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ORIGINAL PAPER

Olfactory identification and preference in bipolar disorder and schizophrenia

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Abstract Olfactory identification deficit appears to be an enduring feature of schizophrenia, but it is unclear whether it is specific to schizophrenia or present in psychotic disorders in general. The aim of the present study was to compare olfactory identification and olfactory preference in schizophrenia and bipolar disorder. Individuals with schizophrenia or bipolar disorder and demographically matched healthy participants were given the University of Pennsylvania Smell Identification Test (UPSIT) to assess olfactory identification ability. To examine olfactory hedonic judgment, participants were also asked to indicate their preference for each UPSIT item on a 5-point rating scale, immediately after odor identification. Clinical symptoms and social competence were also assessed. Both schizophrenic and bipolar groups showed olfactory identification deficits compared with the healthy controls, but schizophrenic patients were more impaired than bipolar patients on the UPSIT accuracy. Interestingly, both bipolar and schizophrenic patients rated odors to be more pleasant than did healthy controls, but all groups preferred odors that they could correctly identify to unidentified smells. Restricted range of preference ratings was associated with the severity of negative symptoms in schizophrenia, and with mania in bipolar disorder. Social competence was associated with better olfactory identification performance. These findings suggest that olfactory identification and preference are compromised in bipolar disorder as well as in schizophrenia, but the precise nature of these abnormalities needs to be further elucidated.

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Introduction

Olfactory deficits have been implicated in major psychiatric disorders including schizophrenia [1–3] and depression [4–6]. Moreover, the brain areas involved in olfactory processing including the orbitofrontal cortex (OFC) and temporal regions overlap with the abnormal neural circuitry implicated in these disorders [7, 8].

Behavioral assessment of olfactory function can occur at "peripheral" (e.g., acuity, detection, and sensitivity) or "central" (e.g., identification and memory) levels [9]. In the case of schizophrenia, deficits in olfactory identification have been most reliably demonstrated [1, 2, 7] compared with problems in more peripheral functions, such as olfactory sensitivity. For example, although some studies have reported reduced olfactory sensitivity or acuity [10–14], there is much greater support for intact odor sensitivity in schizophrenia [15–21]. Evidence for olfactory identification deficit in schizophrenia appears to be more robust and solid. Odor identification deficits have been reported in schizophrenia patients in spite of intact olfactory sensitivity [16, 19]. Odor identification deficits in schizophrenia are not attributable to reduced olfactory sensitivity [11], and there seems to be no consistent relationship between olfactory sensitivity and identification abilities [22]. Moreover, odor identification deficits in schizophrenia are not caused by task complexity [23], smoking [24, 25, 28], medication status [24, 26–28], or illness duration [24, 26], even if these factors partly contribute to the problem in some patients. There is a possibility that cognitive problems could exacerbate odor identification deficits in

schizophrenia. For example, Pantelis and Brewer [29] reported an association between odor identification performance and neuropsychological indices of frontal lobe functions, but simple impairments in attention or executive functions alone cannot account for odor identification deficits [30–32].

Although olfactory identification deficit is clearly established in schizophrenia, it is unclear whether it is a feature of psychosis in general and extends to bipolar disorder. To date, very little is known about olfactory function in bipolar disorder. Hurwitz and colleagues [33] reported intact olfactory identification in 10 bipolar disorder patients, but a more recent study paints a more complicated picture of olfactory functioning in this disorder. Krüger et al. [34] examined event-related potentials (ERP) during olfactory processing in euthymic bipolar disorder participants with and without a history of event-triggered episodes and found that the patients with event-related episodes ($n = 7$) had *increased* olfactory sensitivity than those bipolar patients without such episodes ($n = 9$), but due to the very small sample size, it is difficult to draw any firm conclusions.

However, additional information about olfactory function in bipolar disorder may be gleaned from first-episode psychosis studies. Olfactory deficits have been reported in first-episode affective psychosis patients [35]. These studies indicate that impairment in olfactory identification ability is present at the onset of psychotic illness and is not specific to schizophrenia or schizophreniform disorder, because affective psychosis patients show similar deficits. Moreover, the olfactory identification deficit appears to persist even after the first-episode patients are stabilized on antipsychotic medication. These results suggest that olfactory identification deficit may also be present in chronic bipolar disorder, but this possibility has not been directly examined.

Olfactory deficits in schizophrenia are associated with affective factors, such as the severity of negative symptoms, diminished social drive, and impaired social functioning [36–38]. This pattern of olfactory and socio-affective impairments is consistent with abnormalities of the orbitofrontal cortex [39]. Moreover, the orbitofrontal cortex (OFC) plays an important role in olfactory processing. Neuropsychological studies with OFC lesion patients have shown impaired odor identification with preserved threshold ability in these patients [40, 41]. Similarly, neuropsychological data suggest that the OFC mediates olfactory identification in schizophrenia [42]. In healthy humans, the OFC has been found to be involved in odor identification, odor discrimination, judgment of the hedonic value of odors, and odor memory [43, 44].

The OFC is involved in the monitoring of reward and hedonic processing [45]. Hedonic processing with respect to olfaction is impaired in schizophrenia [46]. Moberg and colleagues [24] reported that schizophrenic patients rated the pleasantness of olfactory stimuli abnormally, despite being nearly identical to controls with respect to intensity judgment. Rupp et al. [11] found that male patients with schizophrenia gave more positive olfactory preference ratings. Similarly, Doop and Park [47] reported that abnormal hedonic preference judgment of odors was correlated with negative symptoms in schizophrenic patients. Specifically, they found that the range of preference ratings was reduced in schizophrenia, even though schizophrenic patients gave more positive ratings than did healthy controls. A PET study [48] reported that schizophrenia patients had deficits in hedonic valence judgment, which was associated with aberrant frontolimbic activation.

There is good evidence for neuropsychological and neuroanatomical deficits in bipolar disorder see [49, 50] that implicate abnormal frontal cortex [51, 52], especially the OFC [53–55]. Individuals with bipolar disorder show alterations of prefrontal cortical volume [56], altered white matter connectivity in the frontal cortex [51], and reduced frontal cortical activity during cognitive challenge tasks [57–59]. Bipolar disorder is also characterized by abnormal hedonic processing [60] and hedonic processing mediated in part by the OFC [44, 61, 62]

Given the accumulating evidence for the involvement of the OFC and abnormal hedonic processing in bipolar disorder, as well as the recent data from first-episode psychosis studies that implicate olfactory deficits in affective psychosis, we hypothesized that individuals with bipolar disorder would show abnormal olfactory processing. The present study investigated olfactory identification and preference in demographically matched groups of bipolar disorder, schizophrenia, and healthy participants.

Methods

Participants

Twenty-two healthy participants (CO) were recruited via advertisement. These individuals were screened for previous history of psychiatric conditions, neurological disorders, drug use, traumatic head injury, and IQ < 75. Twenty individuals who met the DSM-IV [63] criteria for bipolar disorder (BP) and 27 participants with schizophrenia (SZ) who met the DSM-IV criteria for schizophrenia were recruited from local outpatient clinics. Exclusion criteria for BP and SZ were co-morbidity with other Axis-I disorders, neurological disorders, current drug use, traumatic head injury, and IQ < 75.

No participants displayed signs of upper respiratory infections, nasal allergy, or other complications that may

alter olfactory ability. All participants were instructed to not smoke immediately preceding study participation.

There were no significant differences among the three groups in age (F (2, 66) = 0.39, $P = 0.68$), years of education (F (2, 66) = 1.58, $P = 0.21$), IQ (F (2, 66) = 2.19, $P = 0.12$), or the proportion of women ($\chi^2 = 0.20$, $P = 0.90$).

Although there was a group difference in the number of smokers overall ($\chi^2 = 6.80$, $P = 0.04$), this was due to the difference between CO and the psychosis groups, and there was no significant difference between BP and SZ in the proportion of smokers ($\chi^2 = 0.40$, $P = 0.53$).

All SZ and 10 BP patients were taking antipsychotic medications including olanzapine, risperidone, quetiapine, ziprasidone, aripiprazole, and thiothixene. For those who were taking antipsychotic drugs, there was no significant group difference in the chlorpromazine (CPZ) equivalent dose (F (1, 45) = 0.27, $P = 0.61$). Eight BP patients were taking mood stabilizers including carbamazepine, divalproex**,** lithium, and lamotrigine. Two BP patients were unmedicated.

There was a trend towards a significant difference between SZ and BP in the duration of illness (F (1, 45) = 2.93, $P = 0.09$).

Please see Table 1 for participant demographic information. All participants provided written informed consent approved by the Vanderbilt University Institutional Review Board and were paid.

Materials and procedure

After informed consent procedure, all participants filled out a demographics form. They were given instructions for the UPSIT and odor preference tasks before administering the UPSIT [64, 65] to assess odor identification and preference. In addition, the Wechsler Abbreviated Scale of Intelligence (WASI; [66]) was given to estimate general intellectual functioning. BP and SZ patients were interviewed ±2 weeks of the UPSIT administration to evaluate the severity of clinical symptoms. All participants understood the task procedure before they were allowed to begin.

Olfactory identification and preference

The UPSIT is a standardized, recognition-format, multiple-choice measure of odor identification ability. It is reported to have the highest reliability of any olfactory test [64, 65]. Its test–retest reliability in healthy participants is reported as high as 0.92 for 6-month intervals [64]. UPSIT consists of 40 microencapsulated odor patches. On each page of the UPSIT, there is one odor patch accompanied by 4 words. Subjects were asked to scratch the patch with a pencil provided with the UPSIT kit, in order to release the odor and choose from the 4 nouns to identify it. On each page of the UPSIT, we printed a Likert-like scale below the odor patch so that immediately after identifying an odor, participants could make a preference judgment for that particular odor on a five-point rating scale, which ranged from −2 (dislike a lot) to +2 (like a lot). A rating of zero indicated neutral preference, being neither pleasant nor unpleasant.

All participants were administered the UPSIT under supervision, on an item-by-item basis, thus limiting the possibility of errors due to inattention. Each participant worked through the 40 UPSIT items at his/her own pace.

A particular strength of the UPSIT is that it provides an olfactory diagnosis based on comparing the patient's test score with normative data, providing a percentile score of an individual relative to his or her age-matched norm group [64]. Furthermore, a clinician can distinguish individuals

Table 1 Demographic and clinical characteristics of participants

Means (SD)	Schizophrenia $n = 27$	Bipolar $n = 20$	Control $n = 22$	P value (2-tailed)
Age	37.1 (8.4)	34.6 (11.3)	35.5 (9.8)	0.68
I.Q. (WASI)	98.7 (11.6)	105.7 (12.1)	104.1 (12.9)	0.12
Years of education	13.7 (2.6)	14.0 (2.5)	14.9 (2.4)	0.21
Zigler social competence	3.0 (1.6)	4.5 (1.8)	5.8 (1.9)	0.001
BPRS	20.6 (15.0)	16.3 (9.5)	NA	0.14
SAPS	21.9 (20.7)	NA	NA	NA
SANS	23.7 (15.9)	NA	NA	NA
YMRS	NA	9.9 (8.0)	NA	NA
HRSD	NA	11.2 (5.7)	NA	NA
Years of illness	15.9 (7.4)	12.0 (8.2)	NA	0.09
% Smokers	59.3%	50%	22.7%	0.04
% Women	44.4%	50%	50%	0.90
CPZ equivalent (mg/kg/day)	330.6 (301.5)	271.7 (193.9)	NA	0.61

with a normal sense of smell (normosmia) from those with different levels of deficit (mild, moderate, and severe microsmia) or loss (anosmia). The UPSIT can also distinguish probable malingerers from those with true olfactory deficits. Olfactory diagnosis is made from the UPSIT by classifying patients into diagnostic categories, depending on the score achieved. Normosmia is defined by a score >34 for females and 33 for males. Mild microsmia is defined by a score of 31–34 for females and 30–33 for males. Moderate microsmia is defined by a score of 26–30 for females and 26–29 for males. Severe microsmia is defined by a score of 19–25 for females and males. Total anosmia is defined by a score of 6–18. Probable malingering is defined by a score of 0–6. However, a recent Rasch psychometric analysis on schizophrenic and healthy individuals identified three statistically distinct levels of ability that approximately correspond to UPSIT's normosmia, microsmia, and anosmia [2]. For the present study, we decided to categorize our participants according to both schemes, since very little was known about olfactory identification ability in bipolar disorder.

Clinical symptoms

Clinical interviews were conducted ±2 weeks of administering the UPSIT. Symptoms were assessed by the following: Scale for the Assessment of Positive Symptoms (SAPS; [67]), Scale for the Assessment of Negative Symptoms (SANS; [68]), the Brief Psychiatric Rating Scale (BPRS; [69]), the Young Mania Rating Scale (YMRS; [70]), and the Hamilton Rating Scale for Depression (HRSD; [71]). See Table 1 for clinical ratings.

Social competence

The Zigler Social Competence Scale [72] uses demographic information to estimate social functioning based on years of education, occupational status, history of employment, and marital status. See Table 1 for Zigler Scores.

Results

Demographic and clinical information are summarized in Table 1. Olfactory identification accuracy (number of correct items), mean preference ratings, and the range of preference scores were compared across the three diagnostic groups (See Table 2). Since several studies have previously reported sex difference in olfactory identification in schizophrenia [15, 23], we also examined potential gender effects. All tests were two-tailed unless otherwise specified.

Olfactory identification accuracy

We examined the effects of psychiatric diagnostic groups and gender on UPSIT accuracy with MANOVA. There was a significant main effect of diagnostic group (F (2, 63 = 8.30, $P = 0.006$), but there was no main effect of gender (F (1, 63) = 0.44, $P = 0.51$) or interaction between group and gender (F (2, 63) = 0.88, $P = 0.42$). SZ made more errors than did CO (F (1, 47) = 14.12, $P = 0.0005$). BP were more accurate than SZ (F (1, 45) = 5.41, $P = 0.025$). CO were more accurate than BP (F (1, 40) = 4.43, $P = 0.043$). See Table 2.

We then grouped the participants into the five diagnostic UPSIT categories (normosmia, mild microsmia, moderate microsmia, severe microsmia, and total anosmia). There was a significant difference in the distribution of the three groups across the five UPSIT categories ($\chi^2 = 17.2$, $P = 0.025$). Twenty out of 22 CO were normosmic, and 2 were mildly microsmic. Seventeen out of 20 of BP had normosmia, and 3 had mild microsmia. In contrast, only 13 out of 27 of SZ were normosmic. Nine SZ had mild microsmia, 2 had moderate microsmia, 2 had severe microsmia, and 1 had total anosmia.

The results did not change when we categorized our participants according to the three levels of olfactory identification ability as identified by Minor et al. [2]. There was a significant difference in the distribution of SZ, BP, and CO across the three levels of abilities ($\chi^2 = 14.1$,

Table 2 Olfactory identification and preference performance

Mean (SD)	SZ	BP	CO
No. of correct items on UPSIT	32.3 (4.7)	34.9 (2.3)	36.3 (1.9)
Odor preference ratings*	+0.59 (0.42)	+0.54 (0.25)	+0.30 (0.32)
Preference rating for correct items	+0.67 (0.40)	+0.62 (0.25)	+0.38 (0.35)
Preference ratings for incorrect items	+0.11 (0.74)	+0.08 (0.53)	−0.36 (0.62)
Range of preference**	4.67 (0.62)	4.70 (0.57)	4.68 (0.65)

* Preference ratings: −2 *dislike a lot*, −1 *dislike somewhat*, 0 *neutral*, +1 *like somewhat*, and +2 *like a lot*

** Range of preference rating score could vary from minimum of 1 to maximum of 5

Table 3 Distribution of participants across the five UPSIT diagnostic categories as suggested by Sensonics (Doty [65])

	SZ	BP	CO
Normosmia	13	17	20
Mild microsmia	9	3	2
Moderate microsmia	2	0	0
Severe microsmia	2	0	0
Total anosmia	1	0	0
Probable malingering	0	0	0

Table 4 Distribution of participants across the three diagnostic categories proposed by Minor et al. [2]

	SZ	BP	CO
Normosmia	13	17	20
Microsmia	13	3	2
Anosmia	1	0	0

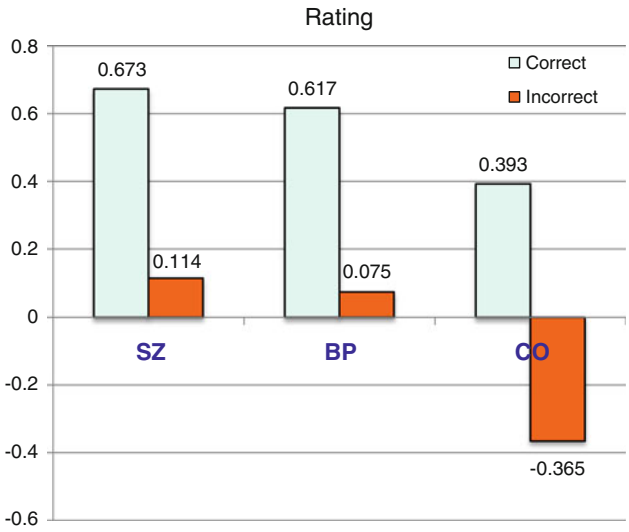

Fig. 1 Mean preference ratings for correctly and incorrectly identified odors

$P = 0.007$). Twenty out of 22 CO were normosmic, and 2 were in the microsmia category. Seventeen out of 20 BP were normosmic, and 3 were microsmic. Thirteen out of 27 SZ had normosmia, but 13 were in the microsmia category and 1 had anosmia.

This pattern of distribution suggests that a greater number of SZ suffer from more severe forms of olfactory identification deficits than do BP. No subject was found in the malingering category. See Tables 3 and 4.

Olfactory preference judgments

There was a significant main effect of psychiatric diagnostic groups on preference ratings (F (2, 63) = 4.08, $P = 0.022$). There was a trend towards significant main effect of gender such that women tended to be more positive (F (1, 63) = 3.92, $P = 0.052$), but there was no interaction between gender and group (F (2, 63) = 1.01, $P = 0.37$).

BP rated odors significantly more positively than did CO (F (1, 40) = 6.91, $P = 0.012$). SZ also rated odors significantly more positively than did CO (F (1, 47) = 6.50, $P = 0.014$). There was no significant difference between the preference ratings of BP and SZ (F (1, 45) = 0.18, $P = 0.67$). These results suggest that psychosis patients tend to judge odors to be more pleasant than do CO. See Table 2.

We then asked whether knowing an odor might affect one's preference for it. We examined the mean preference ratings for correctly identified and incorrectly identified odors with repeated-measures ANOVA. There was a significant main effect of diagnostic group (F (2, 63) = 5.10, $P = 0.01$) and a significant main effect of knowledge of odors (F (1, 63) = 66.7, $P = 0.0001$), but there was no interaction between group and knowledge. All three groups preferred odors that they could correctly identify to unknown smells. See Table 2; Fig. 1.

As shown in Fig. 1, SZ rated correctly identified items more positively than did CO (F (1, 47) = 7.05, $P = 0.01$). BP also rated correctly identified odors more positively than did CO (F (1, 40) = 6.28, $P = 0.017$). There was no significant difference between BP and SZ (F (1, 45) = 0.30, $P = 0.58$) in their preference ratings for correctly identified items. It must be noted that not all participants made UPSIT errors. Nevertheless, there was a group difference in the preference ratings for incorrectly identified items (F (2, 66) = 3.28, $P = 0.044$). BP gave more positive preference ratings than did CO on incorrectly identified items (F (1, 38) = 5.37, $P = 0.026$). SZ also showed more positive ratings than did CO (F (1, 45) = 5.03, $P = 0.03$), but BP and SZ did not differ (F (1, 45) = 0.04, $P = 0.84$).

These results suggest that psychosis patients tend to rate odors to be more pleasant than do healthy controls, regardless of whether they correctly identified these items or not. But their preference for identified odors compared with unknown odors is not different from that of controls. See Fig. 1.

Range of preference ratings

To further examine hedonic processing, we examined the range of preference ratings made by the participants. We hypothesized that restricted hedonic experiences would be reflected in reduced range of preference ratings. There were five possible rating scores that participants could use to

indicate odor preference, ranging from −2 to +2. A range score corresponding to the use of the 5 ratings was determined for each subject; the minimum range score was 1 and the maximum score 5. For example, participants using only three ratings throughout the entire UPSIT (e.g., −1, 0, and +1) received a range score of three. Participants using all ratings received a range score of five. There was no significant difference in the range of preference ratings among the three groups (F (2, 66) = 0.016, P = 0.98). See Table 2.

Olfactory function, social competence, and clinical symptoms

There was no significant difference between BP and SZ on the BPRS (F (1, 45) = 2.25, P = 0.14), which suggests that the two groups were matched on the severity of psychotic symptoms.

Correlations between the Zigler social competence scale scores, UPSIT accuracy, and preference ratings were computed, across the groups and within each group separately. For all groups combined, social competence was correlated with UPSIT accuracy (r = 0.43, P < 0.0008), but this association is likely driven by the fact that CO have much greater Zigler scores compared with the SZ. Within each group, the only significant association observed was between the Zigler score and the range of preference ratings in SZ (r = 0.46, P = 0.026); this is of some interest because it suggests that restricted hedonic preference range may be associated with worse social competence.

Correlations were also computed between clinical symptoms, UPSIT accuracy, and preference ratings for SZ and BP. UPSIT accuracy and BPRS were not correlated, when the two groups were combined (r = −0.005, P = 0.98).

In SZ, the range of preference ratings was inversely correlated with SANS (r = −0.52, P = 0.006), but not with SAPS (r = 0.07, P = 0.73) or BPRS (r = 0.06, P = 0.76). This suggests that those who have more negative symptoms tend to have a more restricted hedonic preference range.

In BP, range of preference scores correlated significantly with YMRS (r = −0.47, P = 0.039) such that increased manic symptoms were associated with a more restricted range of preference ratings. Zigler social competence score was inversely correlated with YMRS (r = −0.49, P = 0.03), and BPRS at a trend level (r = −0.44, P = 0.056). Within BP, we divided them into those with and without psychotic features and found no significant differences between these two groups on the BPRS (F (1, 18) = 2.59, P = 0.13), YMRS (F (1, 18) = 1.09, P = 0.31), HRSD (F 1, 18) = 1.07, P = 0.31), UPSIT scores (F (1, 18) = 1.65, P = 0.22), or preference ratings (F (1, 18) = 0.10, P = 0.76).

Potential effects of smoking

There was a group difference in the proportion of smokers although the % of smokers was not different between BP and SZ groups, so we examined the potential effect of smoking status on UPSIT score. There was no main effect of smoking on olfactory identification (F (1, 63) = 0.44, P = 0.51) or an interaction between group and smoking status (F (2, 63) = 0.59, P = 0.56).

Potential medication effect

All SZ and about half of BP patients were taking antipsychotic drugs. Eight BP patients were on mood stabilizers, and 2 were unmedicated. We examined the patients who were taking antipsychotic drugs and computed correlation between CPZ equivalent dose and UPSIT scores. We found no significant associations among CPZ dose, UPSIT accuracy, preference ratings, or range score (all P values >0.41). We then compared the BP patients on antipsychotic medication with those taking mood stabilizers and found no significant differences on the BPRS (F (1, 17) = 0.03, P = 0.88), YMRS (F (1, 17) = 0.93, P = 0.35), HRSD (F (1, 17) = 1.30, P = 0.27), or UPSIT scores (F (1, 17) = 0.13, P = 0.73). However, from these results, it is premature to draw any conclusions about potential medication effects on olfactory functioning in schizophrenia or bipolar disorder. The potential role of psychotropic medications in olfactory identification and preference must be further examined in the future.

Discussion

Olfactory identification deficits were present in individuals with schizophrenia and bipolar disorder compared with healthy participants, but the effect size of the deficit was much greater for the schizophrenic patients (Cohen's d = 1.16) than for the bipolar patients (Cohen's d = 0.72). In addition, the effect size of the difference between bipolar and schizophrenic groups was also large (Cohen's d = 0.70). The distribution of normosmic, microsmic, and anosmic participants suggests that the frequency of individuals with more severe odor identification deficit may be elevated in schizophrenia compared with bipolar disorder (see Tables 3, 4). These results might reflect a continuum of odor identification ability that varies with the severity of psychosis, since a significant proportion of bipolar patients in our study had a history of psychotic symptoms. However, there was no significant

correlation between BPRS and UPSIT scores, when the two diagnostic groups were combined or examined separately. Moreover, when we compared bipolar patients with and without psychotic features, we found no differences in their UPSIT scores.

With respect to olfactory preference, bipolar and schizophrenic patients showed altered hedonic response to odors, rating them more positively than did the healthy controls. Since there was no group difference in the range of preference ratings, elevated positive preference ratings of schizophrenic and bipolar patients are unlikely to be caused by an incomplete or impaired use of the full preference ratings scale. Regardless of psychiatric diagnosis, there was a strong relationship between odor identification and preference such that correctly identified smells were significantly preferred to unknown odors.

We also asked whether restricted hedonic range might be associated with clinical symptoms and social functioning. The range of preference ratings was not different among the three groups, but nevertheless restricted range may play a role in olfactory hedonic processing in psychotic patients. In schizophrenia, restricted range of preference ratings was related to increased negative symptoms, characterized by blunted affect, anhedonia, avolition, and anergia, but not with positive symptoms. In bipolar patients, restricted range of preference ratings was associated with elevated manic symptoms, but not with depressive symptoms. This finding is counterintuitive at first since mania is associated with euphoria and heightened reward sensitivity, and it is not immediately obvious why restricted repertoire or range of emotional experience should be correlated with mania. However, reduced range of preference ratings might reflect a narrowed window of emotional experiences regardless of valence.

There are several limitations to the present study. First, all schizophrenic and about half of the bipolar patients were taking antipsychotic medication that may influence odor identification and preference, but medication status and CPZ equivalent dose were not associated with odor identification or preference. We did not find any differences in olfactory functioning in bipolar patients who were taking antipsychotic drugs versus those who were taking mood stabilizers. Past research suggests that antipsychotic medication does not cause olfactory identification deficit [25, 35], and there is no evidence that mood stabilizers affect olfactory functioning [73]. However, future studies should examine potential medication effects more closely in a dose-dependent manner.

Another limitation concerns smoking. The proportion of smokers was significantly lower in the control group, although the % of smokers was not different between bipolar and schizophrenic groups. Smoking may reduce odor identification ability depending on the duration and dose [74]. All smokers in our study refrained from smoking immediately before participating in the experiment, so there was no acute effect of smoking on the olfactory performance, but more chronic effect cannot be eliminated since we do not have detailed information on the dose and duration of smoking history on our subjects. Interestingly, smoking may affect olfactory functioning differentially for psychotic patients compared with healthy controls. Smoking appears to normalize olfactory identification ability as assessed by UPSIT in psychotic patients; patients who were smokers scored higher on the UPSIT than did non-smokers, whereas non-smoking healthy controls scored higher than control smokers [75]. A similar phenomenon has been previously observed [25, 36]. Therefore, it is possible that in our bipolar and schizophrenic patients, smoking may have diminished, rather than exacerbated their olfactory identification deficits. But further research is necessary to carefully address the potential effects of smoking on olfactory identification and hedonic processing in schizophrenia and bipolar disorder.

A third limitation is the relatively small sample size of this study. It must be noted that the recruitment of participants was achieved in two waves: 2007–2009 ($n = 62$) and 2009–2010 ($n = 7$). The second wave of recruitment was initiated to increase the sample size and did not change any of the results. Nevertheless, it is important to investigate olfactory functioning in a much larger group of bipolar participants in the future.

To our knowledge, ours is the first study to examine olfactory identification and preference in bipolar disorder and to compare olfactory functioning in demographically matched bipolar and schizophrenia patients. We found olfactory identification deficit and altered hedonic judgment in both disorders, but the odor identification impairment was less severe in bipolar disorder. Future studies are necessary to address the potential limitations of the present study and to extend our understanding of the etiology of olfactory deficits in psychosis.

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