Notes: AD = Alzheimer's disease; PST = Pocket Smell Test.

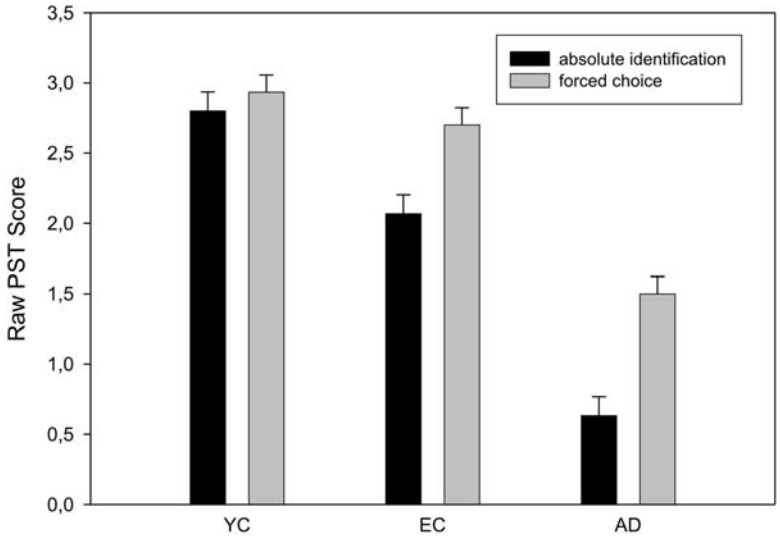

Fig. 1. Comparison of raw PST scores for YC, EC, and AD groups, in the first "absolute identification" and the second "forced choice" sessions (mean, SEM).

Table 3. Measures of diagnostic accuracy of PST for AD patients and elderly controls

Cutoff	Percentage			*p*-value
	Sensitivity	Specificity	Area under the curve	
PST "absolute identification" score				
≤1	83	27	78	<.001
≤2	100	60	70	<.01
PST "forced choice" score				
≤1	50	7	72	<.005
≤2	83	23	80	<.001

Notes: AD = Alzheimer's disease; PST = Pocket Smell Test.

and accuracy for various cutoff scores on the PST. Using a cutoff of ≤1 for the PST scores (McCaffrey, Duff, & Solomon, 2000; Solomon, Petrie, Hart, & Brackin, 1998), we obtained a specificity of 27% and a sensitivity of 83% for "absolute identification" session and specificity of 7% and sensitivity of 50% for "forced choice" session, whereas a cutoff of ≤2 gave a specificity of 60% and a sensitivity of 100% for "absolute identification" session and specificity of 23% and sensitivity of 83% for "forced choice" session (Figure 2).

Relationship between Performance in Olfactory and Cognitive Tests

To investigate possible links between olfactory and neuropsychological performance, the Spearman correlations were calculated for the AD and EC groups separately (Table 4). An examination of correlations in AD patients revealed that the cognitive subscales (ADAS-cog, total scores) were strongly correlated ($r > .6$) with PST scores. When the same correlation analyzes were conducted for particular subtests of the ADAS-cog test, all correlations were significant within the AD group. Performance in the PST also correlated significantly with MMSE scores ($r > .5$) in the AD patient group. As demonstrated in Table 4, olfactory test (PST) scores correlated significantly with performance in most subtests of ADAS-cog in the EC group, except for some of the praxis measures.

Discussion

In this study, the healthy YC subjects identified odors without significant impairment. In addition, they achieved better results in both PST sessions, when compared with the older participants in the healthy and AD groups. These results are in line with those of previous studies conducted in western countries, where participants aged 15–60 achieved comparable results in the B-SIT test (an extended, 12-smells version of the PST test), that is, without any signs of impairment of the ability to identify odors (Doty et al., 1984), or where both detection and identification of olfactory information

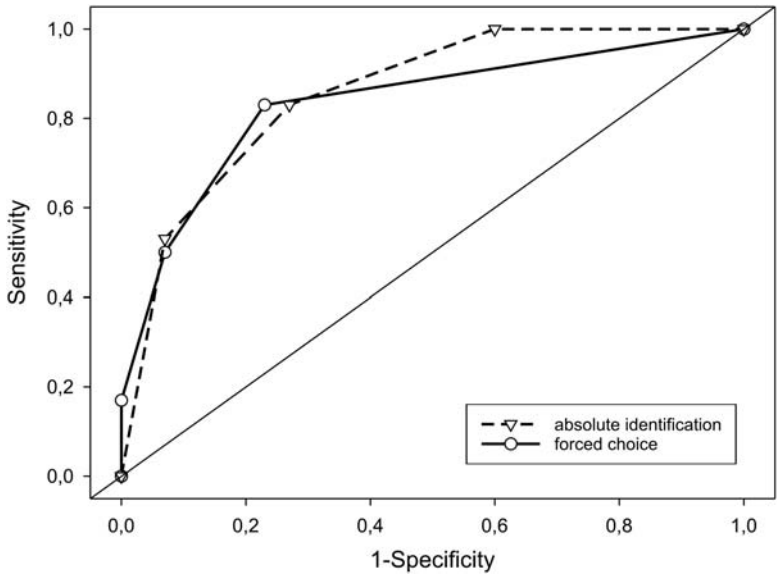

Fig. 2. Receiver operating characteristic curves for the ability of PST to discriminate AD patients from ECs in the first "absolute identification" and the second "forced choice" sessions.

Table 4. Spearman's correlation coefficients between performance in neuropsychological and olfactory tests (for "absolute identification" and "forced choice" sessions) in the AD and EC group

	EC group		AD group	
	PST ("absolute identification" session)	PST ("forced choice" session)	PST ("absolute identification" session)	PST ("forced choice" session)
MMSE	**0.714**†	**0.564****	**0.583**†	**0.571**†
ADAS-cog (total scores)	**−0.665**†	**−0.564****	**−0.698**†	**−0.747**†
ADAS-cog (word recall)	**−0.434***	**−0.397***	**−0.447***	**−0.558****
ADAS-cog (commands)	**−0.660**†	**−0.568****	**−0.468****	**−0.504****
ADAS-cog (constructional praxis)	−0.227	−0.305	**−0.494****	**−0.606**†
ADAS-cog (ideational praxis)	−0.196	**−0.439***	**−0.472****	**−0.601**†
ADAS-cog (orientation)	**−0.605**†	**−0.581**†	**−0.369***	**−0.556****
ADAS-cog (word recognition)	**−0.624**	**−0.424***	**−0.498****	**−0.549****

Notes: AD = Alzheimer's disease; PST = Pocket Smell Test; EC = elderly control; MMSE = Mini-Mental State Examination; ADAS-cog = Alzheimer's Disease Assessment Scale, the cognitive subscale.
*$p < .05$.
**$p < .01$.
†$p < .001$.

were impaired with age (Larsson, Finkel, & Pedersen, 2000). The age of 60 has been identified as the borderline age above which functional impairment of the sense of smell is observed (Economou, 2003). In the present study, we also detected decreased identification of odors in older subjects (over 70 years old). These results are in agreement with the decrease in olfactory functions observed with aging and psychophysical measures at a threshold level (Murphy, 1983), in identification (Doty et al., 1984) and in memory (Larsson & Backman, 1993; Murphy et al., 1997). In tests using odors dissolved in water, Cerf-Ducastel and Murphy (2003) found that odor identification scores were significantly lower in old subjects (over 78 years old), indicating a reduced ability to identify olfactory stimuli; however, olfactory thresholds were not significantly different between young and old subjects. Taken together, our results corroborate previous data showing that normal human aging results in decreased olfactory functions (Cerf-Ducastel & Murphy, 2003). It has been proposed that olfactory identification is more impaired by aging than other olfactory functions (Mesholam et al., 1998). The precise neurophysiological substrate of olfactory deficits that occur with age remains unknown, although structural changes have been identified in the aging brain, especially in the mesiotemporal lobe, including areas that are critical to olfactory processing (Insausti, Insausti, Sobreviela, Salinas, & Martinez-Penuela, 1998; Pruessner, Collins, Pruessner, & Evans, 2001; Tisserand, Visser, van Boxtel, & Jolles, 2000).

Most studies investigating olfactory decline in the process of aging have compared the smell identification test results of elderly people with unimpaired cognitive functioning to those of age-matched patients diagnosed with a syndrome of dementia (McLaughlin & Westervelt, 2008), mostly of the AD type. Typically, participants with AD achieved significantly lower scores in identifying, recognizing, or differentiating odors when compared with their healthy peers (Djordjevic et al., 2008; Royall et al., 2002). Similar results were obtained in this study: the patients suffering from AD were able to correctly identify significantly fewer odors than healthy elderly subjects.

In the present study, a two-stage evaluation of the sense of smell was made for each subject. In the first stage utilizing the test of "absolute identification", the AD patients achieved significantly poorer results than in the second stage, where they could see a list of suggested answers. These results in the "absolute identification" session concur with those of previous studies. According to Zucco and Aiello (1996), the level of wrong answers from AD patients can reach 70% using such a procedure. The difficulty in obtaining exceptional performance in this test may lie in the fact that the participants must access not only their memory of odor, but also they have to provide correct verbal designations to a given smell stimulus. It is well known that in the early stages of AD, language disorders encompass deterioration of the stimulus–signifier connection. Thus, patients find it more difficult to remember the names of various objects. It has been observed that people may correctly recognize more than 85% of odors when they are demanded to name the stimuli (Eibenstein et al., 2005). Over 30 years ago, Engen (1987) asserted that the use of tests of forced choice can give 90% correct identification. He maintained that for the verbal labels to be effective, they have to be highly distinctive. This assumption was confirmed by experimental data indicating significantly higher scores for the PST in its standard version compared with the "absolute" version in all studied groups.

Interestingly, recognition of the smell of roses in the "absolute identification" session was significantly better compared with the other odors. However, with the small sample size and limited number of odors used in this study, this result is difficult to interpret. Although there have been reports of similar differences in identifying levels of a range of odorants, dependent on the stimulus (Duff, McCaffrey, & Solomon, 2002), there has been no attempt to explain this observation. This lack of interpretation could be due to the large number of possible factors that may lie at the root of this phenomenon. However, pleasantness/unpleasantness as well as distinctiveness and familiarity could be one of the factors determining sensitivity/resistance to aging (Konstantinidis et al., 2006). What seems to be supporting this hypothesis is a fact that olfactory processing is mediated by limbic neuroanatomical structures, such as prefrontal cortex, ventromedial temporal lobe, basal forebrain, and diencephalon, which indicates that emotional and olfactory processing are linked (Royet et al., 2000; Zald, Lee, Fluegel, & Pardo, 1998).

It is suggested that olfactory functions, especially odor identification, require subjects to compare their perceptual/olfactory experience with information stored in their memory and to match this information with verbal labels (Djordjevic et al., 2008). In the present study, the average results of the MMSE and ADAS-cog tests (both general and the subscales) were significantly different in the elderly healthy participants (EC group) and the AD patients. In addition, the results of the MMSE scale and the ADAS-cog tests (both general and the subscales) correlated positively with the results of both sessions of smell identification conducted with the group of AD patients. The larger the cognitive impairment of the patient, the more difficulty they had in identifying the correct odors. A similar correlation was observed in the group of elderly participants free from cognitive disorders. Our results are consistent with prior researches (Djordjevic et al., 2008; Kjelvik et al., 2007; Westervelt, Ruffolo, & Tremont, 2005) in which the correlation between the execution of the sense of smell and cognitive functioning has been described. On the other hand, it should be noted that that olfaction impairment is not universal in patients with AD. Westervelt and colleagues (2007) have shown that patients with impaired odor identification could demonstrate neither globally worse cognition nor a greater degree of dementia severity compared with patients with relatively intact olfaction. It seems, therefore, that smell deficit in AD is not solely a function of the patient's cognitive decline. It is possible that AD leads to cognitive and olfactory deficits independently, because the initial neuropathological changes in AD occur in the medial temporal lobe structures (Attems & Jellinger, 2006) that are critical for both cognitive and olfactory functions (Kjelvik et al., 2007).

There is extensive evidence that men of all ages tend to perform worse than women in measures of olfaction (Brand & Millot, 2001; Doty, Marcus, & Lee, 1996). However, the results of the present study revealed no significant difference between men and women in the ability to identify odors. This finding contradicts the results of previous studies, which indicated that women achieve better scores in the B-SIT and the UPSIT than men (Liu et al., 1995). Moreover, Doty and colleagues (1996) found that age-related impairment of the sense of smell was stronger in men; whereas in the study of Larsson and colleagues (2004), such gender differences were absent among the oldest participants (age group of 85 and above). The differences between the findings of the present study and those reported in the literature may be attributable to several causes. First, the tests used in the aforementioned studies employed a larger number of smells (40 in UPSIT and 12 in B-SIT), which makes them more sensitive tools. Second, physiological fluctuations in female hormone levels influence both the performance of women in solving cognitive tasks and their sensitivity to smells. Data on the hormonal functioning of the participants was not collected during the present study. Third, most studies on the identification of smells have been conducted with either younger

participants or older individuals lacking any significant deterioration of cognitive functioning. Overall, it remains a controversial issue whether men and women differ in the incidence of AD and whether there are clearly recognizable sex differences in cognition and behavior among those afflicted. Studies that have examined sex differences in the pathologic indices of AD seem to present mixed results, with some indicating no sex differences (Ghebremedhin et al., 2001; Sandberg, Stewart, Smialek, & Troncoso, 2001), whereas other yield evidences for gender differences (Azad, Al Bugami, & Loy-English, 2007; Barnes et al., 2005; Fleisher et al., 2005). Further work is required to better understand the gender differences in numerous areas of clinical studies.

In summary, the results of the present study indicate that olfactory identification tests could serve as a useful additional tool in neurodegenerative diagnostic protocols, particularly for the differential diagnosis of cognitive functioning disorders in the geriatric population. Schiffman, Graham, Sattely-Miller, Zervakis, and Welsh-Bohmer (2002) suggested that smell measures may have other advantages over traditional neuropsychological tests. For example, participants may not be aware of the link between the ability to recognize smells and the risk of AD, thus they may be less likely to try and compensate for any perceived decline in performance. Moreover, olfactory functions are less prone to practice effects, which is an advantage where patients are assessed periodically (Nordin, Monsch, & Murphy, 1995).

There is ongoing discussion regarding the neurophysiological substrates for olfactory impairment. Some studies have pointed to changes in the peripheral olfactory structures of patients with AD (Arnold, Smutzer, Trojanowski, & Moberg, 1998; Smutzer, Doty, Arnold, & Trojanowski, 2003). Nevertheless, there is a need for further research on the functional impairment of the sense of smell, particularly the mechanisms underlying its development. Such studies should involve a greater number of participants and use a larger panel of odors to test the proficiency of their sense of smell. However, the PST appears to be a simple, reliable, and inexpensive method to detect deficits in olfactory identification in patients with AD.

In our study, a receiver-operating characteristic analyzes showed an excellent sensitivity of 100% only for the "absolute identification" session at a cutoff of ≤ 2 for the PST scores. Although all PST cutoff scores examined were rather disappointing in terms of specificity, it should be noted that the highest specificity index of 60% was also obtained for the "absolute identification" session at a cutoff of ≤ 2. The results suggested that opposite to traditional scoring (i.e., forced choice), nontraditional administration ("absolute identification") could be more useful in differentiating between AD patients and elderly healthy subjects. According to the present study, a cutoff score of ≤ 2 on the "absolute identification" is the best screening tool for AD. However, relatively low specificity of the test suggested that the first screening level (PST) should be followed by a more typical evaluation for AD, such as associative learning tests.

Limitations of the Study

Despite the clinically interesting and potentially useful findings of the study, the authors noted some limitations. First, none of the AD diagnosis was confirmed with neuropathological data via biopsy or autopsy, opening a possibility of erroneous qualification of the participants to a given group. Second, olfactory deficits alone do not represent sufficient specificity as a biomarker for AD. When combined with other markers, however, olfactory perceptual screens could prove to be useful to enhance diagnostic sensitivity and specificity for AD, especially given that they are noninvasive, reflect the functioning of brain circuits affected in AD, and are free of expensive and technical equipment (Wesson, Wilson, & Nixon, 2010). Finally, it should be noted that the group involved in the study was relatively small while the olfactory test used (PST) has a restricted range of only three items.

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Conflict of Interest

None declared.

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