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Associations between olfactory identification and verbal memory in patients with schizophrenia, first-degree relatives, and non-psychiatric controls

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Abstract

Objective: Olfactory identification deficits and verbal memory impairments may represent trait markers for schizophrenia. The aims of this study were to: (1) assess olfactory identification in patients, first-degree relatives, and non-psychiatric controls, (2) determine differences in verbal memory functioning in these three groups, and (3) study correlations between olfactory identification and three specific verbal memory domains.
Method: A total of 106 participants–41 patients with schizophrenia or related disorders, 27 relatives, and 38 controls–were assessed with the University of Pennsylvania Smell Identification Test (UPSIT) and the Wechsler Memory Scale-Third Edition. Linear mixed models, accounting for clustering within families and relevant covariates, were used to compare scores across groups and to examine associations between olfactory identification ability and the three verbal memory domains.
Results: A group effect was apparent for all four measures, and relatives scored midway between patients and controls on all three memory domains. UPSIT scores were significantly correlated with all three forms of verbal memory. Age, verbal working memory, and auditory recognition delayed memory were independently predictive of UPSIT scores.
Conclusions: Impairments in olfactory identification and verbal memory appear to represent two correlated risk markers for schizophrenia, and frontal–temporal deficits likely account for both impairments.

Keywords: First-degree relatives; Olfactory identification; Psychosis; Schizophrenia; Verbal memory; Working memory

1. Introduction

A variety of risk markers, or vulnerability indicators, have been studied in patients with schizophrenia and their first-degree relatives. Similar to the term

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endophenotype (Gottesman and Gould, 2003), a vulnerability indicator denotes any genetic, biological, psychological, or behavioral trait that may reflect an underlying susceptibility toward developing schizophrenia (Kremen et al., 1992). Olfactory identification deficits may be a trait marker for psychotic disorders (Brewer et al., 2001). Similarly, impairments in specific memory domains (including verbal memory and working memory) are putative endophenotypes or vulnerability indicators for schizophrenia (Conklin et al., 2000; Gasperoni et al., 2003; Gottesman and Gould, 2003; Lenzenweger, 1999; Sitskoorn et al., 2004).

Many studies have found that olfactory identification ability, which is most commonly measured with the University of Pennsylvania Smell Identification Test (UPSIT), is impaired in individuals with schizophrenia relative to non-psychiatric controls (Moberg et al., 1999). Olfactory identification deficits also have been documented among first-episode patients and neuroleptic-naïve patients (Kopala et al., 1993; Wu et al., 1993). Olfactory identification ability may even be impaired, relative to healthy controls, in ultra-high-risk adolescents and young adults (with attenuated psychotic symptoms; brief, intermittent psychotic symptoms; or genetic risk along with a significant decrease in functioning) who later develop psychotic disorders (Brewer et al., 2003). A recent study demonstrated that baseline UPSIT scores among 58 antipsychotic-naïve, first-episode patients were predictive of remission of negative and cognitive/disorganized symptoms at 1 year (Good et al., 2006).

Only two prior studies have examined UPSIT performance among relatives of patients with schizophrenia. Kopala and colleagues found that 12 pairs of monozygotic twins discordant for schizophrenia did not differ from one another on the UPSIT, though as a combined group, they performed more poorly than healthy controls (Kopala et al., 1997). In a study of familial schizophrenia, the same researchers found that nonpsychotic first- and second-degree family members ($n=27$) scored midway between patients ($n=19$) and healthy controls ($n=43$) (Kopala et al., 2001).

Memory impairments have been repeatedly demonstrated in schizophrenia, and working memory and verbal learning/memory are among the separable cognitive factors that represent fundamental dimensions of cognitive deficit (Nuechterlein et al., 2004). Such impairments have been shown to be stable, present at the time of the first episode, and demonstrable in neuroleptic-naïve patients (Bilder et al., 1991; Nopoulos et al., 1994; Saykin et al., 1994). Brewer and coworkers recently documented significantly lower performance in verbal memory in ultra-high-risk adolescents and young adults who later developed psychosis compared to symptomatic, help-seeking, ultra-high-risk patients who did not develop psychosis (Brewer et al., 2005a).

Memory impairments also have been identified in first-degree relatives of patients (Conklin et al., 2002; Egan et al., 2001; Kremen et al., 1994; Sponheim et al., 2004). Healthy relatives of patients have verbal memory deficits that are stable traits and that are qualitatively similar, though less severe, than those in patients. A recent meta-analysis revealed that these deficits are apparent across several memory measures, including the Logical Memory, Verbal Paired Associates, and digit span subtests of the *Wechsler Memory Scale* (Trandafir et al., 2006). Such impairments therefore constitute a familial, likely genetic, vulnerability marker for schizophrenia (Sitskoorn et al., 2004; Toulopoulou et al., 2003; Whyte et al., 2005). Relatives from multiply-affected families may exhibit greater verbal memory impairments than those from simplex families (Faraone et al., 2000) indicating an effect of familial loading. Schubert and McNeil recently have shown that offspring (assessed at a mean age of 22.3 years) at genetic high risk for schizophrenia by virtue of having a mother with a history of the disorder, have impairments in verbal memory and other neurocognitive domains (Schubert and McNeil, 2005).

Though there is a dearth of research on associations between the various putative vulnerability indicators, such investigation could enhance understandings of schizophrenia from the perspectives of both pathophysiology and risk for developing the illness. For example, Malaspina et al. found a positive association between UPSIT scores and smooth pursuit eye movement ability (Malaspina et al., 1994). It has been suggested that the study of relationships between olfactory identification ability and neuropsychological functioning may discern distinct groups of schizophrenia patients, thus providing additional insight into the biological underpinnings of the illness (Goudsmit et al., 2004). Several studies have found correlations between olfactory identification and various cognitive domains including executive functioning, intelligence quotient subtests, and processing speed (Brewer et al., 1996; Corcoran et al., 2005; Goudsmit et al., 2004; Malaspina and Coleman, 2003; Saoud et al., 1998; Seckinger et al., 2004; Stedman and Clair, 1998). However, very little research is available on the associations between olfactory identification and memory domains (Brewer et al., 1996; Economou, 2003; Good et al., 2002).

In this study, patients with schizophrenia and related illnesses, their first-degree relatives, and non-psychiatric controls were assessed as part of a study on associations