Chem. Senses 26: 409–417, 2001

Rating of Different Olfactory Judgements in Alzheimer's Disease

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Abstract

Using simple successive tasks we assessed the influence of Alzheimer's disease on the processing of different odours. Fifteen patients with Alzheimer's disease, 15 old control subjects and 15 young control subjects were tested. The experiment included two sessions. Initially 12 odorants were presented, one odorant every minute. For each odour the subjects were asked to rate intensity, pleasantness, familiarity and edibility using linear rating scales. The odorants were then presented a second time and the subjects were asked to identify them. The results show that the intensity scores were lower in old control subjects and Alzheimer patients than in the young control subjects and that familiarity and identification scores were lower in Alzheimer patients than in old control and young control subjects. When we compared the five olfactory tasks the impairment of performance in Alzheimer patients was relatively higher for identification than familiarity, itself higher than the intensity judgement. No difference was observed between the three groups of subjects for pleasantness and edibility judgements.

Introduction

Olfactory dysfunction in Alzheimer's disease (AD) has been the subject of an increasing number of studies. This dysfunction is due to the presence of histological abnormalities in several of the brain areas indispensable to odour information processing. Various studies have shown neurofibrillary tangles, senile neuritic plaques and granulovacuolar degeneration to be found in the olfactory neuroepithelium, the olfactory bulb, the anterior olfactory nucleus, the prepiriform cortex, the entorhinal cortex, the amygdala and the hippocampus (Hooper and Vogel, 1976; Ball, 1977; Herzog and Kemper, 1980; Averback, 1983; Kemper, 1983; Esiri and Wilcock, 1984; Hyman *et al.*, 1984; Pearson *et al.*, 1985; Katzman, 1986; Ohm and Braak, 1987; Reyes *et al.*, 1987; Mann *et al.*, 1988; Talamo *et al.*, 1989; Trojanowski *et al.*, 1991; ter Laak *et al.*, 1994).

Since olfactory dysfunction appears to be one of the earliest signs of AD, an investigation of olfactory function could improve *in vivo* diagnosis of AD and even represent an early marker of disease expression prior to the advent of other clinical manifestations (Knupfer and Spiegel, 1986; Rezek, 1987; Serby, 1987). Various olfactory tasks have been used to rate performance and olfactory deficits have been reported in patients with AD with respect to odour detection, discrimination, recognition memory, identification and naming (Richard and Bizzini, 1981; Corwin *et al.*, 1985; Peabody and Tinklenberg, 1985; St Clair *et al.*, 1985; Serby *et al.*, 1985; Knupfer and Siegel, 1986; Koss, 1986; Doty and Snow, 1987; Doty *et al.*, 1987; Moberg *et al.*, 1987; Rezek, 1987; Serby, 1987; Koss *et al.*, 1988; Murphy *et al.*, 1990; Kesslak *et al.*, 1991; Rhodes *et al.*, 1991; Serby *et al.*, 1991, 1992).

Rather than use the tasks listed above, we proposed a test allowing subjects to rate different types of olfactory judgement. It is well known that objects can be analysed at different levels, ranging from superficial, sensory analyses to deep, semantic analyses (Craik and Lockhart, 1972). Indeed, it has been shown that recognition memory is higher when subjects process stimuli in the encoding phase at a semantic rather than at a phonological or orthographical level. This effect has also been shown for odours (Rabin and Cain, 1984; Royet *et al.*, 1996) and it has been suggested that the process of olfactory identification includes different levels of analysis with individual performance ranging from non-verbal feelings of familiarity to specific object names (Schab, 1991). On the basis of these data we think that intensity, familiarity, hedonicity and edibility judgements could represent some of the olfactory judgements performed by subjects before identifying odours and we postulate that they could involve different olfactory processing. Indeed, in two recent studies using neuroimagery we have shown that these olfactory judgements could activate different cerebral areas (Royet *et al.*, 1999, 2000a, 2001).

The aim of the present study was to examine the influence of AD on these olfactory judgements. The test was divided

into two sessions: in the first session intensity, pleasantness, familiarity and edibility judgements were rated and in the second the subjects were asked to identify the odorants. Intensity, pleasantness, familiarity and edibility were successively assessed using a simple linear rating scale. For the identification task a list of just four odour names was proposed to reduce the difficulty for AD patients. To differentiate between the effects of age and AD olfactory performance was investigated in three groups of subjects: AD patients, old control (OC) subjects matched in age to the AD patients and young control (YC) subjects.

Materials and methods

Subjects

Fifteen AD patients (three men and 12 women, mean age 68.4 ± 8.4 years), 15 OC (three men and 12 women, mean age 71.7 ± 11.6 years) and 15 YC (three men and 12 women, mean age 26.1 ± 3.1 years) participated in this experiment. All the patients had a history of progressive dementia and were diagnosed as having probable AD according to the NINCDS-ADRDA criteria (McKhann *et al.*, 1984), with a mean duration of symptoms of 3.3 ± 1.7 years (range 1–6 years). The OC and YC subjects were healthy volunteers recruited from the community. They were matched with respect to educational level with AD patients.

The evaluation of the AD patients included their history, a physical and neurological examination, a computed tomographic scan or magnetic resonance imaging and laboratory tests. Complete blood counts, serum vitamin B_{12}, folate and calcium levels and thyroid function tests were normal in all patients. Serology for syphilis was negative. Computerised tomography brain scans showed cerebral cortical atrophy and mild ventricular enlargement without focal abnormality. None of the patients had any history of head trauma, brain disease, psychiatric disease, arteriosclerosis, hypertension, alcohol abuse or cerebrovascular disease. The Hachinski Ischaemic Scale scores never exceeded 4 (Hachinski *et al.*, 1975). The patients had a score of on the Hamilton Depression Rating Scale (Hamilton, 1960), i.e. they were not depressed.

All the AD patients underwent a battery of neuropsychological tests (Table 1). The assessment included global intelligence status, dementia severity, language, praxis, constructional abilities, attention, and verbal and non-verbal memory. The Revised-Wechsler Adult Intelligence Scale (Wechsler, 1989) was used to evaluate the global intelligence status. The severity of the illness was assessed using the Mini-mental State Examination (Folstein *et al.*, 1975) and the Blessed Dementia Scale A (Blessed *et al.*, 1968). From the scores obtained it could be stated that the patients had mild to moderate degrees of dementia. The overall level of language function was evaluated using: (i) the Aphasia Battery (Faber-Langendoen *et al.*, 1988); (ii) a 42 item Form I naming task derived from the Boston Naming Test (Huff *et al.*, 1986); (iii) a verbal fluency task (words beginning with the letter P in 1 min and words in the animal category in 1 min, the scores being summed into a

Table 1 Neuropsychological test scores in patients with Alzheimer's disease

Test	Mean (SD)	Range	Max score
Global cognitive tests			
Mini-mental State	20.87 (4.98)	15–29	30
Blessed A	4.4 (2.84)	1–9	28
Revised Wechsler Adult Intelligence Scale			
Full-scale Intelligence Quotient	77.2 (13.72)	61–110	
Verbal IQ	80.4 (14.35)	65–116	
Performance IQ	72.0 (22.73)	57–110	
Language tests			
Boston Naming Test	25.8 (6.24)	13–37	42
Verbal Fluency Task	12.07 (5.99)	4–26	
Praxis			
Limb praxis	20.73 (3.24)	14–24	24
Visuo-constructive abilities			
Signoret's Figure Copy	17.33 (8.59)	0–24	24
Memory and attentional abilities			
Wechsler's Memory Scale	71.73 (13.55)	49–103	
Information	4.14 (1.17)	1–6	
Orientation	3.14 (1.46)	0–5	
Mental control	3.21 (2.86)	0–8	
Logical memory	2.32 (1.81)	0–7	
Digit span	7.14 (1.61)	4–10	
Visual reproduction	2.50 (2.35)	0–7	
Associate learning	6.25 (4.5)	0–14.5	

total fluency score). Limb praxis was evaluated with a 24 item test (eight symbolic and eight non-symbolic gestures on verbal command and eight meaningless movements on visual imitation). Visuo-constructive abilities were studied by asking patients to copy a complex 12 unit picture (Signoret and Whiteley, 1979). Memory evaluation was obtained from the Wechsler Memory Scale (Wechsler, 1969) and consisted of seven subtests: (i) information (personal and current affairs information); (ii) orientation (questions about time and space); (iii) mental control (verbal and arithmetic automatisms); (iv) logical memory (immediate free recall of two paragraphs); (v) digit span (digit forward and backward); (vi) visual reproduction (immediate visual memory drawing task); (vii) associate learning (paired word learning test).

Stimuli

Twelve odorants (Table 2) were chosen from 185 odorants which had been previously evaluated by a large number of subjects (Royet *et al.*, 1999). Odours were recognizable as very familiar, pleasant or unpleasant and either edible or inedible. Seven odorants were supplied by either Givaudan-Roure or International Flavour and Fragrances and were mixtures of odorants. The other five (mushroom, clove, ether, vinegar and gas) were obtained from simple chemical compounds (1-octen-3-ol, eugenol, diethyl ether, acetic acid and tetrahydrothiophene, respectively) and were provided by chemical product manufacturers (Aldrich or Sigma, France).

The odorous products were contained in 15 ml yellow glass jars with polypropylene screw lids (OSI, France). The jars were opaque to mask any visual cues as to identity. The odorants were diluted in mineral oil to prepare 5 ml of odorous solution (1%) and adsorbed on compressed filaments of polypropylene. Because tetrahydrothiophene, acetic acid and ether released a very strong odour, they were diluted 1000 times. Odorants were kept in a refrigerator when not in use and then removed before the experiment began and left to reach room temperature.

Experimental procedures

The whole experiment included two sessions. In the first session the subjects were given instructions concerning the experiment, but not instructed as to the type of task to be performed in the second session. Twelve odorous stimuli were successively presented at a rate of 1 odorant/min. Each odorant was presented twice for 5 s (from 0 to 5 s and from 30 to 35 s). For each odour the subjects were asked to rate intensity, pleasantness, familiarity and edibility using linear 10 cm rating scales. To compensate for the cognitive difficulties of AD patients, the rating scales were not segmented and numbered but continuous. To qualify their judgements, the extremities were marked 'not strong' and 'very strong', 'not pleasant' and 'very pleasant', 'not familiar' and 'very familiar' and 'not edible' and 'very edible', for intensity, pleasantness, familiarity and edibility, respectively.

In the second session the 12 odorants were again presented with one odorant every 30 s. The order of presentation was the same as that used in the first session so that the same interval elapsed between sessions for each odorant. This time each odorant was presented with a written list of four alternative responses (Table 2). The four responses comprised the veridical label, one name evoking a similar odour and two names evoking more distinct, either edible or inedible odours. The subjects had to identify the odorants by selecting the name which seemed correct to them.

Quantitative and statistical analyses

The linear rating scales were segmented into 10 equal parts, thus allowing us to determine the value given by each subject for each odour and each olfactory task. The odour identification scores were determined by attributing value 1

Table 2 List of odorants

	Veridical label	Chemical name	Dilution (%)	Descriptive names		
				1	2	3
1	mushroom	1-octen-3-ol	1	camphor	liquorice	lilac
2	pine	mixture	1	eucalyptus	coffee	tobacco
3	strawberry	mixture	1	pear	rose	petrol
4	smoked salmon	mixture	1	ham	daffodil	glue
5	clove	eugenol	1	garlic	chocolate	grass
6	lemon	mixture	1	apricot	vanilla	manure
7	lavender	mixture	1	violet	caramel	ammonia
8	ether	diethyl ether	0.1	naphthalene	pizza	lily
9	mint	mixture	1	anise	bitter almond	geranium
10	citronella	mixture	1	vervain	banana	tar
11	vinegar	acetic acid	0.1	mustard	orange	gardenia
12	gas	tetrahydrothiophene	0.1	bleach	cheese	carnation

to a response when a subject selected the veridical label and value 0 when he selected any of the three other alternative names indicated in Table 2.

Five two-way analyses of variance (ANOVA) with repeated measurements (Winer, 1962), one per olfactory task, were used to compare scores. The differences between pairs or groups of mean values were assessed by multiple orthogonal contrasts. The normality of the samples and the homogeneity of their variance were controlled with the Lilliefors (Conover, 1971) and Hartley (Winer, 1962) tests, respectively.

To investigate whether the olfactory performance of AD patients could be predicted by their cognitive status and demographic factors, hierarchical multiple regression analyses (stepwise regression) were performed for each odour task. Cognitive status was given by psychometric scores obtained from neuropsychological tests. Demographic factors included age, duration of dementia and educational level. Since the number of variables relative to the number of subjects was too high, cognitive status and demographic factors were analysed separately. In each analysis all the available variables (either psychometric scores or demographic data) were entered in a stepwise fashion. At each step only those predictor variables were retained in the regression equation whose partial correlation with the dependent olfactory measures was significant at $P < 0.05$ or better for the *F*-to-enter statistic. Thus, at each step any improvement in prediction of the resulting equation reflects the contribution of the step after the effects of all previously entered variables have been partially cancelled out.

Results

Olfactory performance

The arithmetic means of the scores obtained for intensity, pleasantness, familiarity, edibility and identification were computed and are shown in Figure 1 as a function of the three groups of subjects (first factor) and the 12 odorants (second factor). We also determined the mean scores for the 12 odours for each one of the three groups of subjects (Table 3). For the intensity measurements a two-way ANOVA revealed a significant effect of the group factor [$F(2,42) = 7.98$, $P < 0.005$] and the odorant factor [$F(11,462) = 14.09$, $P < 0.0005$] and a barely significant interaction between these two factors [$F(22,462) = 1.54$, $P = 0.05$]. Multiple mean comparisons showed that the intensity scores were significantly higher in YC than in OC subjects [$F(1,42) = 15.51$, $P < 0.0005$] and AD patients [$F(1,42) = 6.51$, $P < 0.025$]. No significant difference was observed between OC subjects and AD patient scores [$F(1,42) = 1.920$, n.s.]. Further analysis showed that lower scores in AD patients compared with those of the YC group were mainly due to significant differences for lavender and citronella ($P < 0.005$ and $P < 0.05$, respectively). The lower scores in OC compared with YC were mainly due to significant differences for six odorants: pine, clove, lemon, lavender, mint and gas ($P < 0.05$, at least).

For pleasantness judgements a two-way ANOVA did not reveal any significant effect of the group factor [$F(2,42) = 1.34$, n.s.], but showed a significant effect of the odorant group factor [$F(11,462) = 29.39$, $P < 0.0005$] and also a significant interaction between these two factors [$F(22,462) = 1.97$, $P < 0.01$]. Comparisons by mean pairs showed lower or higher scores in AD than in YC for clove, lavender and mint ($P < 0.025$, at least), but significant differences between OC and AD were only noted for mint and vinegar ($P < 0.025$, at least).

For familiarity judgements a two-way ANOVA revealed the significant effect of the group factor [$F(2,42) = 11.14$, $P < 0.0005$] and the odorant factor [$F(11,462) = 9.81$, $P < 0.0005$] and an interaction between these two factors at the limit of significance [$F(22,462) = 1.58$, $P = 0.05$]. Multiple mean comparisons showed that the familiarity scores were significantly higher in YC than in OC subjects [$F(1,42) = 7.10$, $P < 0.025$] and AD patients [$F(1,42) = 22.14$, $P < 0.0005$] and significantly higher in OC subjects than in AD patients [$F(1,42) = 4.16$, $P < 0.05$]. Further analysis showed that the lower scores in AD patients compared with those of YC subjects were mainly due to significant differences for all the odorants ($P < 0.025$, at least) except three (mushroom, smoked salmon and vinegar). Lower scores in OC compared with those of YC were mainly due to significant differences for six odorants: pine, clove, lavender, mint, citronella and gas ($P < 0.05$, at least). Lastly, lower scores were seen in AD patients compared with the OC subjects for four odorants: strawberry, lemon, lavender and mint ($P < 0.025$, at least).

For edibility judgements a two-way ANOVA revealed the significant effect of the odorant factor [$F(11,462) = 16.94$, $P < 0.0005$], but no significant effect of the group factor [$F(2,42) = 0.36$, n.s.] and no significant interaction between these two factors [$F(22,462) = 1.42$, n.s.].

For odour identification a two-way ANOVA revealed a significant effect of the group factor [$F(2,42) = 21.90$, $P < 0.0005$] and the odorant factor [$F(11,462) = 2.99$, $P < 0.001$], but no significant interaction between these two factors [$F(22,462) = 0.66$, n.s.]. Multiple mean comparisons showed that the identification scores were significantly higher in YC than in OC subjects [$F(1,42) = 10.42$, $P < 0.005$] and AD patients [$F(1,42) = 43.80$, $P < 0.0005$] and significantly higher in OC subjects than in AD patients [$F(1,42) = 11.49$, $P < 0.005$].

Correlation between olfactory performance and cognitive status of AD patients

Hierarchical multiple regression analysis performed with the psychometric variables showed that the Blessed A and orientation tests predicted 49% of the variance in intensity scores. For familiarity scores 57.3% of the variance was

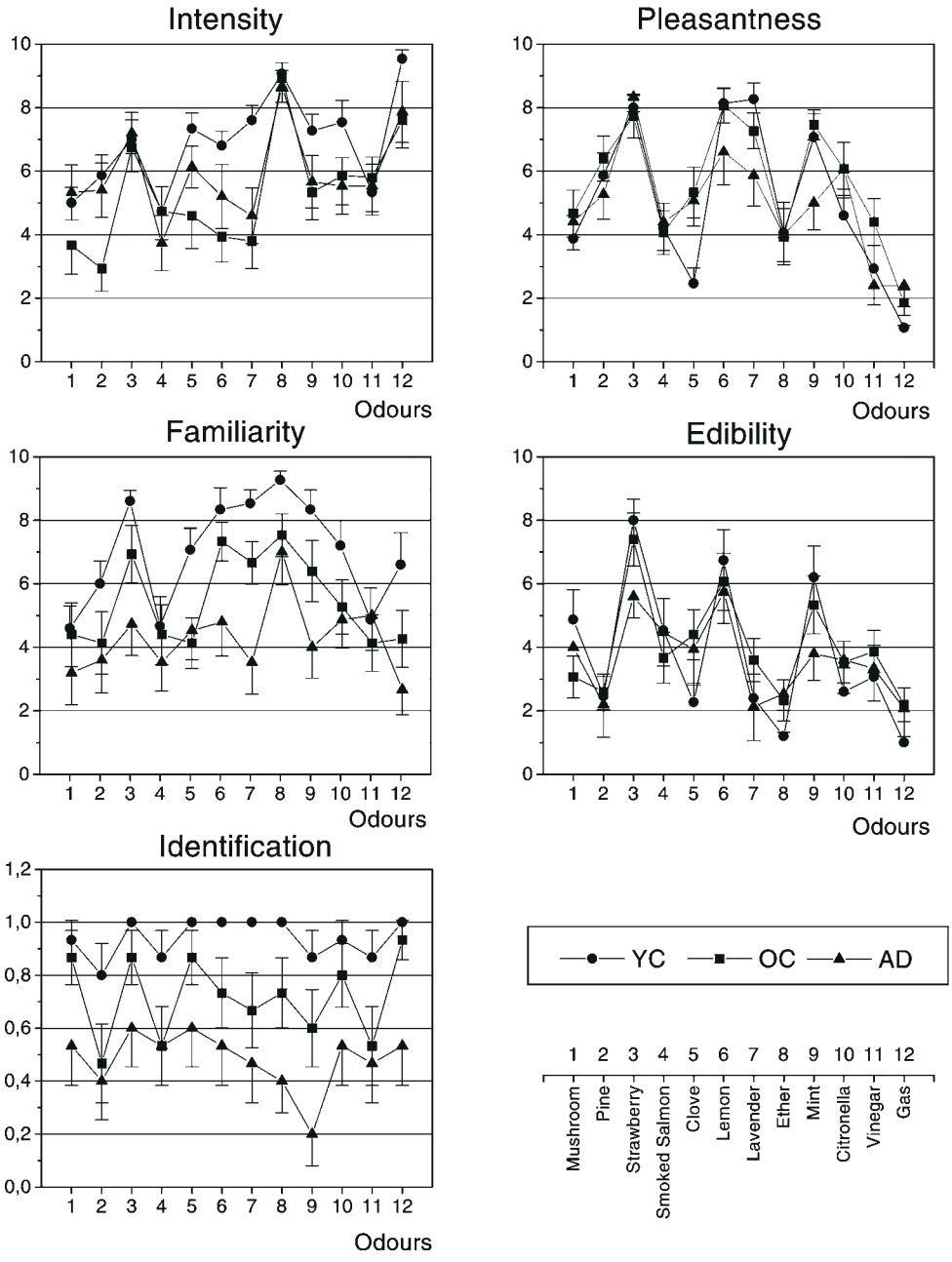

Figure 1 Scores of intensity, pleasantness, familiarity, edibility and identification as a function of the 12 odorants and the subject groups (YC, young controls; OC, old controls; AD, patients with Alzheimer's disease). Error bars indicate standard deviations.

Table 3 Mean scores for the different olfactory judgements in YC and OC subjects and AD patients and ratios of mean scores between the different groups of subjects

Judgement	Mean scores (SD)			Ratios (%)		
	YC	OC	AD	OC/YC	AD/YC	AD/OC
Intensity	6.922 (1.498)	5.328 (1.766)	5.889 (1.389)	77.0	85.1	110.5
Pleasantness	5.045 (2.405)	5.606 (1.888)	4.983 (1.675)	111.1	98.8	88.9
Familiarity	7.006 (1.667)	5.467 (1.392)	4.289 (1.137)	78.0	61.2	78.5
Edibility	3.811 (2.242)	4.006 (1.570)	3.617 (1.253)	105.1	94.9	90.3
Identification	0.939 (0.072)	0.717 (0.156)	0.483 (0.110)	76.4	51.4	67.4

accounted for by the performance in the Blessed A (29.5%) and the logical memory (27.8%) tests. For pleasantness scores the Blessed A variable also accounted for 30% of the variance. For identification scores four variables (logical memory, mental control, information and digit span) accounted for 91% of the variance. No independent variable contributed to any of the regression equations for edibility scores.

Hierarchical multiple regression analysis performed with demographic variables showed that age predicted 60.0% of the variance in intensity scores only. No independent demographic variable contributed to any of the regression equations for familiarity, hedonicity, edibility and identification scores.

Discussion

The present study highlights the influence of AD and age on different odour processing. It showed that intensity, hedonicity, familiarity, edibility judgements and also odour identification were differentially affected in patients with probable AD and elderly subjects when comparisons were made either between or within groups.

Intensity, familiarity and identification

When we compared the intensity scores obtained for the 12 odours and the three groups of subjects (Figure 1, Table 3) we observed that compared with YC subjects performance was similarly reduced in the OC subjects and AD patients (23.0 and 14.9%, respectively). Indeed, no significant difference was observed between OC subject and AD patient scores. The decline in intensity scores in the AD patients could thus be explained by the effect of age. In addition, hierarchical multiple regression analysis showed that 60.1% of the variance of intensity scores in AD patients could be explained by age. So we observed no detectable deficit in intensity judgement, although other researchers have reported sensitivity loss in odour detection in AD patients when compared with age-matched subjects (Richard and Bizzini, 1981; Knupfer and Siegel, 1986; Doty *et al.*, 1987; Rezek, 1987; Koss *et al.*, 1988; Murphy *et al.*, 1990; Serby *et al.*, 1991). The sensitivity loss in AD patients would be larger at weak concentration, near the threshold level, but undetectable at clearly supra-threshold concentrations.

When we compared the familiarity scores between the three groups of subjects (Figure 1, Table 3) we observed that, compared with YC subjects, performance was less reduced in the OC subjects than in the AD patients (22 and 38.8%, respectively). The familiarity scores were therefore an average 16.8% lower in AD patients than in OC subjects. From a statistical point of view our results show a more pronounced significant deficit in familiarity performance in AD patients than in OC subjects with four odours (strawberry, lemon, lavender and mint). While the age effect could explain the low intensity scores in AD patients, we can conclude that the familiarity scores are simply the reflection of a decline in their cognitive abilities. In cognitive psychology it is admitted that the recognition process implies the participation of input mechanisms to representations which provide a feeling of familiarity. Familiarity judgements are thus closely linked to long-term recognition memory, since a feeling of familiarity is closely connected to experience and necessarily involves remote information. Our results therefore corroborate the influence of AD on odour recognition (Moberg *et al.*, 1987). In the controls familiarity scores significantly lower in OC than in YC could also indicate a decline in their cognitive abilities.

The most dramatic effect in AD patients was observed in odour identification and this fact corroborated previous data showing an impairment in performance relative to age-matched control subjects (Peabody and Tinklenberg, 1985; Knupfer and Siegel, 1986; Doty *et al.*, 1987; Rezek, 1987; Serby, 1987; Koss *et al.*, 1988; Kesslak *et al.*, 1991; Serby *et al.*, 1991, 1992). The decline exhibited by AD patients was on average half that of OC (48.6 versus 23.6%) when compared with YC subjects. An age-related impaired ability to identify odours in normal elderly subjects has been reported in several studies (Doty *et al.*, 1984a,b; Doty and Snow, 1987; Serby *et al.*, 1992) and could be explained not only by sensory but also by cognitive deficits. Successful odour identification appears to be at a maximum between 30 and 40 years of age and then begins a monotonic decline (Doty *et al.*, 1984a,b; Eskenazi *et al.*, 1986). Furthermore, correlations were found between identification performance and several memory tasks (logical memory, mental control, information, digit span). However, deficits in odour identification could be partly, but not totally, explained by memory deficits. So when we compared AD patients with OC subjects in the present study the deficits in AD familiarity performance were much less pronounced than those obtained for odour identification (21.5 versus 32.6%, respectively).

A deficiency in odour identification in AD patients could be due to a language dysfunction, but we observed no correlation between the results of the language tests and identification tests. In addition, our results for identification scores were not predicted by age or by any other neuropsychological or demographic variable. These results are consistent with studies demonstrating that poor performance cannot be attributed to the cognitive difficulty of the assessment task (Koss *et al.*, 1988; Morgan *et al.*, 1995). The lexical abilities or cognitive processes involved in matching an odour to its source do not play as great a role in odour identification as the olfactory component itself.

It was recently proposed that the site of initial pathology in AD is the transentorhinal region and that the disease then progressively spreads in a predictable, non-random manner across the hippocampus and isocortex (Braak and Braak, 1995, 1996). These authors stressed that preservation of the entorhinal region is of the utmost importance in main-

taining mnemonic functions, since it predominantly acts as an interface between the neocortex and hippocampus. So a lesion of the entorhinal and hippocampal areas would explain why familiarity ratings in our AD patients were disturbed. In a cerebral imaging study Buschbaum *et al.* showed that AD patients had lower metabolic rates in the anterior portion of the medial-temporal cortex (parahippocampal gyrus) than the normal controls and scored much lower on an olfactory match-to-sample test (Buschbaum *et al.*, 1991). A volumetric study using magnetic resonance imaging also showed a reduction in volume of the entorhinal cortex and hippocampus in AD patients, while at the same time an olfactory deficit was apparent with the identification test (Kesslak *et al.*, 1991).

Pleasantness and edibility

Very few differences were observed between the three groups of subjects when examining their pleasantness judgements. Higher scores for clove and lower scores for lavender and mint in AD than in YC allow us to suppose that AD patients found these three odours less hedonically contrasted, i.e. more neutal than YC subjects. However, only two differences were noted between AD and OC scores. AD patients seemed to find mint more neutral but vinegar more unpleasant than OC subjects. Thus, pleasantness scores were impaired for one odorant only. We can conclude that the AD patients exhibited scores similar to those of the elderly subjects.

Given the presence of histological abnormalities in the amygdala areas of AD patients, it was supposed that their pleasantness scores would be more impaired than those of the elderly subjects. The amygdala is in fact considered to be the key structure in emotion (Le Doux, 1987). Bilateral damage confined to this structure in patients with Urbach–Wiethe disease impairs the processing of emotional visual and auditory stimuli (Adolphs *et al.*, 1995; Cahill *et al.*, 1995; Scott *et al.*, 1997) and in healthy subjects an increase in regional cerebral blood flow is observed in both amygdala in response to pleasant and unpleasant odours (Zald and Pardo, 1997; Royet *et al.*, 2000b). We suggest that the reason we did not observe any effect was because the disease had not yet affected the amygdala of our patients. In a recent study we showed that pleasantness scores are significantly reduced in temporal epileptic patients whose seizures originate in the amygdala and the hippocampus (Hudry *et al.*, 1999).

No difference was shown between the three groups of subjects when examining their edibility judgements. In a previous paper on the functional neuroanatomy of perceptual and semantic processing of odours we suggested that edibility judgement was a semantic task (Royet *et al.*, 1999). Given the olfactory deficits observed for the familiarity judgements and odour identification in the AD patients, it is surprising that we did not observe any modification in edibility scores. It does not appear that patients linked their pleasantness and edibility judgements. Indeed, four odorants (pine, lavender, ether and citronella) actually gave totally different pleasantness and edibility scores in AD patients. The pleasantness and edibility scores were 5.9 and 2.1, respectively, in AD patients for lavender and similar to those obtained for subjects in the other groups. Since the pleasant character of an odour is always described as being the most salient aspect, the edible/not edible dimension could also represent a determining feature for odours which would then be less sensitive to AD. Similarly, in the context of a semiotic hierarchy there appears to be a concomitant inverse relationship in AD between, on the one hand, development sequence in oral language (Emery, 1996), written language (Croisile, 1999) or limb praxis (De Ajuriaguerra and Tissot, 1968) and, on the other hand, their subsequent deterioration. In other words, the more robust a cognitive representation, the later its deterioration in AD.

Olfactory deficiencies have been described as one of the most useful findings for differentiating AD patients from controls (Huff *et al.*, 1987). We present a test using different olfactory tasks which simultaneously and rapidly (in ~30 min) measures several olfactory abilities. We show that the familiarity judgement and identification tasks, but not the intensity, pleasantness and edibility judgements, were notably affected in AD patients. We further think that these tasks could be discriminative depending on the pathology considered. A study is now in progress to rate olfactory deficiencies in Parkinson's disease using the same test. The first results clearly show different deficiencies from those seen in AD patients.

Acknowledgements

We thank anonymous reviewers for helpful comments on a draft of this manuscript and are grateful to W. Lipski for correcting the English language of the paper. This research was supported by a grant (BQR) from the Université Claude-Bernard Lyon 1. The Laboratoire des Neurosciences et Systèmes Sensoriels and the Service de Neuropsychologie belong to the Institut Fédératif des Neurosciences de Lyon.

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Accepted November 28, 2000