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Ratings of Different Olfactory Judgements in Schizophrenia

Julie Hudry, Mohamed Saoud[1,2], Thierry d'Amato[1], Jean Daléry[1] and Jean-Pierre Royet

Neuroscience and Sensory Systems, Claude-Bernard University (UMR CNRS 5020), 50, Avenue Tony Garnier, F-69007 Lyon Cedex 07, [1]Psychopathology and Neurobiology of Schizophrenia and Psychosis Vulnerability (EA 3092), Claude-Bernard University, Hôpital du Vinatier, 95, Boulevard Pinel, Bron-Lyon, F-69677 and [2]INSERM U534, 16 Avenue Lépine, Bron-Lyon, F-69676, France

Correspondence to be sent to: J. Hudry, Neuroscience and Sensory Systems (UMR CNRS 5020), Université Claude-Bernard Lyon 1, 50, Avenue Tony Garnier, 69366 Lyon Cedex 07, France. e-mail: hudry@olfac.univ-lyon1.fr

Abstract

We assessed the influence of schizophrenia on different olfactory tasks. Forty patients with schizophrenia (20 males and 20 females) and 40 control subjects (20 males and 20 females) were tested. The experiment included two sessions. Initially, 12 odorants were presented at a rate of one per minute. The subjects were asked to rate intensity, pleasantness, familiarity and edibility for each odour using linear rating scales. The odorants were then presented a second time and the subjects were asked to identify them. The results showed that the scores for pleasantness, familiarity, edibility and identification but not intensity were disturbed in patients when compared with control subjects. Furthermore, the familiarity judgement of male patients was more often deficient than that of female patients and they rated odorants as being inedible when the women judged them as neutral. Considered together, these data show that our olfactory test may be used in patients with schizophrenia for evidencing various dysfunctions specific to different types of olfactory processing that represent steps in the odour name identification process.

Introduction

Olfactory dysfunction in patients with schizophrenia has been the subject of an increasing number of studies. With a few exceptions (Campbell and Gregson, 1972; Bradley, 1984) olfactory deficits in schizophrenia have been reported in odour detection (Gross-Isseroff *et al*., 1987; Kopala *et al*., 1989, 1992; Geddes *et al*., 1991), similarity judgement and discrimination (Gregson and Fearnley, 1974; Malaspina *et al*., 1994), recognition memory (Wu *et al*., 1993), identification (Kopala *et al*., 1989, 1992, 1994; Hurwitz and Clark, 1990; Kopala and Clark, 1990; Serby *et al*., 1990; Seidman *et al*., 1992; Wu *et al*., 1993; Houlihan *et al*., 1994; Stedman and Clair, 1998) and naming (Saoud *et al*., 1998).

Deficits in odour identification have been found to be more common in men than in women (Kopala *et al*., 1992), more marked in post-menopausal than in pre-menopausal women with schizophrenia (Kopala *et al*., 1995) and closely linked to illness duration (Moberg *et al*., 1997b). Thus, independently of the normal ageing effect and cognitive deficit, elderly patients with schizophrenia displayed a greater magnitude of olfactory deficit than younger patients and this effect was not related to medication (Serby *et al*., 1990; Kopala *et al*., 1992). Conducting a meta-analytic review of the English language literature on olfaction in schizophrenia, Moberg *et al*. found no significant influence of medication status or smoking on differential deficits across the domains of detection threshold sensitivity, discrimination, memory and identification. They concluded that their findings support the hypothesis of a primary dysfunction in the olfactory system (Moberg *et al*., 1999).

Using the University of Pennsylvania's Smell Identification Test (UPSIT), Moberg *et al*. found pronounced deficits in patients with Alzheimer's disease as well as in elderly patients with schizophrenia (Moberg *et al*., 1997a). They suggested that, since performance on an odour identification test did not discriminate between these two disorders, similar pathological processes in olfactory brain regions might be involved. In a recent study that investigated patients with Alzheimer's disease we proposed an original test that allowed us to assess different olfactory judgements in addition to the classic olfactory identification test (Royet *et al*., 2001a). Taking into account cognitive psychology concepts (Craik and Lockhart, 1972; Craik and Tulving, 1975; Schab, 1991; Kosslyn and Koenig, 1992) we suggested that subjects assessed intensity, familiarity, pleasantness and edibility before identifying odours (Royet *et al*., 1999, 2000a,b, 2001b). We then showed that patients with Alzheimer's disease presented lower familiarity and identification scores than age-matched control subjects. In contrast, no difference was observed between either group of subjects for intensity, pleasantness and edibility judgements.

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The aim of the present study was to examine, for the first time, the influence of schizophrenia on the performance of these alternative olfactory judgement tasks. The test was divided into two sessions: a first one in which intensity, pleasantness, familiarity and edibility judgements were rated for several odorants and a second one in which the subjects were additionally asked to identify these odorants. Intensity, pleasantness, familiarity and edibility were successively assessed using linear rating scales. A list of five alternative odour names was proposed for the identification task. We postulated that, in addition to the well-documented impairment in identifying the odours, more specific deficits could be observed in the various olfactory judgements. Knowing that schizophrenia patients commonly present a disturbed experience of pleasure (Becker *et al*., 1993; Brewer *et al*., 1996) we could also presume that these patients would display an impaired pleasantness judgement

Methods

Subjects

Forty schizophrenia patients (20 males and 20 females) and 40 control subjects (20 males and 20 females) participated in this experiment (Table 1). All patients were recruited from the Vinatier Hospital in Lyon, France and met the criteria of the fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV) for schizophrenia (American Psychiatric Association, 1994). They were clinically stable with no change in medication for at least 1 month before the study. The control subjects were group matched in age and gender to the schizophrenia patients. The experiments were conducted on fully informed subjects who had given their written consent.

Psychiatric diagnoses were established on the basis of the Schedule for Affective Disorders and Schizophrenia (SADS) (Fyer *et al*., 1985) and a review of medical records. The SADS was used for selecting healthy comparison subjects who were confirmed to have neither current DSM-IV Axis I psychiatric disorder or schizophrenia spectrum personality disorder. The Positive and Negative Syndrome Scale (PANSS) (Kay *et al*., 1987) was also used for assessing psychopathology in patients (Table 1). Furthermore, no comparison subject had any family history of psychopathology as assessed by family research diagnostic criteria (Endicott *et al*., 1975). The exclusion criteria for all subjects included possible brain damage, major medical problems, current substance abuse, lithium medication, known anosmia or a current cold.

Stimuli

A set of 12 odorants (Table 2) was chosen from 185 odorants previously evaluated by a large number of control subjects (Royet *et al*., 1999). The odours were recognized as rather familiar, but either strong or weak, either pleasant or unpleasant and either edible or inedible. Seven odorants were furnished by Givaudan-Roure (France) or International Flavor and Fragrances (France) and were mixtures of odorants (lemon, lavender, citronella, strawberry, mint, pine and smoked salmon). 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 manufacturers of chemical products (Aldrich or Sigma, France).

The odorous products were contained in 15 ml yellow glass jars with screw lids in polypropylene (Fisher, Erlancourt, France). The jars were opaque in order to mask any visual cues as to identity. The odorants were diluted in mineral oil to prepare 5 ml of odorous solution (1%) and absorbed by compressed filaments of polypropylene. Because tetrahydrothiophene, acetic acid and ether released a very strong odour they were diluted 1000 times. The odorants were kept in a refrigerator when not in use and

Table 1 Demographic and clinical data of the patients and controls

Test	Control subjects		Schizophrenia patients	
	Male (n = 20)	Female (n = 20)	Male (n = 20)	Female (n = 20)
Demographic variables				
Age (years)	33.85 (9.41)	37.55 (9.71)	33.40 (8.57)	38.40 (10.21)
Education (years)	12.21 (2.68)	11.75 (3.02)	10.50 (1.86)	11.70 (1.35)
Personal psychiatric history				
Length of psychiatric history (months)			11.73 (11.06)	8.15 (5.34)
Medication				
Antipsychotic (mg/day CPZ Eq.)			405.45 (145.20)	389.20 (158.71)
PANSS scores				
Negative symptoms score			27.95 (8.34)	29.25 (6.06)
Positive symptoms score			22.45 (6.12)	20.50 (5.95)

Values are mean (SD). CPZ Eq., chlorpromazine equivalent.

Table 2 List and order of the odorants presented in the two sessions of the olfactory test

No.	Veridical label	Chemical name	Dilution (%)	Descriptive names			
				1	2	3	4
1	mushroom	1-octen-3-ol	1	mould	camphor	liquorice	lilac
2	lemon	mixture	1	hyacinth	grapefruit	vanilla	apricot
3	vinegar	acetic acid	0.1	orange	mustard	gardenia	cider
4	lavender	mixture	1	incense	caramel	mothballs	thyme
5	citronella	mixture	1	banana	lychee	tar	verbena
6	clove	eugenol	1	grass	garlic	chocolate	cinnamon
7	ether	diethyl ether	0.1	chloroform	lily	pizza	nail varnish
8	strawberry	mixture	1	biscuit	raspberry	petrol	passion fruit
9	gas	tetrahydrothiophene	0.1	carnation	gas	cheese	turpentine
10	mint	mixture	1	bitter almond	rose	liquorice	anise
11	pine	mixture	1	eucalyptus	wax	tobacco	gingerbread
12	smoked salmon	mixture	1	prawn	ham	glue	jonquil

were removed before the experiment began and left to reach room temperature.

Experimental procedure

The whole experiment included two sessions that were separated by an interval of a few minutes. Before the first session, the subjects were only given instructions concerning the tasks to be performed immediately. The experimenter then presented 12 odorants to the subjects at a rate of one per minute, with each odorant being presented for ~5 s. The subjects were asked to rate the intensity, pleasantness, familiarity and edibility of each odorant in order using linear 5 cm rating scales that were regularly segmented and numbered from 1 to 10. In order to indicate further the degree of judgement demanded, the extremities were marked 'very weak and 'very strong', 'very unpleasant' and 'very pleasant', 'very unfamiliar' and 'very familiar' and 'very inedible' and 'very edible' for intensity, pleasantness, familiarity and edibility respectively. The four linear rating scales were presented on the same page for each odorant. The subjects were not allowed to adjust their previous ratings while making a current judgement.

The same 12 odorants were presented again in the same order in the second session and with the same inter-stimulus interval as in the first session. The subjects had to choose one name for each odorant presented among a written list of five alternative proposals that comprised the veridical label, one name evoking a similar odour and three names evoking more distinct odours, either edible or not (Table 2). The presentation order of the odorants was the same for all subjects for both sessions. Each session lasted ~12 min and the entire test lasted 30 min.

Quantitative and statistical analyses

The scores obtained for intensity, pleasantness, familiarity and edibility were directly deduced from the value selected on the rating scales for each odour by each subject. The odour identification scores were determined by attributing the value 1 to a response when a subject selected the veridical label and the value 0 to that response when they selected one out of the four other alternative names indicated in Table 2. We chose to code the five alternative choices simply as correct or incorrect responses instead of distributing the responses into the categories of veridical label, near miss and far miss (Rabin and Cain, 1984; Lyman and McDaniel, 1984) because we felt that extracting near misses from incorrect responses could give redundant information with those processed in the four other tasks of olfactory judgement, particularly that of the edibility judgement. In the frame of our hypotheses emanating from cognitive psychology (Royet *et al*., 1999), the intensity, hedonicity, familiarity and edibility judgements represent different categories of odour processing, all of which contribute to the identification process.

The intensity, pleasantness, familiarity and edibility judgements and odour identification were considered as being different olfactory tasks involving different olfactory processing. However, it has previously been shown that there is a significant correlation between these tasks (Henion, 1971; Doty *et al*., 1984; Distel *et al.*, 1999; Royet *et al.*, 1999). Therefore multivariate analysis of variance (MANOVA) with group (patient versus control), gender (male versus female) and judgement type (intensity, hedonicity, familiarity, edibility and identification) was performed with repeated measurements on the odorant factor. Three-way analyses of variance (ANOVA) (group × gender × odorants) with repeated measurements (Winer, 1962) were then used for separately analysing the scores relative to the different olfactory judgement tasks. The differences between groups of means 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 the Hartley (Winer, 1962) tests respectively.

The relationships between olfactory performances and the demographic or clinical characteristics of the schizophrenia patients were assessed using Spearman correlations. They were performed on the results observed for each odour judgement task, for age, for PANSS positive and PANSS negative performances, duration of illness and for the educational level of the schizophrenia patients.

Results

Olfactory performances

All subjects provided the required ratings so that no data were missing. The arithmetic means of the scores obtained for intensity, pleasantness, familiarity, edibility and identification were computed as a function of the subject groups (schizophrenia versus control), of gender (male versus female) and of the 12 odorants (Figure 1). The results of the MANOVA showed a significant effect of the group [Wilks' $\lambda(11,370) = 5.982$ and $P < 0.0001$] and judgement factors [Wilks' $\lambda(44,1417) = 23.705$ and $P < 0.0001$], but not the sex factor [Wilks' $\lambda(11,370) = 1.314$ and non-significant]. Significant interactions between the group and judgement [Wilks' $\lambda(44,1417) = 2.090$ and $P < 0.0001$] and group and gender factors [Wilks' $\lambda(11,370) = 3.025$ and $P < 0.0007$], but not between the sex and judgement [Wilks' $\lambda(44,1417) = 1.180$ and non-significant] and group, gender and judgement factors [Wilks' $\lambda(44,1417) = 1.274$ and non-significant] were also observed. A Bonferroni test showed significant differences between the different olfactory tasks (intensity, hedonicity, familiarity, edibility and identification) compared by pair ($P < 0.05$ at least). Univariate tests with three-way ANOVAs were then performed for these five olfactory tasks.

We observed that only the odorant factor had a significant effect for the intensity judgements [$F(11,836) = 27.74$ and $P < 0.0005$]. The ANOVA for the pleasantness judgements revealed that the odorant factor had a significant effect [$F(11,836) = 52.17$ and $P < 0.001$] and that there were significant interactions ($P < 0.05$ at least) between three factors (group × gender × odorant). Multiple orthogonal comparisons of the means showed that the pleasantness performances were significantly lower in the schizophrenia patients than in the control subjects for both genders. The ANOVA for the familiarity judgements revealed a significant effect of the group [$F(1,76) = 14.29$ and $P < 0.0005$] and odorant [$F(11,836) = 16.83$ and $P < 0.0005$] factors and a significant interaction between these two factors [$F(11,836) = 2.54$ and $P < 0.005$]. Multiple orthogonal comparisons showed that the familiarity scores were significantly lower in the male than in the female schizophrenia patients [$F(1,76) = 5.29$ and $P < 0.025$] and also significantly lower in the male schizophrenia patients than in the male control subjects [$F(1,76) = 15.86$ and $P < 0.0005$]. The ANOVA revealed a significant effect of the odorant [$F(11,836) = 42.92$ and $P < 0.0005$] factor and a significant interaction between the group and gender [$F(1,76) = 7.75$ and $P < 0.005$] and the group and odorant factors [$F(11,836) = 2.80$ and $P < 0.0005$] for the edibility judgements. Multiple orthogonal comparisons showed that the edibility scores were significantly lower in the male than in the female schizophrenia patients [$F(1,76) = 9.01$ and $P < 0.005$] and significantly less contrasted in the male schizophrenia patients than in the male control subjects [$F(1,76) = 5.76$ and $P < 0.025$]. The ANOVA revealed a significant effect of the group [$F(11,836) = 28.68$ and $P < 0.0005$] and odorant factors [$F(11,836) = 6.07$ and $P < 0.0005$] and a significant interaction between the three factors [$F(11,836) = 1.95$ and $P < 0.05$] for the identification scores. Multiple orthogonal comparisons showed that the identification scores were significantly lower in the male and female schizophrenia patients as compared with their respective control groups [$F(1,76) = 17.96$ and $P < 0.005$ and $F(1,76) = 11.13$ and $P < 0.001$ respectively]. The identification scores of the male and female patients within the schizophrenia group were not significantly different [$F(1,76) = 0.293$ and non-significant] and those seen in the male and female subjects within the control group were also not significantly different [$F(1,76) = 2.081$ and non-significant].

The percentages of the schizophrenia patient performances were further rated in comparison to those of the control subjects. The mean scores for the 12 odorants were directly computed for the schizophrenia and control groups as a function of gender for the intensity, familiarity and identification tasks (Table 3). Differences between the performances observed in the schizophrenia patients and control subjects were then calculated for each odorant and expressed as a percentage of the control group performance. The percentages were indirectly calculated after normalization of the data for the pleasantness and edibility judgements. Given that the pleasantness judgement is a bipolar dimension, from unpleasant to neutral and from neutral to pleasant (Moskowitz and Barbe, 1976; Doty, 1991), the calculation of the mean scores for the 12 odorants could suppress differences between the groups. The pleasantness data were therefore standardized into normalized scores by computing the deviation of each score (absolute value) relative to the middle score (value 5). We applied the following empirical formula:

$$M = 1 - \frac{1}{n}\sum_{i=1}^{n}\left|\frac{(X_i - 5) - (Y_i - 5)}{5}\right|$$

where M was the mean score of the patients compared with that of the control group for all the odorants, X_i and Y_i were the mean respective scores for the control subjects and patients for the ith odorant and n was the number of odorants. As for the pleasantness judgement, we considered

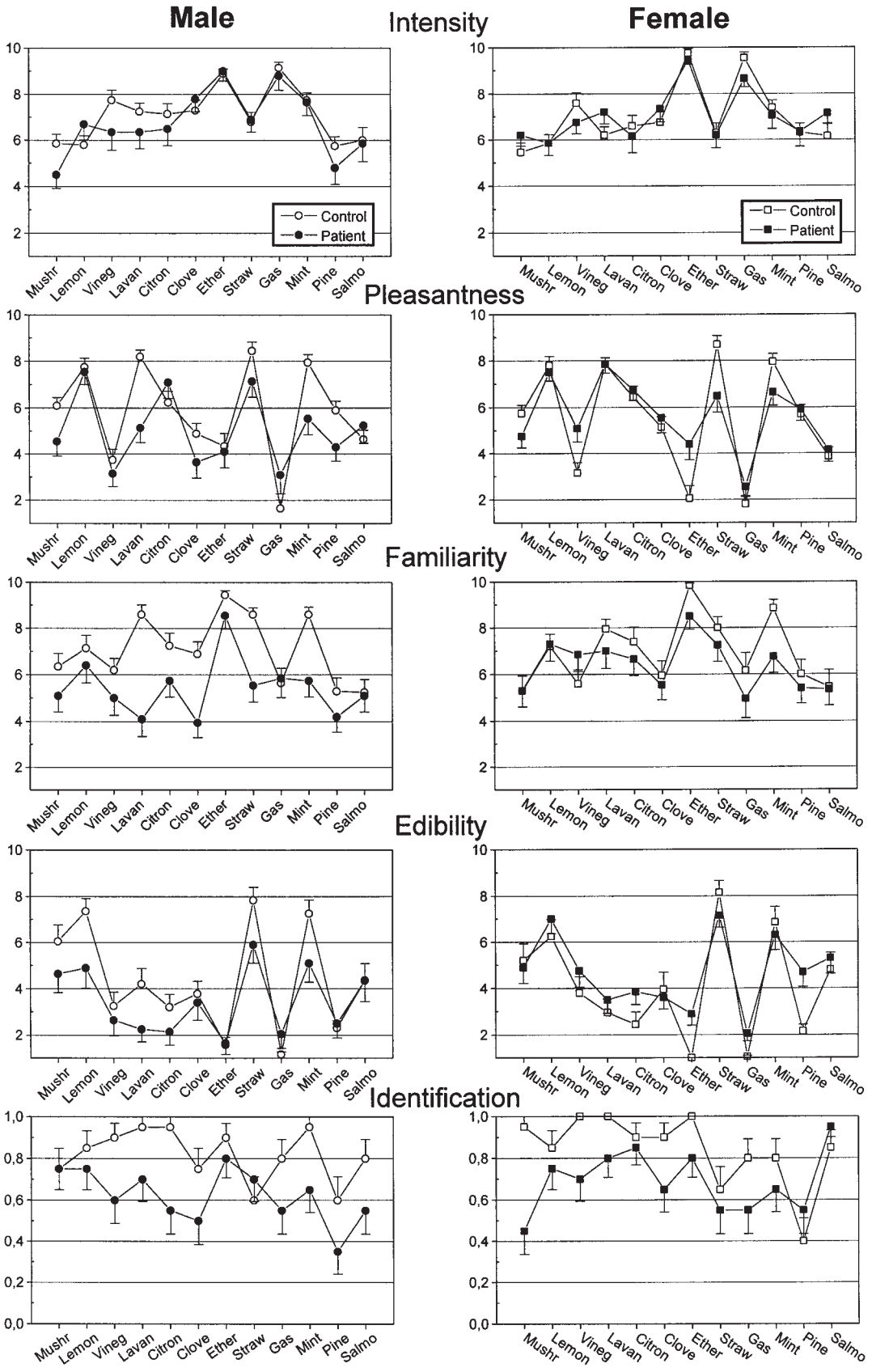

Figure 1 Scores of intensity, pleasantness, familiarity, edibility and identification as a function of gender, the subject groups (patient versus control) and the 12 odorants. The vertical bars are standard errors of the mean.

Table 3 Mean scores (± SD) for the intensity and familiarity judgements and identification in male and female control subjects and schizophrenia patients (left) and ratios of the mean scores of the schizophrenia patients when compared with those of the control subjects (right)

Judgement	Control subjects		Schizophrenia patients		Mean scores (%) of the patients relative to those of the controls	
	Male	Female	Male	Female	Male	Female
Intensity	7.12 (0.84)	6.99 (1.18)	6.77 (1.32)	7.03 (1.08)	95.0	100.5
Familiarity	7.11 (1.24)	6.98 (1.81)	5.44 (1.85)	6.40 (0.99)	76.6	91.8
Identification	0.82 (0.06)	0.84 (0.11)	0.62 (0.20)	0.69 (0.16)	76.0	81.7
Pleasantness					74.8	77.2
Edibility					76.8	80.3

The mean scores for the pleasantness and edibility judgements were obtained from the deviation of each score relative to the middle score (value 5).

the edibility judgement as also being a bipolar dimension and computed the deviation of each score relative to the middle score.

Demographic and clinical variables and olfactory performances

The mean age and educational level of the subjects were compared as a function of the group (schizophrenia versus control) and gender factors (male versus female) with two-way ANOVAs. The analysis did not show any significant effect for both variables of group factor [age, $F(1,76) = 0.01$ and non-significant and education, $F(1,76) = 2.90$ and non-significant] and gender factor [age, $F(1,76) = 3.74$ and non-significant and education, $F(1,76) = 0.51$ and non-significant] or any significant interaction between the two factors [age, $F(1,76) = 0.08$ and non-significant and education, $F(1,76) = 2.58$ and non-significant]. PANSS negative and PANSS positive scores, duration of illness and education levels were compared between the male and female schizophrenia patients. No significant difference was noted between either sex as a function of PANSS negative scores [$F(1,38) = 0.03$ and non-significant], PANSS positive scores [$F(1,38) = 1.04$ and non-significant] and duration of illness [$F(1,38) = 0.242$ and non-significant].

With regard to the within-group correlations between the demographic/clinical variables and olfactory scores, Spearman correlations only revealed a few significant associations between the olfactory scores and demographic and clinical variables. We mainly found weak but significant correlations between the intensity scores and the PANSS positive scores ($r = 0.097$ and $P = 0.034$) and between the familiarity scores and the PANSS positive and negative scores ($r = –0.108$ and $P = 0.018$ and $r = 0.096$ and $P = 0.036$ respectively).

Discussion

Olfactory performances in schizophrenia

The present study highlighted the influence of schizophrenia on different odour processing. It showed that the pleasantness, familiarity and edibility judgements and also odour identification but not the intensity judgement were differentially affected in the schizophrenia subjects when compared with the control subjects. Thus, although it has previously been shown that there is correlation between these olfactory tasks (Henion, 1971; Doty *et al*., 1984; Distel *et al*., 1999; Royet *et al*., 1999), they can underlie different odour processing and, as a consequence, involve different olfactory neural networks. Since deficits of odour identification in schizophrenia have largely been reported in the literature (Kopala *et al*., 1989, 1992, 1994; Hurwitz and Clark, 1990; Kopala and Clark, 1990; Serby *et al*., 1990; Seidman *et al*., 1992; Wu *et al*., 1993; Houlihan *et al*., 1994), the deficits observed in the present study for olfactory pleasantness, familiarity and edibility judgements are demonstrated for the first time. However, at a recent congress Moberg *et al*. also described impairment of odour hedonics in patients with schizophrenia (Moberg *et al*., 2001). Moreover, in a previous work (Royet *et al*., 2001a) we claimed that familiarity judgement can represent long-term recognition memory because familiarity feelings are closely related to experience and necessarily involve remote information. From this assumption, our results are coherent with data established in an earlier study (Wu *et al*., 1993) demonstrating that medicated or never-medicated schizophrenia patients performed worse than control subjects on an odour match-to-sample test.

A performance decrease in pleasantness judgement can be related to physical anhedonia, a well-known schizophrenia symptom corresponding to a ‘disturbed experience of pleasure, *i.e.* a gradual loss of the ability to feel emotionally moved, or to experience physical or psychic pleasure’ (Becker *et al*., 1993). Conversely to their expectations, these authors (Becker *et al*., 1993) could not prove this relation between anhedonia and pleasantness rating in psychosis-prone subjects. However, it is worth noting that these authors only used one odour.

It does not appear that the schizophrenia patients linked the edibility judgement to the pleasantness one, since several

odorants (lemon, lavender and smoked salmon) actually gave totally different edibility and pleasantness scores. Thus, both the schizophrenia patients and control subjects could judge an odorant as pleasant, although inedible (e.g. lavender and citronella). However, this dysfunction in edibility judgement can be linked to that found for familiarity judgement. The loss of familiarity judgement ability, which was mainly in the male schizophrenia patients, could lead them to consider odorants as being inedible. In other words, an unknown odorant could not be correctly judged edible or inedible, but could just be perceived as inedible.

The current study furthermore showed a clear dissociation between the olfactory performances of the male and female schizophrenia patients in their familiarity and edibility judgements. Thus, these performances for familiarity judgement mainly revealed score decreases in the males but not the females when compared with those of control subjects of the same gender (23.4 and 8.2% respectively). Although such ratio differences were not observed for the edibility judgement (due to its bipolar dimension), the analyses also proved lower edibility scores in the males than in the females. This also supports P.J. Moberg's (personal communication) observations showing that male but not female patients also modified their pleasantness ratings. The gender differences found in the present study were not related to age, since both groups were age matched. In contrast, they could be related to Kopala's studies indicating that the deficit in odour identification was more marked in male than in female patients and more marked in post- than pre-menopausal women with schizophrenia (Kopala *et al*., 1989, 1992, 1995). These authors suggested the involvement of a mechanism related to sex hormones such as oestrogen that could play a protective role in schizophrenia females. They emphasized the higher concentrations of oestrogen receptors in the amygdala, hippocampus and orbitofrontal cortex, which are all structures involved in olfaction and which are found to be abnormal in post-mortem studies of schizophrenia patients. However, several other studies did not show such gender differences using an odour identification test (Houlihan *et al*., 1994; Malaspina *et al*., 1994; Moberg *et al*., 1997a,b; Seidman *et al*., 1997). We suggest that these gender differences, which are not systematically observed, are due to a dysfunction in brain areas in male patients. These areas participate in familiarity and edibility judgements that are supposed to be steps in the odour name identification process. Finally, we showed that the identification scores were inversely related to the duration of illness and age. The identification scores were lower when the illness duration was increased, thus corroborating previously reported results (Moberg *et al*., 1997b). The identification performances were also lower in the oldest schizophrenia patients. However, this last relationship is rather tentative and explains why this data has not been previously published.

Schizophrenia and neural networks involved in odour processing

No histochemical or morphological abnormalities of the olfactory epithelium were observed in an immunohistochemical analysis of post-mortem olfactory tissues removed from schizophrenia patients (Smutzer *et al*., 1998). The olfactory bulb volume has been found to be smaller in schizophrenia patients than in comparison subjects, but no correlation between the olfactory bulb volume and odour threshold sensitivity was observed in patients (Turetsky *et al*., 2000). Thus, any olfactory deficits observed in schizophrenia were likely to present a central origin. There is indeed a growing body of evidence suggesting that schizophrenia is a neurobehavioural disorder resulting partly from brain temporolimbic dysfunctions (Fuster, 1989; Arnold *et al*., 1991, 1997, 1998; Seidman *et al*., 1995; Moberg *et al*., 1999). The limbic system is a well-known region of olfactory projection in mammals (Shipley and Reyes, 1991) and damage to this system in schizophrenia could explain a reduction in performance with pleasantness and familiarity judgements. The amygdala is considered to be the key structure in emotion (LeDoux, 1987) and cerebral imaging of healthy subjects has for instance revealed an increased amygdalian regional cerebral blood flow in response to both pleasant and unpleasant odours (Zald and Pardo, 1997; Royet *et al*., 2000b). We have also recently shown that pleasantness scores are significantly reduced in epileptic patients whose seizures originate in the amygdala and the hippocampus (Hudry *et al*., 1999). Finally, the left temporal lobe volume has recently been shown to be significantly smaller in male schizophrenia patients than in male comparison subjects (Bryant *et al*., 1999). These data are consistent with our own recent findings obtained from cerebral imaging, which has shown strong lateralization of the emotional processing of odours, i.e. that in healthy subjects the left hemisphere was clearly activated (Royet *et al*., 2000b).

It is usually hypothesized that aspects of schizophrenic symptomatology can reflect differential expressions of the disorder in two partially independent frontal subcortical regions: the left dorsolateral and the right ventral prefrontal systems (Seidman *et al*., 1992; Brewer *et al*., 1996; Purdon, 1998). The left dorsolateral part is reported to be involved in executive functions (Weinberger *et al*., 1986; Seidman *et al*., 1994), whereas the right ventral part, that is the orbitofrontal cortex, is implicated in olfactory processing (Jones-Gotman and Zatorre, 1988; Zatorre and Jones-Gotman, 1991; Zatorre *et al*., 1992). However, there appears to be discrepancies since two recent studies concluded that odour identification ability might be associated with the function of the dorsolateral prefrontal cortex (Brewer *et al*., 1996; Saoud *et al*., 1998).

Only a few studies have used cerebral imaging in patients with schizophrenia (Clark *et al*., 1991; Wu *et al*., 1993;

Bertollo *et al*., 1996; Malaspina *et al*., 1998). They indicated lower rates of metabolism relative to healthy controls in the frontal lobe and more particularly in the inferior frontal gyrus or the orbitofrontal cortex. Such a hypometabolism could explain olfactory deficits in schizophrenia, but unfortunately no olfactory performances were measured in patients by these authors during imaging scans. However, it has recently been demonstrated that the pattern of activation in the right and left orbitofrontal cortices of healthy subjects varies depending on whether odour processing is related to familiarity or pleasantness judgements (Zald and Pardo, 1997; Zald *et al*., 1998; Royet *et al*., 1999, 2000a,b, 2001b). The right orbitofrontal cortex activity was highest during the familiarity judgement, whereas the left orbitofrontal cortex activity increased significantly during the pleasantness judgement. We would like to suggest that the lower metabolism observed in these areas in patients with schizophrenia could explain the poor olfactory performances observed in the present study for the familiarity and pleasantness judgements.

Comparisons of data in patients with Alzheimer's disease and schizophrenia

Substantial olfactory deficits have been found in Alzheimer's disease and schizophrenia in the domain of odour detection threshold sensitivity, discrimination, memory and identification. However, a meta-analytic study of the English language literature on olfactory dysfunction in schizophrenia did not find differential deficits in these olfactory domains (Moberg *et al*., 1999). Neither was any difference found between either disease, Alzheimer's disease and elderly schizophrenia using the UPSIT (Moberg *et al*., 1997a). In a previous study with Alzheimer's disease patients, we showed deficits for familiarity judgement and the identification of odours, but not for intensity, pleasantness and edibility judgements when their performances were compared with those of control subjects matched in age (Royet *et al*., 2001a). In the present study we found deficits for the familiarity, pleasantness and edibility judgements and odour identification. Thus, even without further comparative statistical analysis, we can underline the differences in olfactory performances found between Alzheimer's disease and schizophrenia patients with our test for pleasantness and edibility judgements. We can therefore conclude that the present olfactory test, as a function of the olfactory judgements investigated, is suitable for demonstrating differential deficits in olfactory functioning in Alzheimer's disease and schizophrenia and for allowing us to evidence the involvement of different neuronal circuits. Furthermore, this test could be sensitive enough to differentiate schizotypic and at-risk groups and we feel that this may deserve further investigation.

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