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Automatization and working memory capacity in schizophrenia

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Abstract

Working memory (WM) dysfunction in schizophrenia is characterized by inefficient WM recruitment and reduced capacity, but it is not yet clear how these relate to one another. In controls practice of certain cognitive tasks induces automatization, which is associated with reduced WM recruitment and increased capacity of concurrent task performance. We therefore investigated whether inefficient function and reduced capacity in schizophrenia was associated with a failure in automatization. FMRI data was acquired with a verbal WM task with novel and practiced stimuli in 18 schizophrenia patients and 18 controls. Participants performed a dual-task outside the scanner to test WM capacity. Patients showed intact performance on the WM task, which was paralleled by excessive WM activity. Practice improved performance and reduced WM activity in both groups. The difference in WM activity after practice predicted performance cost in controls but not in patients. In addition, patients showed disproportionately poor dual-task performance compared to controls, especially when processing information that required continuous adjustment in WM. Our findings support the notion of inefficient WM function and reduced capacity in schizophrenia. This was not related to a failure in automatization, but was evident when processing continuously changing information. This suggests that inefficient WM function and reduced capacity may be related to an inability to process information requiring frequent updating.

Keywords: Functional MRI; Schizophrenia; Working memory; Automatization; Dual-task

1. Introduction

Cognitive dysfunction is a core characteristic of schizophrenia (Elvevag and Goldberg, 2000) and associated with deficits in working memory (WM). WM refers to the temporary maintenance and utilization of information (Baddeley, 1986) and is considered important for complex cognitive performance (Miller and Cohen, 2001). WM dysfunction in schizophrenia is characterized by inefficient prefrontal function as most patients exhibit excessive activity when performing a moderately difficult WM task (Callicott et al., 2003, 2000a; Manoach et al., 1999, 2000, 2003; Jansma et al., 2004; Perlstein et al., 2001). When performing a more difficult WM task (i.e. with more information that has to be memorized and processed), they generally exhibit poor performance and lower levels of WM activity than controls (Berman et al., 1992; Andreasen et al., 1992b; Karlsgodt et al., 2007; Van Snellenberg et al., 2006),

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indicating that their WM capacity is quite limited (Callicott et al., 1999, 2000a, 2003; Jansma et al., 2004). In spite of structural abnormalities in the prefrontal cortex (Callicott et al., 2000b; Bertolino et al., 2000), and of genetic variation contributing to prefrontal activation levels (Egan et al., 2001; Bertolino et al., 2006a,b, 2004) it is not clear what causes inefficient WM function and reduced WM capacity in schizophrenia.

Recently we demonstrated that the ability to reduce demands on WM with practice is closely related to the capacity to perform an additional task simultaneously in controls (Ramsey et al., 2004). If a cognitive task involves a constant relationship between stimuli and responses, practice can induce a shift from demanding to effortless processing, which is referred to as automatization. In a previous study we demonstrated that automatization is associated with improved performance and reduced activity in WM. In a related study we compared the difference in WM activity after practice to the ability to perform two tasks simultaneously. It was found that subjects with a larger reduction in WM activity after practice were better at performing two tasks concurrently (Ramsey et al., 2004). This suggests that the drop in WM activity induced by practice may reflect an increase of available WM capacity to accommodate concurrent task performance.

Although behavioral tests of automatization indicate that schizophrenic patients improve performance with practice (Harvey et al., 2000; Serper et al., 1990) several studies have shown that patients are either unable to process a second task concurrently (Granholm et al., 1991, 1996) or need significantly more practice to achieve normal dual-task performance (Gold and Harvey, 1993; Serper et al., 1990; Granholm et al., 1991, 1996; Harvey et al., 2000). This suggests that schizophrenic patients may fail to reduce neural activity in spite of improved performance after practice and are therefore unable to liberate sufficient neural resources to perform additional tasks simultaneously.

This raises the question whether inefficient WM function and limited capacity in schizophrenia could be associated with a failure in automatization. To test this, brain activity was examined with fMRI using a verbal WM task with novel and practiced stimulus sets (Sternberg, 1966). Subjects subsequently participated in a behavioral dual-task paradigm to measure their ability of concurrent task performance.

2. Methods and materials

2.1. Subjects

Patients were recruited from the Department of Psychiatry of the University Medical Center Utrecht. DSM-IV diagnosis of schizophrenia was confirmed using The Comprehensive Assessment of Symptoms and History (CASH) (Andreasen et al., 1992a) and severity of symptoms was assessed with The Positive And Negative Syndrome Scale (PANSS) interview (Kay et al., 1987). Controls were recruited through advertisement

Table 1
Demographic and illness-related variables in healthy controls and subjects with schizophrenia

	Patients with schizophrenia				Healthy controls				
	N	Mean	SD	Range	N	Mean	SD	Range	*p*-value[a]
Male	14				13				–
Female	4				5				–
Age (yr)		28.4	7.4	19.6–41.8		26.0	5.8	18.9–43.8	n.s.
EHI index		0.80	0.19	0.42–1.00		0.86	0.20	0.33–1.00	n.s.
Education (yr)		13.1	1.94	9–15		13.4	1.50	10–16	n.s.
PANSS (item mean)									
Positive scale		1.77	0.57	1.00–2.83					
Negative scale		2.10	0.72	1.00–3.29					
General scale		1.59	0.32	1.06–2.19					
Length of Illness (yr)		5.23	4.36	0.77–17.53					
Age of Onset (yr)		23.17	5.04	15–33					
Medication (mg/day)									
Clozapine	7	145.36	179	0–400					
Quetiapine	1	700	–	700					
Risperidon	3	1.33	0.58	1–2					
Olanzapine	6	10.75	7.64	2–20					

N: number of subjects, SD: standard deviation. PANSS:Positive and Negative Syndrom Scale (Kay et al., 1987), EHI: Edinburgh Handedness Index (Oldfield, 1971).

[a] Significance of differences calculated by using *t*-tests and nonparametric Kolmogorov–Smirnov *Z*-test, two-tailed.