Olfactory Identification Deficits in First-Episode Psychosis May Predict Patients at Risk for Persistent Negative and Disorganized or Cognitive Symptoms

Kimberley P. Good, Ph.D.
David Whitehorn, Ph.D., M.Sc.N.
Qing Rui, M.D.
Heather Milliken, M.D., F.R.C.P.C.
Lili C. Kopala, M.D., F.R.C.P.C.

Objective: One-third of patients with a schizophrenia spectrum disorder have a measurable olfactory identification deficit at first examination. The authors studied the relationship of this deficit to symptom remission after 1 year of treatment.

Method: Fifty-eight patients naive to antipsychotic medication who entered the Nova Scotia Early Psychosis Program were symptomatically rated with the Positive and Negative Syndrome Scale (PANSS) (at baseline and 1 year). At baseline, the University of Pennsylvania Smell Identification Test (UPSIT) was also completed. Remission was determined for four symptom factors derived from the PANSS (positive, negative, cognitive/disorganized, and anxiety/depression). Patients with and without remission were compared on UPSIT scores.

Results: Patients with nonremission of negative and cognitive/disorganized symptoms had significantly lower baseline UPSIT scores compared with pateints with remission. UPSIT scores were unrelated to remission of positive or anxiety/depression symptoms.

Conclusions: UPSIT scores can be used to identify patients at risk for persistent negative and disorganized/cognitive symptoms.

(Am J Psychiatry 2006; 163:932–933)

Impairment in odor naming, as measured by the University of Pennsylvania Smell Identification Test (UPSIT) (1), has been reported in patients with a first episode of a schizophrenia spectrum disorder (2). However, the clinical significance of this olfactory identification deficit and the relevance of the UPSIT to clinical practice are less clear.

The use of the UPSIT results to identify clinically relevant subgroups has been examined in a study with patients at "ultra-high risk" of developing a psychotic disorder (3). When followed prospectively, the patients who eventually developed a psychotic illness had poorer premorbid UPSIT performance than those who developed other psychiatric disorders or who remained well.

In the current study, first-episode patients with psychosis who had not previously received antipsychotic medications were studied. UPSIT scores, measured shortly after the onset of treatment, were examined in relation to remission of symptoms after 1 year of treatment.

Method

Fifty-eight antipsychotic-drug-naive patients were recruited as they entered the Nova Scotia Early Psychosis Program, where they received clinical care based on best-practice standards (4). Written informed consent was obtained. Exclusion criteria included head injury with a loss of consciousness exceeding 5 minutes, nasal or facial fracture, and current rhinitis or sinusitis.

The Positive and Negative Syndrome Scale (PANSS) (5) was given by trained raters (with an interrater reliability of 0.8 or greater) at baseline (a drug-naive state) and after patients had received 1 year of treatment. A five-factor model of the PANSS was used (6). The factors were positive (P1, P3, P5, P6, G9), negative (N1, N2, N3, N4, N6, G7, G12), cognitive/disorganized (P2, N5, N7, G11, G12, G13, G15), anxiety/depression (G1, G2, G3, G4, G6), and excitement (P4, P7, G8, G14).

The subjects were tested with the UPSIT (1), which is composed of 40 cards, each containing a scratch-activated scent-impregnated patch and four possible answers. All subjects had a normal olfactory threshold, as assessed by the compound phenyl ethyl alcohol (score: mean=9.3, SD=2.6, normal range=8–11; unpublished data of Good et al.).

Olfactory assessment was carried out as soon as it was judged that the subject could participate without direct interference from psychotic symptoms. On average, this occurred 4 weeks after treatment initiation. Olfactory performance appears to be unaffected by exposure to antipsychotic medications (7).

Symptom remission for each PANSS-derived factor was defined as no item within the factor rated as more severe than a 3 (mild) (6, 8). With PANSS ratings at 1 year for each factor, remitted and nonremitted groups were identified. Note that this criterion for remission, while identifying patients with persistent symptoms, does not assess treatment response, defined as a change in symptom severity.

For each factor, the remitted and nonremitted groups were compared on baseline UPSIT scores with independent t tests (with correction for heterogeneity of variance where applicable). The excitement factor was not analyzed due to a 97% remission rate.

Results

The 58 patients (18 women, 40 men) were a mean age of 22.5 years (SD=4.7). After 1 year, 75% (N=44) met DSM-IV criteria for schizophrenia or schizoaffective disorder, and the remainder were diagnosed with psychosis not otherwise specified. The mean baseline UPSIT score was 34.1 (SD=4.7). After we used standardization data (1), 31% (N=18) were considered microsmatic (UPSIT score <34 of 40).

TABLE 1. University of Pennsylvania Smell Identification Test Scores for First-Episode Psychosis Remitters and Nonremitters on Each Symptom Factor

	Remitters			Nonremitters			Analysis		
Factor	N	Mean	SD	N	Mean	SD	t	df	p
Positive	43	34.0	5.2	15	34.5	3.0	0.4	56	n.s.
Negative	42	35.2	3.4	16	31.4	6.3	2.3	19[a,b]	<0.04
Cognitive-disorganized	33	35.5	3.0	25	32.3	5.8	2.6	34[a,b]	<0.02
Anxiety/depression	42	34.8	3.7	16	32.5	6.5	1.3	19[a]	n.s.
Excitement[c]	56			2					

[a] Degrees of freedom were adjusted to correct for heterogeneity of variance.
[b] Both analyses remained significant when patients who met criteria for remission at baseline were excluded from the analysis.
[c] Excitement factor was not analyzed due to a 97% remission rate.

When we compared baseline olfactory test scores, they revealed no differences between remitters and nonremitters based on positive (n.s.) or anxiety/depression (n.s.) symptoms (Table 1).

The patients who met remission criteria for the negative symptom factor had significantly higher olfactory test scores than those who did not ($p<0.04$), as did patients who met criteria for remission on the cognitive/disorganized factor ($p<0.02$) (Table 1).

Because status at baseline may have influenced the results of the 1-year analysis, the patients who met criteria for remission at baseline were excluded, and the same analyses were conducted. The results were identical to those observed by examining the total group.

The patients were also stratified based on olfactory status. For the patients who were normosmatic, 80% (N=32) had remission of negative symptoms, and 68% (N=27) had remission on cognitive/disorganized symptoms. Among microsmatic patients, the corresponding remission rates were lower: 56% (N=10) and 33% (N=6), respectively. Remission groups did not differ in terms of baseline symptom severity, except that negative symptom remitters had less severe baseline negative symptoms.

Discussion

The results highlight the clinical utility of assessing patients for olfactory identification deficits early in the course of a psychotic disorder. Olfactory identification deficits appear to serve as one marker for a subtype of patients who are characterized by less frequent remission of negative and cognitive/disorganized symptoms. In contrast, the UPSIT results were not predictive of persistent positive or anxiety/depression symptoms.

It is beyond the scope of this study to determine the relative importance of the UPSIT for other variables, including the duration of untreated psychosis, premorbid adjustment, and affective flattening (9) that may characterize patients with enduring negative symptoms. Larger groups are needed to support meaningful multivariate analysis, and such a study is currently under way in our center.

In the field of schizophrenia spectrum disorders research, few easily measured behavioral markers exist. Olfactory performance, as measured at the first episode by the UPSIT, clearly warrants further study.

Presented in part at the fourth annual meeting of the International Early Psychosis Association, Vancouver, B.C., Canada, Sept. 28, 2004 to Oct. 1, 2004. Received Nov. 4, 2004; revisions received April 15, June 29, and Aug. 29, 2005; accepted Sept. 19, 2005. From the Nova Scotia Early Psychosis Program, Department of Psychiatry, Dalhousie University, Halifax, N.S., Canada; and the Department of Psychiatry, University of British Columbia, Vancouver, B.C., Canada. Address correspondence and reprint requests to Dr. Good, AJLB, 4th Floor, 5909 Veteran's Memorial Lane, Halifax, N.S., B3H 2E2 Canada; kimpgood@dal.ca (e-mail).

Funded in part by the Canadian Institutes for Health Research (grant MOP-42461) and the National Alliance for Research on Schizophrenia and Depression, Department of Psychiatry Research Fund, Schizophrenia Society of Canada.

References

1. Doty R, Shaman P, Dann M: Development of the University of Pennsylvania Smell Identification Test: standardized microencapsulated test for olfactory function. Phys Behav 1984; 32: 489–502
2. Kopala L, Clark C, Hurwitz T: Olfactory deficits in neuroleptic naive patients with schizophrenia. Schizophr Res 1992; 8:245–250
3. Brewer WJ, Wood SJ, McGorry PD, Francey SM, Phillips LJ, Yung AR, Anderson V, Copolov DL, Singh B, Velakoulis D, Pantelis C: Impairment of olfactory identification ability in individuals at ultra-high risk for psychosis who later develop schizophrenia. Am J Psychiatry 2003; 160:1790–1794
4. Spencer E, Birchwood M, McGovern D: Management of first-episode psychosis. Adv Psychiatr Treat 2001; 7:133–142
5. Kay SR, Opler LA, Lindenmayer JP: The Positive and Negative Syndrome Scale (PANSS): rationale and standardisation. Br J Psychiatr 1989; 155:59–67
6. Whitehorn D, Brown J, Richard J, Rui Q, Kopala L: Multiple dimensions of recovery in early psychosis. Int Rev Psychiatry 2002; 14:273–283
7. Brewer WJ, Pantelis C, Anderson V, Velakoulis D, Singh B, Copolov DL, McGorry PD: Stability of olfactory identification deficits in neuroleptic-naive patients with first-episode psychosis. Am J Psychiatry 2001; 158:107–115
8. Addington J, Leriger E, Addington D: Symptom outcome 1 year after admission to an early psychosis program. Can J Psychiatry 2003; 48:204–207
9. Malla A, Norman R, Takhar J, Manchanda R, Townsend L, Scholten D: Can patients at risk for persistent negative symptoms be identified during their first episode of psychosis? J Nerv Ment Dis 2004; 192:455–463