



The effect of odor valence on olfactory performance in schizophrenia patients, unaffected relatives and at-risk youth



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ABSTRACT

Given the presence of odor identification impairment in individuals with schizophrenia and recent evidence of aberrant odor hedonic processing, the aim of this investigation was to examine the influence of valence and intensity on odor identification in schizophrenia patients, their first-degree family members, and young persons at clinical risk for psychosis. Participants completed the 16-item Sniffin' Stick Odor Identification Test. A logistic regression was conducted to assess the influence of valence and intensity on odor identification accuracy. Identification performance in the schizophrenia patients and youths at clinical risk for psychosis was significantly influenced by odor valence, but not intensity. Identification accuracy in first-degree family members was not influenced by valence or intensity. These data suggest that abnormalities in odor valence perception may represent an environmentally-mediated marker for hedonic disturbance that could have predictive utility in future conversion to psychosis. Further research examining the utility of odor valence measures as markers for psychosis risk is warranted.

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1. Introduction

Prior studies have indicated that the ability to assign valence ratings to pleasant, but not unpleasant, odors is aberrant in schizophrenia (Crespo-Facorro et al., 2001). Notably, deficit syndrome patients under-rated the pleasantness of pleasant odors relative to non-deficit patients and controls (Strauss et al., 2010). We previously examined how schizophrenia patients rate the pleasantness of amyl acetate, a banana-like odor, at varying concentrations (Kamath et al., 2013; Moberg et al., 2003). Patients under-appreciated the pleasantness of amyl acetate at concentrations judged as pleasant by controls and over-rated its pleasantness at the concentration judged by controls, as relatively unpleasant (Kamath et al., 2013). In contrast, first-degree family members of

schizophrenia patients showed normal odor hedonic ratings (Kamath et al., 2013; Schneider et al., 2007).

Given that odor hedonic processing and odor identification performance are disrupted in schizophrenia (Moberg et al., 2013), recent studies have examined whether odor identification is influenced by valence. In one prior study, we found that patients were less accurate when identifying pleasant and neutral odors, but were not impaired in their ability to identify unpleasant odors (Kamath et al., 2011c). Similarly, schizophrenia inpatients showed a selective deficit for identifying pleasant, but not unpleasant, odors on a brief measure of odor identification (Kamath et al., 2011a). However, a third study, which used only a limited subset of these odorants, found no influence of valence on odor identification ability (Strauss et al., 2010). Results are thus somewhat inconsistent. It is also unclear if this pattern of deficits extends to first-degree relatives of schizophrenia patients or to at-risk samples, two cohorts in which attenuated odor identification performance has been repeatedly observed (Brewer et al., 2003; Kopala et al., 2001). The aim of the current study was to examine the influence of valence and intensity on odor identification performance in a larger cohort of schizophrenia patients and separate cohorts of

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non-ill first-degree relatives and youths at risk for psychosis. One limitation of all prior studies was the use of a categorical classification of odors as either pleasant or unpleasant. We therefore examined the influence of valence and intensity using continuous, rather than categorical, normative ratings of both odor attributes.

2. Method

2.1. Participants

2.1.1. Adult cohort

The sample included sixty-four individuals meeting DSM-IV criteria for schizophrenia, 27 first-degree relatives of schizophrenia patients, and 54 healthy individuals drawn from the available subject pool at the University of Pennsylvania Schizophrenia Research Center (SRC). All subjects who participate in SRC studies are screened for any history of neurological disorder, head trauma with loss of consciousness, substance abuse within the preceding six months, positive urine drug screen, or medical conditions affecting cerebral functioning. Subjects who present with any of these conditions are not enrolled. On average 22.6% of potential subjects are excluded. None of the participants in this study had any obvious craniofacial abnormality (e.g., septal deviation) or acute respiratory condition. All study procedures were approved by the University of Pennsylvania Institutional Review Board (IRB), in compliance with the Declaration of Helsinki's ethical standards in the treatment of human research participants. Participants provided written informed consent following a full explanation of the study procedures. Data from these subjects were included in a previous publication (Kamath et al., 2011b).

Consensus best-estimate DSM-IV diagnoses for schizophrenia were established using a semi-structured diagnostic interview (Structured Clinical Interview for DSM-IV – Patient Edition; First et al., 1996), medical record review, and available information from family and care providers. Patients were administered Scales for the Assessment of Negative Symptoms (SANS; Andreasen, 1984a) and Positive Symptoms (SAPS; Andreasen, 1984b). Controls and family members were assessed for current or past DSM-IV Axis I or Axis II disorders (First et al., 1995) and excluded for any current Axis I disorder, psychotropic medication use, or history of substance abuse or dependence in the preceding 6 months. Controls were also excluded if they had an Axis II cluster A disorder or a first-degree relative with a psychotic illness. A prior history of depression (major depressive disorder or depression not otherwise specified) was not exclusionary, provided there was no current clinical symptomatology or pharmacologic treatment. Three controls and 3 family members had diagnoses of past depression.

The family member cohort was comprised of 5 parents, 18 siblings, and 4 offspring of schizophrenia patients. Four subjects from our family member cohort were biological relatives of our schizophrenia cohort.

Groups did not differ in age [$F(2,142) = 1.52, p = 0.22$], sex composition [$\chi^2 = 4.50, df = 2, p = 0.11$], or race [$\chi^2 = 9.64, df = 6, p = 0.14$]. Groups differed in educational attainment [$F(2,142) = 8.64, p < 0.01$]. Controls had more education than patients [$F(1,142) = 17.27, p < 0.01$]. Family members had an intermediate level of education, but did not differ significantly from either controls [$F(1,142) = 3.04, p = 0.08$] or patients [$F(1,142) = 2.42, p = 0.12$]. The three groups did not differ in parental education [Wilks' Lambda = 0.95, $F(4,228) = 1.35, p = 0.25$], an estimate of potential that minimizes the confound of illness (Resnick, 1992). Group differences in smoking (packs/day) were statistically significant [$F(2,142) = 6.02, p < 0.01$]. Patients reported a higher smoking burden than controls [$F(1,142) = 10.96, p < 0.01$] and family members [$F(1,142) = 4.77, p = 0.03$; see Table 1]. Schizophrenia patients were either unmedicated ($n = 4$), taking atypical antipsychotic medication ($n = 8$), typical antipsychotic medication ($n = 39$), a combination of both typical and atypical antipsychotic medications ($n = 2$), or other psychotropic medications at the time of testing ($n = 10$). Medication dosages were converted to chlorpromazine equivalents using published reference tables (Kroken et al., 2009). Medication data were unavailable for one individual and medication dosages were unknown for three individuals.

2.1.2. Adolescent and young adult cohort

Individuals who exhibited prodromal symptoms but did not meet criteria for a DSM-IV axis I psychotic disorder (Clinical Risk; CR, $n = 15$), and symptom-free comparison subjects (Low Risk; LR, $n = 14$) were recruited to the Neurodevelopment in Adolescence and Young Adulthood (NAYA) research program at the University of Pennsylvania. Informed consent was obtained from all young adult participants; parental consent and child assent were obtained for subjects under the age of 18. Exclusion criteria noted for the adult cohort above were applied, except that DSM-IV substance use and mood or anxiety disorders were not exclusionary for CR subjects. Five CR subjects had a depressive disorder and 2 had substance use disorders. Two CR subjects had a prior history of depression. Individuals were administered the Wechsler Test of Adult Reading (WTAR; Wechsler, 2001) to obtain an estimate of verbal intellectual functioning. Participants with a standard score below 70 were excluded.

Trained diagnosticians administered the Diagnostic Interview for Genetic Studies (DIGS; Nurnberger et al., 1994), the Structured Clinical Interview for DSM-IV-F (Anxiety) Module (SCID; First et al.,

Table 1

Demographic and clinical characteristics for schizophrenia patients, first-degree family members, and healthy comparison subjects.

Characteristic	Schizophrenia probands ($n = 64$)			Family members ($n = 27$)			Healthy controls ($n = 54$)		
	Mean	SD	n	Mean	SD	n	Mean	SD	n
Age (years)	36.97	10.82		36.30	16.33		33.20	10.87	
Sex (Males/females)			36 28			9 18			30 24
Education level ^a (years)	12.67	2.28		13.44	1.93		14.33	2.14	
Mother's education (years)	13.02	2.91		12.33	2.73		14.16	2.42	
Father's education (years)	13.04	3.90		13.14	3.72		13.69	3.06	
Packs/day ^a	0.47	0.65		0.21	0.37		0.15	0.37	
Illness duration (years)	15.51	10.19							
Age of onset (years)	21.47	6.70							
SANS ^b total	27.70	17.05							
SAPS ^c total	18.25	16.66							

^a Significant difference ($p < 0.05$).

^b SANS = Scale for the Assessment of Negative Symptoms (Andreasen, 1984a).

^c SAPS = Scale for the Assessment of Positive Symptoms (Andreasen, 1984b).

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