



Identification of pleasant, neutral, and unpleasant odors in schizophrenia

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ABSTRACT

Recent work on odor hedonics in schizophrenia has indicated that patients display abnormalities in hedonic judgments of odors in comparison to healthy comparison participants. In the current study, identification accuracy for pleasant, neutral, and unpleasant odors in individuals with schizophrenia and healthy controls was examined. Thirty-three schizophrenia patients (63% male) and thirty-one healthy volunteers (65% male) were recruited. The groups were well matched on age, sex, and smoking status. Participants were administered the University of Pennsylvania Smell Identification Test, which was subsequently divided into 16 pleasant, 15 neutral, and 9 unpleasant items. Analysis of identification z-scores for pleasant, neutral, and unpleasant odors revealed a significant diagnosis by valence interaction. Post-hoc analysis revealed that schizophrenia participants made more identification errors on pleasant and neutral odors compared to healthy controls, with no differences observed for unpleasant odors. No effect was seen for sex. The findings from the current investigation suggest that odor identification accuracy in patients is influenced by odor valence. This pattern of results parallels a growing body of literature indicating that patients display aberrant pleasantness ratings for pleasant odors and highlights the need for additional research on the influence of odor valence on olfactory identification performance in individuals with schizophrenia.

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1. Introduction

The relationship between olfactory and emotional processing is an area of increasing interest in schizophrenia research, due to the involvement of overlapping neural substrates in the orbitofrontal and temporo-limbic brain regions. Emotional disturbances such as flat affect and anhedonia are prominent and well-characterized clinical features of the illness. Structural and functional abnormalities in olfactory networks are also robust neurobiological findings (Turetsky et al., 2009). How individuals with schizophrenia process the hedonic characteristics of odors is therefore a relevant yet understudied probe of frontotemporal limbic dysfunction and the resulting emotional disturbances observed in schizophrenia.

While schizophrenia deficits in odor identification have been widely replicated (Moberg et al., 1999), considerably less attention has been given to odor hedonic processing. There are, though, an increasing number of studies which suggest that patients' ability to appreciate the hedonic quality of odors is impaired. The precise nature of this abnormality, however, remains unclear. Schizophrenia patients have been variously reported to exhibit a nonspecific attenuation of their hedonic responses (Hudry et al., 2002) though a selective decrease in their ability to appreciate the pleasantness of odors

(Crespo-Facorro et al., 2001; Plailly et al., 2006) as well as an exaggerated assessment of odor pleasantness has been shown (Rupp et al., 2005; Doop and Park, 2006). Consistent with these latter reports, previous work from our laboratory (Moberg et al., 2003) found that male patients failed to appreciate the increasing negative valence associated with higher concentrations of an odorant, even as they correctly perceived the increase in odor intensity. This finding, that schizophrenia patients mis-assign hedonic valence even as they correctly rate the intensity of odors, is one that has been observed repeatedly (Crespo-Facorro et al., 2001; Hudry et al., 2002; Moberg et al., 2003; Doop and Park, 2006). Recent data suggest that the tendency to over-rate vs. under-rate the pleasantness of odors may reflect the extent of a patient's negative symptomatology though here, too, contradictory results have been reported. In a study that was limited to 12 olfactory probe items, but which examined both deficit syndrome and nondeficit patients, Strauss et al. (2010) reported that both groups undervalued the unpleasantness of negative odors, but only deficit syndrome patients undervalued the pleasantness of pleasant odors. In contrast, Doop and Park (2006) found that patients with greater negative symptomatology were more likely to judge an odor as pleasant.

Differences in methodology and sample characteristics are likely to underlie some of the specific differences in these study results. Cumulatively, though, they suggest that schizophrenia patients not only fail to identify odors correctly, but also fail to appreciate their hedonic qualities appropriately. This raises the intriguing question of whether these two domains of olfactory impairment might interact

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with each other. In particular, since olfactory identification performance is also highly correlated with negative symptomatology (Ishizuka et al., 2010), it is plausible that differences in the hedonic qualities of different odors affect the ability of patients to correctly identify them. Only two studies have actually attempted to look at the interaction of odor valence and identification performance in schizophrenia. Doop and Park (2006) reported that both patients and controls rated correctly identified items as being more pleasant than incorrectly identified items, consistent with the idea that familiarity is associated with liking. More interestingly, Strauss et al. (2010) considered whether identification performance was different for positive and negative valence odors, based on an established normative assessment of each odor's hedonic attributes (Doty et al., 1984). Although they found no difference in the ability to identify pleasant vs. unpleasant odors, this study was limited by the fact that only 12 items (7 pleasant, 5 unpleasant) were included. Also, because there were so few items, odors considered to be on the pleasant side of a neutral categorization were included in the pleasant group and, similarly, odors on the unpleasant side of neutral were considered unpleasant. This may have militated against the likelihood of finding an association between odor valence and identification performance.

The current study was designed to investigate, in greater detail, the effects of odor valence on odor identification deficits in schizophrenia patients, and to address the weaknesses noted above. We used a well-established 40-item measure of odor identification that included normative data to classify the odors as pleasant, unpleasant, or neutral (Doty et al., 1984). Patients were characterized with multiple clinical assessment tools to examine the relationship between specific clinical measures and valence-modulated odor identification performance.

2. Method

2.1. Participants

Thirty-three patients (21 males and 12 females) diagnosed with schizophrenia using DSM-IV criteria (American Psychiatric Association, 2000) and thirty-one healthy volunteers (20 males and 11 females) were recruited by the Schizophrenia Research Center at the University of Pennsylvania Medical Center. All participants underwent a medical and psychiatric evaluation that included a physical examination and the administration of standardized clinical scales. Exclusion criteria included history of psychiatric disorder (other than schizophrenia), neurological disorder, head trauma, loss of consciousness, substance abuse history, or the presence of one of the following: a medical condition that could alter cerebral functioning, an upper respiratory infection, or a condition that could affect olfactory functioning (e.g., common cold). Normal participants were screened for a history of Axis I psychiatric illness in themselves and in their first-degree relatives. After providing a complete description of the study to participants, written informed consent was obtained.

Of the patients with schizophrenia, nine were taking atypical antipsychotic medication, 10 were taking typical antipsychotic medication, and six were taking a combination of both typical and atypical antipsychotic medications at the time of testing. Patients and controls did not differ with regard to age ($F[1,62] = 3.37, P = 0.11$), sex composition ($\chi^2 = 0.01, df = 1, P = 0.94$), or smoking status ($\chi^2 = 2.84, df = 2, P = 0.24$). They did, however, differ with regard to ethnic background ($\chi^2 = 7.80, df = 3, P = 0.05$) and educational attainment ($F[1,62] = 27.65, P < 0.001$). Sample demographics are provided in Table 1.

2.2. Clinical assessment

Clinical rating scales were completed on all patients prior to testing, by trained raters with an inter-rater reliability (ICC) greater than 0.85. Patients were administered the following instruments to characterize their clinical and emotional status: Scale for the Assessment of Negative Symptoms (SANS; Andreasen, 1983), Scale for the Assessment of Positive Symptoms (SAPS; Andreasen, 1984), Brief Psychiatric Rating Scale (BPRS; Overall and Gorham, 1962), Quality of Life Scale (QOLS; Heinrichs et al., 1984), and the Hamilton Rating Scale for Depression (HAM-D; Hamilton, 1960). Clinical rating scale scores are presented in Table 1.

2.3. Odor identification assessment

Odor identification ability was assessed using the University of Pennsylvania Smell Identification Test (UPSIT; Doty et al., 1984). The 40-item UPSIT is a standardized, four-alternative, forced-choice test of olfactory identification comprised of four booklets containing ten odorants apiece, one odorant per page. The stimuli are embedded in "scratch and sniff" microcapsules fixed and positioned on strips at the bottom of each

Table 1
Sample characteristics for schizophrenia (SZ) and healthy comparison (HC) groups.

Variable	SZ (N = 33)	HC (N = 31)
	Mean ($\pm$ SD)	Mean ($\pm$ SD)
Age (years)	34.9 (10.2)	30.7 (10.3)
Gender		
Male	N = 21	N = 20
Female	N = 12	N = 11
Education (years) ^a	12.0 (2.0)	14.7 (2.1)
Ethnic background ^b		
Caucasian	N = 15	N = 23
African-American	N = 17	N = 7
Asian-American	N = 0	N = 1
Other	N = 1	N = 0
UPSIT ^a (total score)	31.0 (4.1)	35.8 (3.6)
Pleasant odors ^a (N = 16)	12.5 (2.0)	14.4 (1.7)
Neutral odors ^a (N = 15)	11.1 (2.3)	13.4 (1.7)
Unpleasant odors (N = 9)	7.5 (1.6)	8.0 (1.1)
Illness duration (years)	11.1 (7.6)	–
Age of onset (years)	22.5 (7.7)	–
SANS total score	39.4 (21.9)	–
SAPS total score	23.2 (21.3)	–
BPRS total score	35.4 (12.4)	–
HAM-D total score	11.2 (7.7)	–
QOLS total score	29.9 (20.0)	–

SANS and SAPS: Scales for the Assessment of Negative Symptoms (Andreasen, 1983) and Positive Symptoms (Andreasen, 1984); BPRS: Brief Psychiatric Rating Scale (Overall and Gorham, 1962); QOLS: Quality of Life Scale (Heinrichs et al., 1984); HAM-D: Hamilton Rating Scale for Depression (Hamilton, 1960).

^a patient – control difference, $P < 0.00001$.

^b patient – control difference, $P = 0.05$.

page. A multiple-choice question with four response alternatives for each item is located above each odorant strip. The specific stimuli, basis for their selection, as well as the reliability and sensitivity of the test, have been described in detail elsewhere (Doty et al., 1984; 1989). The UPSIT was administered birhinally by a trained technician, who released the microencapsulated stimuli, placed the stimuli under the participant's nares, and recorded the answer following the subject's response.

To assess the effect of valence on identification performance, the 40 odorants were divided into pleasant, neutral, and unpleasant valence categories using published pleasantness ratings from the UPSIT manual (Doty et al., 1984). UPSIT items from Doty's original study (1984) were rated on a Likert scale ranging from 1 to 9 with 5 designated as the neutral point. Mean item ratings were obtained and odors with mean item ratings between 4 and 6 were classified as neutral, greater than 6 were classified as pleasant, and less than 4 were classified as unpleasant. In total, 16 items were categorized as pleasant (bubble gum, cherry, banana, fruit punch, licorice, cinnamon, strawberry, chocolate, root beer, pineapple, lime, orange, wintergreen, watermelon, grape, and lemon), 15 items were categorized as neutral (menthol, mint, clove, coconut, cheddar cheese, cedar, ginger bread, lilac, peach, dill pickle, grass, pine, soap, rose, and peanut), and 9 items were categorized as unpleasant (pizza, motor oil, leather, onion, gasoline, turpentine, paint thinner, smoke, and natural gas).

2.4. Data analysis

Analysis of variance (ANOVA) was used to examine differences in the odor identification total score, with diagnosis and sex as grouping factors. To examine differences in the odor identification performance by valence category, the raw scores for pleasant, neutral, and unpleasant odors were rescaled to standard equivalents (Z-transformation) using the means and standard deviations of the healthy control group to control for differences in the number of items in each category. A multivariate repeated measures analysis of variance (MANOVA) was used to examine differences in the identification of pleasant, neutral, and unpleasant odors with diagnosis and sex as grouping factors and valence as the repeated measures factor. Within the patient group, relationships between olfactory performance and clinical measures (duration of illness, age of onset, negative symptoms, positive symptoms, general psychiatric symptoms, quality of life, and depression ratings) were assessed using Spearman rank order correlations, since several of the scales were not normally distributed.

3. Results

3.1. Odor identification

Consistent with the extant literature, patients demonstrated a significant deficit in total UPSIT performance relative to controls ($F[1,60] = 24.33, P < 0.001$). No main effect was seen for sex ($F[1,60] =$

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