

The neuroanatomical basis of affective mentalizing in schizophrenia: Comparison of patients with schizophrenia and patients with localized prefrontal lesions

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Abstract

Patients with schizophrenia show impaired emotional and social behavior, such as misinterpretation of social situations and lack of Theory of Mind (ToM). However, the neuroanatomical basis of impaired ToM and its nature in schizophrenia is still largely unknown. Based on previous findings, the present study suggests that impaired social cognition observed in schizophrenic patients may be similar to that observed in patients with prefrontal (PFC) damage due to impaired ‘affective ToM’ abilities, rather than to a general impairment in ToM. We examined the behavioral and neural mechanisms that underlie the social and communicative impairments observed in patients with schizophrenia and with PFC damage, by looking at differential patterns of ToM impairment in these individuals. The performance of 24 patients with schizophrenia was compared to the responses of patients with localized lesions in the ventromedial (VM) or dorsolateral PFC, patients with non-frontal lesions, and healthy control subjects. Patients with schizophrenia and those with VM lesions were impaired on ‘affective ToM’ tasks but not in cognitive ToM conditions. It was concluded that the pattern of mentalizing impairments in schizophrenia resembled those seen in patients with lesions of the frontal lobe, particularly with VM damage, providing support for the notion of a disturbance of the fronto-limbic circuits in schizophrenia.

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1. Introduction

Impaired social cognition has been observed in patients with schizophrenia and found to be linked to

their social functioning and behavior (Penn et al., 1999). Although deficits in emotional and social behavior in schizophrenia have been extensively investigated, the scientific literature shows little agreement as to the neuroanatomical basis of impaired social cognition in schizophrenia (Morrison et al., 1988; Mandal et al., 1998). Recently, attempts to explain the behavioral disturbances in schizophrenia have emphasized the breakdown of ‘theory of mind’ (ToM) processes in

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these individuals. ToM refers to the ability to understand and predict the behavior of other people through the process of making inferences regarding their mental states: their knowledge, intentions and beliefs (Premack and Woodruff, 1978). It has been shown that individuals with schizophrenia perform poorly on ToM tasks relative to clinical and non-clinical control groups (Frith and Corcoran, 1996; Sarfati et al., 1997).

Important corroboration for the idea of impaired ToM in schizophrenia may arise from studying the neuroanatomical bases of social impairment in individuals with brain damage. Evidence from patients with cortical lesions shows that individuals with prefrontal (PFC) damage show impaired social behavior and functioning, despite the retention of intact cognitive skills. Patients with PFC damage may show misinterpretation of social situations, especially when the damage is located in the orbitofrontal/ventromedial (VM) PFC region (Rolls, 1996). This selective deficit might suggest that a unique neural circuit that involves the PFC subserves social cognition (Pinkham et al., 2003). Indeed, evidence from both lesion (Stone et al., 1998; Stuss et al., 2001; Rowe et al., 2001) and neuroimaging (Fletcher et al., 1995; Goel et al., 1995; Baron-Cohen et al., 1994; Gallagher et al., 2000; Calarge et al., 2003; Grezes et al., 2004; Vollm et al., 2006) studies reported the contribution of specific prefrontal regions to ToM abilities.

Operationally, subjects are usually credited with ToM if they succeed in tasks designed to test their understanding of beliefs. However, we have recently found that tasks involving inference regarding *cognitive* mental states and tasks that involve inference regarding *affective* mental states are differentially impaired in individuals with schizophrenia (Shamay-Tsoory et al., in

press) and in individuals with VM damage (Shamay-Tsoory et al., 2005).

Interestingly, the same cortical regions, involved in ToM are also known to be impaired in schizophrenia. Recently, there has been particular interest in the possible contribution of the PFC to schizophrenic symptomatology (for review: Pantelis et al., 2005). Neuropsychological studies of patients with schizophrenia have consistently identified deficits of executive function, traditionally considered sensitive to frontal lobe damage (Morris et al., 1995). While most studies focused on dorsolateral prefrontal dysfunction in schizophrenia (Weinberger et al., 1986), schizophrenic patients also appear to show deficits in the VM and prefrontal regions (Convit et al., 2001; Pantelis et al., 2005). However, although abnormal function has been demonstrated in the PFC, there is limited evidence of anatomical pathology of this brain area (Shelton et al., 1988).

Taken together, it appears that a dysfunction in the PFC and particularly the VM may underlie impaired ToM in schizophrenia. While studies to date have reported impaired ToM and empathy in both schizophrenia (Frith and Corcoran, 1996) and VM damage (Stone et al., 1998; Shamay-Tsoory et al., 2005), no previous study has directly compared these two groups. Therefore, the goal of the present study was to examine the role of PFC cortices in impaired ToM in schizophrenia.

2. Methods

2.1. Subjects

Ethical approval was granted by both hospitals (Rambam medical center and Shalvata Mental Health Care Center) Ethics Committees. All subjects signed informed consent.

Table 1
Demographic details

	Schizophrenia N=24	VM N=9	DLC N=7	MIX N=11	NF N=16	HC N=28	Sig
Gender							
Males	15	8	6	9	11	15	NS
Females	9	1	1	5	4	13	
Age, mean (SD)	32.47 (10.66)	40.11 (15.55)	33.57 (7.28)	34.63 (15.74)	37.87 (16.28)	28.35 (7.44)	NS
Years of education, mean (SD)	12.90 (3.38)	13.25 (3.41)	13.42 (1.81)	13.00 (2.36)	13.66 (2.22)	13.39 (1.13)	NS
Similarities, mean (SD)	9.95 (3.00)	9.55 (1.13)	11.80 (1.30)	8.92 (1.49)	10.75 (1.815)	11.08 (2.29)	NS
Recognition of emotions, mean % of correct responses (SD)	85.43 (8.02)	77.89 (11.69)	78.17 (8.54)	81.92 (2.08)	85.31 (8.79)	88.18 (11.37)	$p=0.034$
Perspective taking scale, mean (SD)	1.75 (4.60)	-4.00 (6.58)	2.40(3.36)	1.57 (4.43)	5.00 (5.85)	5.9 (3.48)	$p=0.0001$

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