OLFACTORY IDENTIFICATION IN SCHIZOPHRENIA

by

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Olfactory Identification in Schizophrenia

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Abstract

Olfactory identification performance and olfactory thresholds in patients with schizophrenia were investigated in this study. Three primary questions were raised: (a) Do neuroleptically medicated schizophrenic patients demonstrate significant olfactory identification deficits in the absence of olfactory acuity (threshold) deficits when compared with (i) non-schizophrenic, neuroleptically unmedicated psychiatric controls, (ii) non-schizophrenic, neuroleptically medicated psychiatric controls, and (iii) non-psychiatric controls? (b) Is there a significant difference in olfactory identification performance in the absence of a difference in olfactory acuity performance between non-schizophrenic psychiatric subjects receiving neuroleptic medication and those not receiving neuroleptic medication? (c) Do male schizophrenic patients perform significantly worse than female schizophrenic patients on olfactory identification? Seventeen male and two female schizophrenic patients from a chronic care psychiatric hospital were evaluated with the University of Pennsylvania Smell Identification Test (SIT), the pyridine test of olfactory acuity, and a questionnaire assessing medical and demographic histories. Results indicated that schizophrenic patients demonstrated significant olfactory identification deficits but no olfactory acuity deficits when compared with both (i) neuroleptically unmedicated psychiatric controls, and (ii) non-psychiatric controls, but did not demonstrate significant olfactory identification or acuity performance deficits when compared with neuroleptically medicated psychiatric controls. For non-schizophrenic psychiatric subjects receiving neuroleptic medication, olfactory identification performance but not acuity was significantly lower than that of psychiatric subjects not receiving neuroleptic medication. Both female

schizophrenic patients scored in the microsmic (below normal range) olfactory identification range, however this did not provide sufficient data to support a statistical analysis of gender differences for olfactory identification performance. The results are discussed in the context of the notion that olfactory identification deficits may be related to psychosis generally rather than to schizophrenic psychosis specifically. The relationships between the presence of olfactory hallucinations and (i) olfactory identification performance and (ii) olfactory acuity in schizophrenic patients were investigated and no statistically significant associations were observed. Future research into the effects of atypical neuroleptic medication on olfactory identification is suggested.

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Olfactory Identification in Schizophrenia

Olfactory dysfunction has been linked with a variety of neuropsychiatric disorders, including Parkinson's and Alzheimer's diseases (Doty, Deems, & Stellar, 1988; Doty, Reyes, & Gregor, 1987; Ward, Hess, & Calne, 1983; Warner, Peabody, Flatter, & Tinklenberg, 1986), Korsakoff's syndrome (Mair et al., 1986) and Huntington's disease (Moberg, Pearlson, Speedie, & Lipsey, 1987). Olfactory symptoms were also recognized as features of schizophrenic illness in the early nineteen hundreds (Kraepelin, 1919). Since Kraepelin's description of such symptoms, however, little research has been conducted with regard to the neurophysiology of olfactory changes in schizophrenia. This may be due to (a) a lack of standardized experimental methods, making comparability of results across studies difficult to achieve (Doty, Shaman, Kimmelman, & Dann, 1984), and (b) the elusive understanding of the nature of olfactory stimuli and their associated transduction mechanisms (Richardson & Zucco, 1989). Although olfaction has long been considered the least consequential of the human senses, it remains unequivocally involved in such aspects of human life as emotion and memory, digestion and respiration, and personal safety (Schneider, 1974). With the development of Doty's University of Pennsylvania Smell Identification Test (SIT) in 1984, the "Cinderella of the senses" (Moore-Gillon, 1987) has enjoyed a resurgence of research interest, particularly in experimental neuropsychiatry.

It would seem reasonable to expect a link between olfactory function and schizophrenia since olfactory hallucinations can appear as symptoms of the illness (American Psychiatric Association, 1987; Goodwin, Alderson, & Rosenthal, 1971; Kraepelin, 1919; Pryse-Phillips, 1975). The limbic system has its evolutionary

origins in the rhinencephalon, or the "nose brain", a primitive olfactory system (Vilensky, Van Hosen, & Damasio, 1982), and is also thought to represent one of the brain systems affected in schizophrenia (Levin, Yurgelun-Todd, & Craft, 1989). Kopala and Clark (1990) and Kopala, Clark and Hurwitz (1992) have asserted that those structures of the brain serving olfactory functioning are often found to be abnormal in the brains of schizophrenic patients. For example, olfactory projections to the frontal cortex thought to be involved in the ability to discriminate between odors (Harrison & Pearson, 1989; Potter & Butters, 1980) have been implicated in the neuropathology of schizophrenic illness (Andreasen et al., 1986; Williamson, 1987). Temporal lobe (Rausch, Serafetinides, & Crandall, 1977; Sreenivasan, Abraham, & Verghese, 1987) and limbic system (Bogerts, Meertz, & Schonfeldt-Bausch, 1985; Falkai, Bogerts, & Rozumek, 1988) pathologies have also been reported in both olfactory dysfunction and schizophrenia (Eskenzai, Cain, Novelly, & Friend, 1983).

In 1984, olfaction and psychosis again became linked in the literature in a study by Bradley who investigated the possibility that psychotic patients possess heightened sensitivity to pheromonal stimuli. Bradley found that psychotic male subjects demonstrated significantly greater olfactory acuity scores than normal non-psychiatric male subjects. Isserhoff, Stoler, Ophir, Lancet and Sirota (1987) failed to replicate Bradley's findings in a larger sample consisting of only schizophrenic subjects and no other forms of psychotic illness. The authors concluded that Bradley's findings had likely been due to chance. In both of these studies, however, olfactory acuity (the ability to detect the presence of an odor) was investigated, and not olfactory identification (the ability to identify an odor by

name), which is thought to define a distinct phenomenon (Kopala & Clark, 1990).

The first study to investigate olfactory identification performance in schizophrenic patients (Hurwitz, Kopala, Clark, & Jones, 1988) employed Doty's SIT. This study reported significant olfactory identification deficits in schizophrenic patients compared to both non-psychiatric and non-schizophrenic psychiatric controls. Two studies (Kopala et al., 1992; Serby, Larson, & Kalkstein, 1990) replicated this finding. One study (Warner, Peabody, & Csernansky, 1990) reported no significant differences between schizophrenic patients and either psychiatric or non-psychiatric control groups. However, Hurwitz and Clark (1990) re-analyzed these data, combining Warner et al.'s (1990) normal and psychiatric control groups, and found significant olfactory identification deficits in schizophrenic patients compared to the combined control groups.

Recently, research in this area has begun to focus on olfactory identification differences *within* the schizophrenic population. For example, in two follow-up studies conducted by Kopala, Clark and Hurwitz (1989, 1992), the authors investigated olfactory identification differences between male and female schizophrenic patients (1989) and the effects of neuroleptic medication on olfactory identification performance (1992). They found olfactory identification deficits to be confined to a subgroup of male schizophrenic patients and not related to neuroleptic medication regime. A study by Wu et al. (1993) that employed unmedicated schizophrenic patients, supported Kopala et al.'s (1992) findings.

Other studies have looked at olfactory functioning in the positive syndrome (characterized by delusions, hallucinations and thought disorder) versus the

negative syndrome (characterized by flattened affect, poverty of speech and generally diminished motivation and interest) of schizophrenia (Geddes, Huws, & Pratt, 1991; Wray, Mayr, Clark, & Malaspina, 1993) and in the context of dorsolateral prefrontal cognitive deficits (Seidman et al., 1992).

Geddes et al. (1991) reported that although schizophrenic patients with negative symptoms demonstrated significantly better olfactory acuity performance than those with positive symptoms, there were no significant differences between either group and a non-psychiatric control group. In contrast, Wray et al. (1993) reported no significant differences in olfactory performance between patients with positive and negative symptoms. These authors also found no relationships between olfactory identification performance and age at onset or neurologic soft signs.

Seidman et al. (1992) reported significant deficits in both olfactory identification and cognitive tasks in schizophrenic patients compared to non-psychiatric controls, but found that these deficits were largely unrelated. Correlations between olfactory identification and dorsolateral prefrontal functioning as measured by the Wisconsin Card Sorting Test were also nonsignificant. The authors suggested that olfactory identification deficits in patients with schizophrenia are unrelated to generalized cognitive deficits and independent of dorsolateral prefrontal dysfunction.

Early research on olfactory identification in schizophrenia was often characterized by relatively small sample sizes, inconsistent or non-existent psychiatric control groups, and discordant findings and interpretations. Since these original studies of olfactory identification deficits in the schizophrenic population

provided the impetus for the current interest in differential deficits within the schizophrenic population, the present study was designed in order to provide a firmer foundation for these extensions. The purpose was to re-examine the original contention that olfactory identification deficits do exist in the schizophrenic population.

The following *a priori* hypotheses were proposed:

1. Medicated schizophrenic patients will demonstrate significant *olfactory identification* deficits when compared with (a) non-schizophrenic, neuroleptically unmedicated psychiatric controls, (b) non-schizophrenic, neuroleptically medicated psychiatric controls, and (c) non-psychiatric controls.

2. Medicated schizophrenic patients will not demonstrate significant *olfactory acuity* (i.e., olfactory threshold) differences when compared with (a) non-schizophrenic, neuroleptically unmedicated psychiatric controls, (b) non-schizophrenic, neuroleptically medicated psychiatric controls, and (c) non-psychiatric controls.

3. Non-schizophrenic psychiatric patients who are receiving neuroleptic medication will not demonstrate significant *olfactory identification* or *acuity* differences when compared with non-schizophrenic psychiatric patients who are not receiving neuroleptic medication.

4. Olfactory identification deficits will be apparent only in male schizophrenic patients.

The relationships in schizophrenic patients between olfactory hallucinations and (a) olfactory identification performance and (b) olfactory acuity were also examined. Historically, olfactory hallucinations have been associated with

schizophrenia and other psychotic illness (American Psychiatric Association, 1987; Goodwin et al., 1971; Kraepelin, 1919; Malasi, El-Hilu, Mirza, & El-Islam, 1990; Pryse-Phillips, 1975). However, only one study (Kopala et al., 1992) was found that investigated the possibility of a relationship between olfactory identification performance and olfactory hallucinations and this study reported no significant relationship. In light of the paucity of previous research into this putative relationship, this aspect of the study was considered exploratory in nature and therefore no specific hypotheses were proposed.

The following *post hoc* hypothesis was investigated:

A significantly higher proportion of medicated schizophrenic patients will score in the microsmic olfactory identification range than (a) non-schizophrenic, neuroleptically unmedicated psychiatric controls, (b) non-schizophrenic, neuroleptically medicated psychiatric controls, and (c) non-psychiatric controls.

Method

Subjects

Four groups of participants were recruited through Riverview Hospital, Coquitlam, B.C. and St. Paul's Hospital, Vancouver, B.C.. All subjects gave informed consent (see Appendix 1) and the study was approved by the Simon Fraser University Research Ethics Review Committee and by the Riverview Hospital Research Advisory Committee.

Group 1 consisted of 17 male and two female (n = 19) patients with schizophrenia who were receiving neuroleptic medication at the time of participation. The mean age of this group was 34 years (SD = 9.45; range = 20-57). All but three patients in this group were refractory to traditional neuroleptic

treatment and were therefore receiving the atypical neuroleptic medications risperidone or clozapine at the time of participation.

Group 2 consisted of nine male and ten female (n = 19) psychiatric patients who had been diagnosed with a non-schizophrenic illness on Axis I (American Psychiatric Association, 1987) and were receiving neuroleptic medication at the time of participation. Only two patients were receiving atypical neuroleptic medication while all others were receiving traditional neuroleptic medication. This group consisted of 18 bipolar patients and one depressed patient, all presenting with psychosis. The mean age of this group was 46 years (SD = 10.51; range = 24-67).

Group 3 consisted of 11 male and nine female (n = 20) psychiatric patients who had been diagnosed with a non-schizophrenic illness on Axis I (American Psychiatric Association, 1987) and were not receiving neuroleptic medication at the time of participation. This group consisted of 12 bipolar patients and eight depressed patients. None of these patients presented with psychosis. The mean age of this group was 46 years (SD = 11.83; range = 23-65).

All diagnoses had been made according to DSM-III-R criteria, by a team of attending physicians, nursing staff, social workers and researchers in accordance with hospital diagnostic procedures, or by the participating patient's physician.

Group 4 consisted of 15 male and three female (n = 18) hospital employees who had never been diagnosed with a psychiatric illness and were therefore considered never to have received neuroleptic medication and who were in continuing contact with patients participating in this study. The mean age of this group was 34 years (SD = 10.27; range = 23-55).

Potential subjects suffering from any significant olfactory symptoms such as those associated with the common cold, influenza, or nasal allergies, or any other organic condition such as upper respiratory tract infection, current hypothyroidism or chronic cocaine use (past or current), which could have compromised their sense of smell, were excluded from the study. Patients concurrently suffering from organic mental disorders, current psychoactive substance use disorders, dissociative disorders, sexual disorders, anxiety disorders, somatoform disorders, and / or water intoxication syndrome were also excluded from the study. Group profiles for smoking, head and nasal injury are presented in Table 1.

Insert Table 1 about here

Both patients and hospital employees were personally recruited by the experimenter with permission of the attending physician (where applicable) and the head nurse of the hospital ward where recruiting took place.

Materials and Procedures

All subjects underwent the same three procedures outlined below. The same examiner administered all tests. Tests were administered in adequately ventilated interview rooms, with only the subject and the examiner present during testing.

Smell Identification Test. The University of Pennsylvania Smell Identification Test (SIT) (Doty, Shaman, & Dann, 1984) was administered to subjects to determine olfactory identification ability. The SIT consists of four

Table 1

Frequency of Smoking, Head and Nasal Injury

		Dependent Measures			
Group	N	Smokers	Average Cigarettes Per Day	Head Injured	Nasal Injured
Schizophrenic	19	12	15.31	5	11
Neuroleptically Medicated (Psychiatric)	19	10	10.79	9	5
Neuroleptically Unmedicated (Psychiatric)	20	7	6.20	7	7
Non-Psychiatric	18	4	3.33	5	9

booklets, each of which contains ten different scent-impregnated microencapsulation patches, colloquially known as "scratch-and-sniff" patches. (See Appendix 2.) Examinees are instructed to scratch and smell each patch, then select the name of each released odor from among the four alternatives listed above each target patch. Although the SIT is designed to be a self-administered test, due to the clinical nature of the population under investigation, subjects were tested individually and asked to respond verbally to the examiner to ensure comprehension of, and compliance with, instructions. The examiner scratched one target patch for each trial, releasing the odor. The subject was then instructed to smell the patch and indicate which of the four alternatives, read aloud by the examiner, best described the odor released. Subjects were also instructed to indicate to the examiner if they were unable to detect any odor on a given trial. In such cases, the examiner would release additional odor by scratching the target patch again until the subject reported experiencing an odorous sensation. Subjects required 10-20 minutes to complete this test.

Results on the SIT were scored out of a possible total of 40. Scores of 34 or less for females and 33 or less for males were considered microsmic (below the normal range). This was based on standardized data by Doty, Shaman and Dann (1984). No subject was excluded from this study on the basis of SIT score.

Smell Acuity Test. A psychophysical test of olfactory threshold was administered to subjects as the olfactory acuity measure. This test was patterned after the Olfacto-Labs Smell Sensitivity test kit (Amoore & Ollman, 1983) and was chosen because of the relative stability and longevity of the pyridine in mineral oil test solution which it employs. (See Appendix 3.) Subjects were exposed to

varying concentrations of the chemical compound pyridine in a forced choice "method of limits" paradigm to determine their ability to detect this compound at each concentration presented. Opaque nalgene plastic squeeze bottles of 60 ml capacity were used to contain the pyridine solutions. These bottles were fitted with analytical delivery nozzle tops that would direct a stream of the odorant in aerosol when the bottle was squeezed. The pyridine bottles contained 30 ml of stimulus liquid incrementally decreasing in concentration from a three percent solution (step 6) to a 1×10^{-7} percent solution (step 28) (Sherman, Amoore, & Weigel, 1979). (See Appendix 3.) Each bottle of pyridine solution was paired with a control bottle identical in appearance but containing only an equal amount of odorless light mineral oil (the solvent used in the pyridine solutions). The bottles were arranged in ascending order of concentration in front of the subject. Identification of active and control members of the pair and concentration level was accomplished by plading numbers on the bottom of each bottle which were not visible to the subject. Left-right position of active and control bottles on the table was varied randomly. Prior to presenting each stimlus pair, the examiner agitated the solutions in the botttles (to promote equilibration between liquid and vapor in the bottles) and randomized the order of the bottles within the pair (to eliminate memory effects from previous trails). The examiner then directed a gentle puff of air from the bottles of each pair, individually, at the subject's nose. Both of the subject's nostrils were stimulated birhinally. The subject was instructed to inhale the expelled odorant through the nose and to report which bottle from each pair produced the strongest odor. Typically step 10 or 12 was the first solution pair to be presented followed by pairs of increasing or decreasing concentration as

required by the subject. Subjects required 10-15 minutes to complete this test.

Olfactory threshold was defined as the weakest concentration of solution for which the subject was able to identify the pyridine-containing bottle correctly on three consecutive trials (Amoore et al., 1983). Data gathered by Amoore et al. (1983) indicate that 96 percent of healthy persons between the ages of 20 and 60 years score between steps 14 and 21, with a mean score of 18 (SD = 2). Subjects who cannot detect step 10 pyridine may still be able to correctly identify the pyridine-containing bottle at lower than step 10, due to sensations resulting from partial stimulation of the trigeminal nerve. Hence, as outlined by Amoore et al. (1983), any subject scoring below step 14 was considered hyposmic (below the normal range) regardless of performance below step 10. One subject in group 1 (schizophrenic) was unable to provide an olfactory acuity score. No subject was excluded from this study on the basis of olfactory acuity score.

History and Hallucinations Questionnaire. Subjects responded to the questionnaire contained in Appendix 4. This questionnaire includes items about subjects' age, smoking habits, histories of head and nasal trauma, olfactory conditions, drug use, and the type of hallucination (visual, auditory, olfactory, gustatory or tactile), if any, they most commonly experienced. These questions were adapted from the Structured Clinical Interview for the Positive and Negative Syndrome Scale (SCI-PANSS) (Opler, Kay, Lindenmayer, & Fiszbein, 1992). Additional information on current medication and number of years since first onset of illness, where applicable and available, was also collected from the patients' medical records or through self-report. To ensure comprehension of questions, subjects were asked to respond verbally to items of the questionnaire read aloud by

the examiner. Subjects required 5-15 minutes to complete this questionnaire.

Responses to questions were coded as a head or nasal injury only if the subject had at any time, sustained an insult to the head or nose resulting in loss of consciousness or sutures, or a broken or bloody nose, respectively.

Any sensory experience for which the subject could not locate a physical cause (at any time during the subject's illness) was coded as a hallucination. Hallucinations in each of the modalities (auditory, visual, olfactory, gustatory and tactile) were coded separately.

Only those subjects who were active smokers at the time of participation in the study were coded as smokers. The mean number of cigarettes smoked per day was calculated for each group.

Analyses

The following contrasts were conducted to test the *a priori* hypotheses:

(1) To test the hypothesis that patients with schizophrenia would demonstrate olfactory identification deficits, t-tests were conducted on SIT scores contrasting schizophrenic patients with (a) non-schizophrenic psychiatric patients not receiving neuroleptic medication, (b) non-schizophrenic psychiatric patients receiving neuroleptic medication, and (c) non-psychiatric controls.

(2) To test the hypothesis that olfactory identification deficits exist in the absence of olfactory acuity deficits (i.e, absolute olfactory threshold differences), t-tests were conducted on olfactory acuity scores comparing schizophrenic patients with (a) non-schizophrenic psychiatric patients not receiving neuroleptic medication, (b) non-schizophrenic psychiatric patients receiving neuroleptic medication, and (c) non-psychiatric controls.

(3) To determine whether olfactory deficits are related to exposure to neuroleptic medication, t-tests were conducted on SIT and olfactory acuity scores of non-schizophrenic patients receiving neuroleptic medication and non-schizophrenic patients not receiving neuroleptic medication.

Due to the insufficient number of female schizophrenic patients available to be tested, the planned comparison between male and female schizophrenic patients' SIT scores was not feasible. This comparison would have tested the hypothesis that olfactory identification deficits are confined to male patients with schizophrenia.

To investigate the relationship between olfactory hallucinations and olfactory functioning, t-tests between schizophrenic patients experiencing olfactory hallucinations and schizophrenic patients not experiencing olfactory hallucinations were conducted on SIT and olfactory acuity scores.

The continuous dependent variables, age, smoking, and olfactory acuity were analyzed for relatedness to the dependent variable of interest (SIT scores) by computing a Pearson r correlation. The categorical variables, head injury, nasal injury and gender, were analyzed for relatedness to SIT scores by conducting three t-tests on SIT scores between (a) head injured and not head injured subjects, (b) nasal injured and not nasal injured subjects, and (c) male and female subjects.

The following comparisons were conducted to test the *post hoc* hypothesis:

(1) To test the hypothesis that a significantly higher proportion of schizophrenic patients would score in the microsmic olfactory range than the other groups, comparisons were conducted on the proportion of subjects scoring in the microsmic olfactory identification range between schizophrenic patients and (a)

non-schizophrenic psychiatric patients not receiving neuroleptic medication, (b) non-schizophrenic psychiatric patients receiving neuroleptic medication and (c) non-psychiatric controls.

Results

Ten planned contrasts were conducted to test the *a priori* hypotheses and three contrasts were conducted to test the *post hoc* hypothesis as follows. Where multiple tests were conducted, a familywise α of 0.1 was adopted. Individual α values were adjusted using the Bonferroni correction to prevent capitalizing on Type I errors.

Olfactory Identification

In order to test the significance of differences in olfactory identification performance (SIT scores) among the groups, three t-tests, with α adjusted to .025, were conducted on SIT scores. As predicted, schizophrenic patients scored significantly lower than (a) non-schizophrenic psychiatric patients not receiving neuroleptic medication ($t(37) = 2.23$, $p = .016$) and (b) non-psychiatric controls ($t(35) = 2.50$, $p = .008$). Schizophrenic patients did not differ significantly from non-schizophrenic patients receiving neuroleptic medication ($t(36) = 0.61$, $p = .273$).

Olfactory Acuity

In order to test the significance of differences in olfactory acuity (i.e., absolute olfactory threshold on the pyridine scale) among the groups, three t-tests, with α adjusted to .025, were conducted on olfactory acuity scores. As predicted, no significant threshold differences were found between schizophrenic patients and

(a) non-schizophrenic psychiatric patients not receiving neuroleptic medication ($t(36) = 1.96$, $p = .058$), (b) non-schizophrenic psychiatric patients receiving neuroleptic medication ($t(35) = 1.49$, $p = .144$), and (c) non-psychiatric controls ($t(34) = 1.29$, $p = .206$).

Medication Effects

In order to investigate the effects of neuroleptic medication on olfactory functioning, two additional t-tests, with α adjusted to .025, were conducted on SIT and olfactory acuity scores of the non-schizophrenic psychiatric groups. Contrary to expectations, non-schizophrenic patients receiving neuroleptic medication scored significantly lower on the SIT than non-schizophrenic patients not receiving neuroleptic medication ($t(37) = 3.13$, $p = .003$). No significant difference was found between these two groups for olfactory acuity scores ($t(37) = .30$, $p = .768$).

Table 2 presents means, standard deviations and ranges for olfactory identification (SIT) scores and olfactory acuity scores for each of the groups.

Insert Table 2 about here

Gender

Although both female schizophrenic patients scored in the microsmic olfactory identification range (SIT scores of 32 and 34), these were insufficient data to support a statistical analysis of sex differences for olfactory identification performance.

Table 2

Group Means, Standard Deviations and Ranges for Olfactory Identification and Acuity Scores

		Olfactory Identification (SIT Scores)			Olfactory Acuity (Pyridine Scale Scores)		
Group	N	Mean	SD	Range	Mean	SD	Range
Schizophrenic	19*	32.84	3.89	25-39	15.89	4.36	6-26
Neuroleptically Medicated (Psychiatric)	19	32.10	3.53	21-36	18.32	5.43	12-28
Neuroleptically Unmedicated (Psychiatric)	20	35.20	2.61	29-38	18.80	4.74	10-28
Non-Psychiatric	18	35.72	3.04	28-39	17.67	3.90	12-28

Note. SD = Standard Deviation.
* N = 18 for Olfactory Acuity

Olfactory Hallucinations

Fourty-two percent of patients with schizophrenia reported experiencing hallucinations in the olfactory modality.

Two t-tests ($\alpha = .05$) were conducted in order to investigate the relationship between presence of olfactory hallucinations and olfactory functioning. The SIT and olfactory acuity scores of schizophrenic patients experiencing olfactory hallucinations and schizophrenic patients not experiencing olfactory hallucinations did not differ significantly ($t(17) = 1.81$, $p = .09$) and ($t(16) = .31$, $p = .76$), respectively). (See Tables 3 and 4.)

Insert Tables 3 and 4 about here

Although it was not statistically significant, hallucinating schizophrenic patients scored higher on both olfactory identification and acuity measures than non-hallucinating schizophrenic patients.

Three *post hoc* tests for significant differences in the proportions of subjects who scored in the microsmic olfactory identification range ($\alpha = .03$) among the groups revealed that a significantly higher proportion of schizophrenic patients scored in the microsmic olfactory identification range than (a) non-schizophrenic psychiatric patients not receiving neuroleptic medication ($z = 2.08$, $p = .01$) and (b) non-psychiatric controls ($z = 2.50$, $p = .003$). The proportion of subjects scoring in the microsmic olfactory identification range did not differ significantly between schizophrenic patients and non-schizophrenic psychiatric patients receiving neuroleptic medication ($z = .23$, $p = .205$). (See Table 5.)

Table 3

Means and Standard Deviations of Olfactory Identification Scores for Schizophrenic Patients Experiencing Olfactory Hallucinations and Schizophrenic Patients not Experiencing Olfactory Hallucinations

	Schizophrenic Patients			
Olfactory Identification (SIT Scores)	Experiencing Olf Hal's n = 9	Not Experiencing Olf Hal's n = 10	t	p
Mean	34.44	31.40	1.81	.09
SD	2.79	4.30		

Note. SD = Standard Deviation. Olf Hal's = Olfactory Hallucinations.
* $p < .05$.

Table 4

Means and Standard Deviations of Olfactory Acuity Scores for Schizophrenic Patients Experiencing Olfactory Hallucinations and Schizophrenic Patients not Experiencing Olfactory Hallucinations

	Schizophrenic Patients			
Olfactory Acuity (Pyridine Scale Scores)	Experiencing Olf Hal's n = 8	Not Experiencing Olf Hal's n = 10	t	p
Mean	16.25	15.60	.31	.76
SD	2.71	5.48		

Note. SD = Standard Deviation. Olf Hal's = Olfactory Hallucinations.
* $p < .05$.

Insert Table 5 about here

Confounding Variables

In order to determine whether there were confounding influences of the variables, age, smoking, olfactory acuity, head or nasal injury, and gender on SIT scores, two types of analyses were conducted. (1) For the continuous variables age, smoking and olfactory acuity, Pearson r correlations were computed (α = .01). (2) For the dichotomous variables, head or nasal injury and gender, three t-tests (α = .03) were performed. As indicated in Table 6, there were no significant relationships between age, smoking, olfactory acuity and SIT scores.

Insert Table 6 about here

As indicated in Table 7 there were no significant differences between SIT scores of (a) head-injured and not head-injured subjects ($t(74) = .54$, $p = .588$), (b) nasal-injured and not nasal-injured subjects ($t(74) = .57$, $p = .574$), and (c) male and female subjects ($t(74) = .27$, $p = .787$).

Insert Table 7 about here

Table 5

Proportion of Subjects with Microsmic Olfactory Identification Scores

Group	N	Olfactory Identification (SIT Scores) Normosmic	Microsmic	Proportion of Subjects with Microsmic SIT Scores
Schizophrenic	19	7	12	.63
Neuroleptically Medicated (Psychiatric)	19	5	14	.74
Neuroleptically Unmedicated (Psychiatric)	20	14	6	.30
Non-Psychiatric	18	14	4	.22

Note. Normosmic = within normal range. Microsmic = below normal range.

Table 6

Correlations between Olfactory Identification Scores and Age, Smoking and Olfactory Acuity Scores

	Olfactory Identification (SIT Scores)	Olfactory Acuity (Pyridine Scale Scores)	Age	Smoking
Olfactory Identification (SIT Scores)	____	.1204	-.1932	-.2062
Olfactory Acuity (Pyridine Scale Scores)		____	.0101	.0159
Age			____	-.2158
Smoking				____

N = 76
* $p < .01$.

Table 7

Differences between Groups on Olfactory Identification Scores

	Group			
Olfactory Identification (SIT Scores)	Head Injured n = 25	Not Head Injured n = 51	t	p
Mean	33.64	34.12	.54	.59
SD	3.21	3.76		
	Nasal Injured n = 32	Not Nasal Injured n = 44		
Mean	33.69	34.16	.57	.57
SD	3.36	3.75		
	Male n = 25	Female n = 51		
Mean	33.88	34.12	.27	.79
SD	3.99	2.60		

Note. SD = Standard Deviation.
* $p < .03$.

Discussion

The cardinal finding of the present study was that the olfactory identification performance of medicated patients with schizophrenia was significantly impaired when compared to both non-schizophrenic psychiatric patients who were not receiving neuroleptic medication and non-psychiatric control subjects. However, when medicated schizophrenic patients were compared with non-schizophrenic psychiatric patients who were receiving neuroleptic medication, there was no significant difference in olfactory identification scores. As predicted, no differences in absolute olfactory threshold on the pyridine scale were found between schizophrenic patients and the three comparison groups. These results are consistent with previous findings (Hurwitz et al., 1988; Kopala et al., 1992; Serby et al., 1989 & 1990) that schizophrenic patients demonstrate significant olfactory identification deficits when compared to non-psychiatric control subjects. They are contrary, however, to the further findings of Hurwitz et al. (1988), that medicated schizophrenic patients demonstrate inferior olfactory identification performance when compared to non-schizophrenic psychiatric patients receiving neuroleptic medication. Furthermore, the average SIT scores of both the schizophrenic group and the non-schizophrenic psychiatric group receiving neuroleptic medication were microsmic, while the average SIT scores of both the non-psychiatric group and the non-schizophrenic psychiatric group not receiving neuroleptic medication were normosmic (within the normal range). Similarly, the proportion of schizophrenic patients who scored in the microsmic olfactory identification range was significantly higher than both non-schizophrenic psychiatric patients who were not receiving neuroleptic medication

and non-psychiatric controls, but not significantly different from non-schizophrenic psychiatric patients who were receiving neuroleptic medication.

Differences in SIT scores between these groups cannot be accounted for by olfactory acuity deficits as no differences in olfactory threshold among groups were found.

Despite reported evidence of a decrease in SIT scores with increases in age and smoking habits (Doty, Shaman, Applebaum, Giberson, Siksorski, & Rosenberg, 1984; Doty, Shaman, & Dann, 1984; Schiffman, 1983), in the present study, olfactory acuity, age and smoking were unrelated to olfactory identification performance. Although no relationship was found to exist between the mean number of cigarettes smoked per day and SIT scores, the patients with schizophrenia group contained three times as many smokers as the non-psychiatric group (twelve and four smokers respectively). Hence, smoking cannot be entirely ruled out as a possible contributor to the low SIT scores of the schizophrenic patients group.

Similarly, despite reported evidence of a difference in SIT scores between males and females (Doty, Shaman, & Dann, 1984; Kopala, et al. 1989), no significant gender effects were found. No differences in SIT scores were found between subjects who had suffered from head or nasal trauma and those who had not.

The olfactory identification deficits in patients with schizophrenia may have reflected more general cognitive and attentional deficits (Levin et al., 1989) or overt psychopathology (Hurwitz et al., 1988). As indicated by Levin et al. (1989), these attentional deficits are often consistent with frontal system dysfunction

models of schizophrenia. Although the possibility of these confounds was not addressed in the present study, previous research has shown no significant relationships between olfactory identification performance and many cognitive deficits often associated with schizophrenia or dorsolateral prefrontal functioning as measured by the Wisconsin Card Sorting Test (Seidman et al., 1992) or overt psychopathology as measured by the Global Assessment Scale (Hurwitz et al., 1988; Kopala et al., 1989). Wray et al. (1993) reported that olfactory identification deficits were unrelated to clinical or demographic variables or to neurologic soft signs.

With the exception of Hurwitz et al. (1988), no studies to date have examined olfaction in psychiatric control subjects receiving neuroleptic medication at the time of participation. Kopala et al. (1992) and Wu et al. (1993), however, have investigated olfactory identification performance in neuroleptically-naive schizophrenic patients and schizophrenic patients who were unmedicated for a minimum of three weeks prior to participation, respectively. They found olfactory identification deficits to exist in the absence of exposure to neuroleptic medication. Serby et al. (1990) and Warner et al.(1990) also examined schizophrenic patients who were discontinued from treatment with antipsychotic medication for a minimum of ten days and two weeks, respectively. Although Serby et al. (1990) found olfactory identification deficits in schizophrenic patients compared to psychiatric controls, Warner et al. (1990) did not. In sum, the majority of previous studies support the notion that olfactory identification deficits are unrelated to exposure to neuroleptic medication.

To investigate further the notion that neuroleptic exposure is unrelated to

olfactory identification performance, in the present study, SIT and olfactory acuity scores of non-schizophrenic psychiatric patients not receiving neuroleptic medication were compared to non-schizophrenic psychiatric patients who were receiving neuroleptic medication. Contrary to predictions, patients receiving neuroleptic medication performed significantly worse on olfactory identification than those not receiving neuroleptic medication. As predicted, however, there were no significant differences in olfactory acuity performance.

In view of previous findings that olfactory identification deficits are independent of exposure to neuroleptic medication, it seems unlikely that in the current sample of non-schizophrenic psychiatric patients, olfactory identification deficits were related to neuroleptic medication usage. Alternatively, the presence of psychotic symptoms (for which the treatment with neuroleptic medication is primarily prescribed), rather than the effects of neuroleptic medication itself, may have influenced olfactory identification performance. While it must be considered that psychiatric control patients may have received neuroleptic medication for treatment of symptoms other than psychosis, it is suggested that olfactory identification deficits currently seen in schizophrenic populations could also exist in other psychotic populations but may have gone undetected due to relatively small sample sizes and inconsistent, non-existent, or neuroleptically unmedicated (and therefore, largely non-psychotic) psychiatric control groups. In order to test this hypothesis more rigorously, future research is encouraged with larger, more carefully selected psychiatric control groups where the criteria for inclusion involve the presence of psychotic symptoms comparable in nature and chronicity to those of the schizophrenic patient group. Due to the ethical difficulty of recruiting

neuroleptically-naive patients with psychosis, the administration of comparable dosages of neuroleptic medication across groups would provide a more feasible approach to the medication confound.

Taken together, the present study's unexpected findings of (a) no differences in SIT scores between schizophrenic patients and non-schizophrenic psychiatric patients receiving neuroleptic medication, and (b) significant differences in SIT scores between non-schizophrenic psychiatric patients receiving neuroleptic medication and those not receiving neuroleptic medication, must be considered in light of the following caveats: Chronicity of psychosis, and therefore duration of exposure to neuroleptic medication, is likely to have been discrepant in psychiatric groups receiving neuroleptic medication. Schizophrenic patients in the present study were suffering from chronic psychosis while the non-schizophrenic psychiatric patients receiving neuroleptic medication were suffering from psychosis *at the time of participation*, but were not necessarily chronically psychotic. Hence this group may have comprised a more heterogeneous sample in terms of chronicity of psychosis than the schizophrenic patient group. Furthermore, although all psychiatric groups in the present study were diagnosed according to DSM-III-R criteria (American Psychiatric Association, 1987), both non-schizophrenic psychiatric groups were recruited from an out-patient facility and were therefore not diagnosed in the same manner as the schizophrenic patients who were recruited from a research ward of a psychiatric hospital. In addition to diagnostic reliability, diagnostic validity of these groups must also be considered, as indicated by Smith, MacEwan, Ancill, Honer and Ehmann (1992), who have asserted that psychiatric diagnoses in the community are often inaccurate.

The hypothesis that olfactory identification deficits are apparent only in male patients with schizophrenia could not be formally tested in the present study as only two female patients with schizophrenia participated in the study. Kopala et al. (1992) have acknowledged similar discrepancies in sex ratio of patients admitted to hospital with psychosis. Although there were insufficient data to permit a statistical analysis of gender, both female schizophrenic patients were microsmic with respect to SIT scores. This trend is contrary to previous findings that female schizophrenic patients do not demonstrate significant olfactory identification deficits (Kopala et al., 1989, 1992) and therefore merits attention in future research.

Consistent with past research (Kopala et al., 1992), no significant relationship was found between olfactory hallucinations and either olfactory identification performance or olfactory acuity in the schizophrenic patients of the current study. Although not statistically significant, it is interesting to note that hallucinators scored higher on both olfactory identification and threshold than non-hallucinators.

To date, olfactory identification research involving medicated patients with schizophrenia has employed only patients receiving traditional or typical neuroleptic medication such as haloperidol or chlorpromazine. The present study is the first study to examine treatment-refractory schizophrenic patients who are receiving atypical neuroleptic medication such as risperidone or clozapine. Since it has been suggested that treatment-refractory schizophrenic patients may comprise a unique and possibly more homogeneous subgroup of patients (Meltzer, 1990; Smith et al., 1992), the schizophrenic patients who participated in the current

study, as well as their medication regime, may be considered divergent from patients in prior studies. This should be considered a caveat to the interpretation of present findings.

Furthermore, as is often the case with psychiatric research, sample size was limited due to the clinical nature of the population under investigation. Future research is therefore suggested with larger samples, thereby identifying small but reliable effects that could not reach statistical significance in a small sample.

In summary, the results of the present study largely support previous findings of an olfactory identification deficit in patients with schizophrenia in that a deficit was found in comparison to (a) psychiatric subjects not receiving neuroleptic medication and (b) non-psychiatric subjects. However, medicated schizophrenic patients did not demonstrate a significant olfactory identification deficit when compared to other psychiatric subjects who were also receiving neuroleptic medication. These results raise some questions. Do olfactory identification deficits also exist in the non-schizophrenic psychotic patient population? If so, what differentiates a psychotic patient exhibiting olfactory identification deficits from one that does not? Kopala et al. (1992) have suggested that olfactory identification deficits are confined to a subgroup of male schizophrenic patients. Could this subgroup reflect part of a larger subgroup of psychotic patients? Further research is required to answer these questions.

Appendix 1

SUBJECT CONSENT FORM-RIVERVIEW HOSPITAL

If you agree to be a part of this study, entitled "SMELL IDENTIFICATION", you will be asked by KIM STRIEBEL of the Psychology Department of Simon Fraser University, to do the following things:

1) You will smell a number of different fragrances and be asked

   i) whether you can smell each one or not and
   ii) to pick the name of each fragrance from a short list of possible names.

These are harmless, everyday fragrances commonly used in research.

2) You will be asked to answer a few questions about yourself.

3) Your medical records may be consulted during the course of this study.

All the information gathered in this study will remain STRICTLY CONFIDENTIAL.

You may withdraw from the study AT ANY TIME WITHOUT COMPROMISING YOUR TREATMENT.

If you have any concerns about this study, you may contact DR. R. BLACKMAN of the Psychology Department of Simon Fraser University.

I _____, agree to participate in the study,
(signature of participant)

_____
(print name)
SMELL IDENTIFICATION, at Riverview Hospital, during the period of November 1992 to December 1993.

DATE: _____

WITNESS: _____

SUBJECT CONSENT FORM-ST. PAUL'S HOSPITAL

If you agree to be a part of this study, entitled "SMELL IDENTIFICATION", you will be asked by KIM STRIEBEL of the Psychology Department of Simon Fraser University, to do the following things:

1) You will smell a number of different fragrances and be asked

   i) whether you can smell each one or not and
   ii) to pick the name of each fragrance from a short list of possible names.

These are harmless, everyday fragrances commonly used in research.

2) You will be asked to answer a few questions about yourself.

3) Your medical records may be consulted during the course of this study.

All the information gathered in this study will remain STRICTLY CONFIDENTIAL.

You may withdraw from the study AT ANY TIME WITHOUT COMPROMISING YOUR TREATMENT.

If you have any concerns about this study, you may contact DR. R. BLACKMAN of the Psychology Department of Simon Fraser University.

I _____, agree to participate in the study,
(signature of participant)

_____
(print name)
SMELL IDENTIFICATION, at St. Paul's Hospital, during the period of November 1992 to December 1993.

DATE: _____

WITNESS: _____

Appendix 2

SMELL IDENTIFICATION TEST

ques #	A	B	C	D	cor / incor
1	gasoline	pizza	peanuts	lilac	
2	dill pickle	bubble gum	wintergreen	watermelon	
3	tomato	licorice	strawberry	menthol	
4	whiskey	honey	lime	cherry	
5	grass	pizza	motor oil	pineapple	
6	skunk	mint	fruit punch	cola	
7	banana	garlic	cherry	motor oil	
8	licorice	clove	chili	banana	
9	clove	lilac	leather	apple	
10	skunk	coconut	cedar	honey	
11	chocolate	banana	onion	fruit punch	
12	soap	fruit punch	menthol	pumpkin pie	
13	licorice	pineapple	cheddar cheese	cherry	
14	paint thinner	cherry	coconut	cheddar cheese	
15	cola	cinnamon	pine	coconut	
16	rose	lemon	peach	gasoline	
17	strawberry	dill pickle	chocolate	cedar	
18	cedar	gasoline	lemon	root beer	
19	lemon	chocolate	root beer	black pepper	
20	menthol	apple	gingerbread	cheddar cheese	

• 21	lilac	chili	coconut	whiskey	
22	turpentine	soap	skunk	chili	
23	chocolate	peach	leather	pizza	
24	root beer	watermelon	banana	smoke	
25	pineapple	dill pickle	root beer	black pepper	
26	smoke	whiskey	pineapple	onion	
27	musk	garlic	turpentine	lime	
28	cheddar cheese	orange	bubble gum	turpentine	
29	lime	wintergreen	pumpkin pie	leather	
30	chili	menthol	orange	watermelon	
31	watermelon	peanut	rose	paint thinner	
32	mint	gingerbread	grass	strawberry	
33	dill pickle	grass	smoke	peach	
34	pine	smoke	lilac	orange	
35	pizza	turpentine	clove	grape	
36	motor oil	pumpkin pie	rose	lemon	
37	soap	black pepper	licorice	peanut	
38	orange	musk	cola	natural gas	
39	lime	rose	mint	bubble gum	
40	peanut	lemon	apple	root beer	

Tot Correct: _____

Appendix 3

SMELL ACUITY TEST

test step #	test 1	test 2	test 3
6			
8			
10			
12			
14			
16			
18			
20			
22			
24			
26			
28			

Pyridine threshold is Step # ____

PYRIDINE OLFACTORY SENSITIVITY SCALE
TOTAL SOL'N: 30 ML

binary step #	mineral oil (mL)	pyridine (ml)	(effective) conc. pyridine (%)
6	29.1	0.93	3.2
8	49.81	0.39	0.78
		step 8 sol'n	
10	22.5	7.5	0.195
12	28	2	0.05
14	29.5	0.5	0.012
16	50	0.20	0.003
		step 16 sol'n	
18	22.5	7.5	0.00075
20	28	2	0.00019
22	29.5	0.5	0.0000469
24	50	0.20	0.0000117
		step 24 sol'n	
26	22.5	7.5	0.00000293
28	28	2	0.000000733

Appendix 4

HALLUCINATION QUESTIONNAIRE

Do you once in a while have strange or unusual experiences?_____

AUDITORY

Sometimes people tell me that they can hear noises or vioces inside their head that others can't hear. What about you?

YES NO

IF YES: What do you hear?

_____

Are these as clear and loud as my voice?

_____

How often do you hear these voices (noises, messages, etc.)?

_____

Does this happen at a particular time of day or all the time?

_____

VISUAL

Do ordinary things sometimes look strange or distorted to you?

_____

Do you sometimes have "visions" or see things that others can't see?

YES NO

IF YES:
For example?_____

Do these visions seem very real or life-like?

_____

How often do you have these experiences?

_____

Does this happen at any particular time of the day or all the time?

_____

OLFACTORY

Do you sometimes smell things that are unusual or that others don't smell?

YES NO

IF YES:
Please explain._____

GUSTATORY

What about tasting things that other people couldn't taste?

YES NO

IF YES:
Please explain._____

TACTILE

Do you get any strange or unusual sensations from inside your body?

YES NO

IF YES:
Tell me about this_____

SUBJECT HISTORY QUESTIONNAIRE

subject #:

male ☐ female ☐

age: _____ years _____ months B / d:_____

subject diagnosis (where applicable) Axis I_____
Axis II_____
Axis III _____
Axis IV_____

IF NOT psychiatric patient, have you ever been diagnosed with a psychiatric illness?

YES NO

Have you ever suffered a head injury? DESCRIBE:
(In an accident, for example)

YES NO

Have you ever been hit in the face / head area? DESCRIBE:
(In a fist fight, for example)

YES NO

Have you ever been hit directly in the nose? DESCRIBE:

YES NO

Are you currently suffering from any of the following? (Circle applicable ailments)

COLD

FLU

NASAL ALLERGY

If yes, what kind(s)?

_____

Have you ever or are you now using cocaine through the nose?
(In excess of once / week on an on-going basis.)

YES NO

Consult medical records for the following if necessary:

HYPOTHYROIDISM
If yes, medication:

_____

UPPER RESPIRATORY INFECTION

Do you smoke?

YES NO

IF YES, how long have you been smoking?

_____

Current medications:

_____

_____

# of months / years from first onset:

_____

Additional comments:

_____

_____

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