ELSEVIER

International Journal of Psychophysiology 27 (1997) 147–151

INTERNATIONAL JOURNAL OF PSYCHOPHYSIOLOGY

Short communication

Association of an oculomotor delayed response task and the Wisconsin Card Sort Test in schizophrenic patients

Sohee Park*

Department of Psychology and Institute for Neuroscience, Northwestern University, 2029 Sheridan Road, Evanston, IL 60208, USA

Received 15 July 1996; revised 15 December 1996; accepted 5 March 1997

Abstract

The relationship between a widely-used neuropsychological test of frontal lobe function, the Wisconsin Card Sort Test, and spatial working memory, as assessed by the oculomotor delayed response task, was examined in schizophrenic patients. Schizophrenic patients were impaired compared with bipolar and normal control subjects on both tasks and their working memory performance was significantly correlated with their WCST measures. The spatial working memory and the WCST deficits in schizophrenia may reflect disrupted circuitry mediated by the dorsolateral prefrontal system. © 1997 Elsevier Science B.V.

Keywords: Schizophrenia; Working memory; Frontal lobe; Wisconsin Card Sort Test; Delayed response

1. Introduction

Neuropsychological testing of schizophrenic patients typically yields symptom profiles that are similar to frontal and temporal lobe dysfunctions but dissimilar to parietal lobe disorders (e.g. Kolb and Wishaw, 1983). Patients with frontal lobe lesions also tend to display anergia, inappropriate affect, attention deficits and recall problems (Stuss and Benson, 1984, 1987), similar to that observed in a large proportion of chronic schizophrenic patients.

Functional imaging studies also indicate frontal lobe dysfunction in schizophrenia. Medicated schizophrenic patients do not show 'hyperfrontal'

* E-mail: shp@nwu.edu

PII S0167-8760(97)00045-7

regional cerebral blood flow (rCBF), typically manifested by normals at resting state (Ingvar and Franzen, 1974; Ingvar, 1980). In addition, hypofrontality is related to the negative symptomatology, as well as specific cognitive deficits (Andreasen et al., 1992; Wolkin et al., 1992). During the Wisconsin Card Sort Test (WCST), the regional cerebral blood flow to the dorsolateral prefrontal cortex was significantly increased in normal controls but not in schizophrenic patients (Weinberger et al., 1986, 1988; Sagawa et al., 1990). However, during a number matching task, which is not mediated by the prefrontal cortex but still requires cognitive effort, there was no difference between the normal controls and patients in the rCBF pattern (Weinberger et al., 1986, 1988; Berman et al., 1988).

A variety of cognitive experiments, especially those involving the control of eye movements, also implicate the role of frontal lobe deficit in schizophrenia. Lesions in the dorsolateral prefrontal region in the rhesus monkey lead to profound deficits in spatial working memory, as assessed by delayed response tasks (e.g. Jacobsen, 1936; Goldman-Rakic, 1987; Funahashi et al., 1989). Humans with prefrontal lesions also show analogous deficits in delayed response tasks (Freedman and Oscar-Berman, 1986) or in memory-guided eye movement tasks (Pierrot-Deseilligny et al., 1991). Similarly, schizophrenic patients show deficits in oculomotor and haptic delayed response tasks, whereas bipolar patients do not show any impairments on the same tasks (Park and Holzman, 1992, 1993). Thus, working memory deficit, as assessed by the delayed-response tasks, provide additional evidence for the presence of prefrontal pathology in schizophrenic patients, who seem unable to regulate behavior by means of working memory, mediated by the prefrontal cortex (see Goldman-Rakic, 1991).

The WCST is a complex neuropsychological task with multiple neurocognitive components, some of which require active working memory. Spatial working memory, as assessed by the delayed response task is mediated by the dorsolateral prefrontal system in the monkey and although the evidence is mixed, the ability to perform well on the WCST also seems to be mediated by the dorsolateral prefrontal system rather than the orbitofrontal system. Therefore, delayed response and WCST performances should be associated, if they both share the same underlying neural and psychological mechanisms. Indeed, data from psychometrically ascertained schizotypic subjects indicate that their WCST performance is associated with deficits in spatial working memory (Park et al., 1995). It was hypothesized that the spatial working memory deficit would be associated with the WCST performance in schizophrenia patients.

2. Subjects and methods

2.1. Subjects

Fourteen schizophrenic out-patients (four women) and 13 bipolar out-patients (three women) who met the DSM-III-R diagnosis (Spitzer and Williams, 1985) participated in the study. They had no evidence of organic brain damage and were not mentally retarded. All patients were medicated. Scores of working memory function from 12 of these patients have been reported in Park and Holzman (1992). Fif-

Table 1
Mean age, years of education, IQ and the duration of illness

	Age (S.D.)	Years of education (S.D.)	WAIS verbal (S.D.)	Duration of illness (S.D.)
Schizophrenic (n = 14)	31.8 (5.0)	12.4 (1.5)	102.1 (14.1)	11.6 (3.6)
Bipolar (n = 13)	33.5 (9.5)	13.2 (1.8)	102.9 (11.9)	12.6 (7.8)
Normal (n = 15)	34.6 (8.8)	13.8 (1.8)	108.2 (8.8)	Not applicable

teen normal control subjects (five women) who did not have a history of mental illness in the family, were recruited. Demographic variables are summarized in Table 1. There were no statistical differences in age, years of education and IQ scores among the three subject groups. The two patient groups did not differ in the duration of illness.

2.2. Procedure

2.2.1. Oculomotor delayed response task (ODR)

Only a brief description of the ODR is given here. Details of the ODR paradigm and a description of the ISCAN eye monitoring equipment are found in Park and Holzman (1992) (1993). The target, a black circle (2°) was flashed for 200 ms in the periphery while the subject fixated on a dot (0.5°) in the center of the stimulus display monitor. The distance between the fixation point and the target was 12°. Target locations were presented in a random order. Immediately following the target presentation, there was a delay period of 15 s, during which subjects performed an intervening verbal task, introduced to prevent them from using idiosyncratic mnemonic strategies and also to make sure that they maintained fixation in the center during the delay. The intervening task does not interfere with the spatial working memory performance (Park, 1991). After the delay, subjects were required to move their eyes to the remembered position of the target. Eye positions were recorded every 20 ms. There were 64 trials (see Fig. 1).

2.2.2. Wisconsin Card Sort Test

The Nelson Revised version of the WCST was used. It makes less cognitive demands because the rules are made explicit to the subject so that errors are less likely to be due to the failure to grasp the rules of sorting (Lezak, 1983).

3. Results

Schizophrenic patients performed worse than the two control groups on the working memory task and on the WCST. The results are summarized in Table 2.

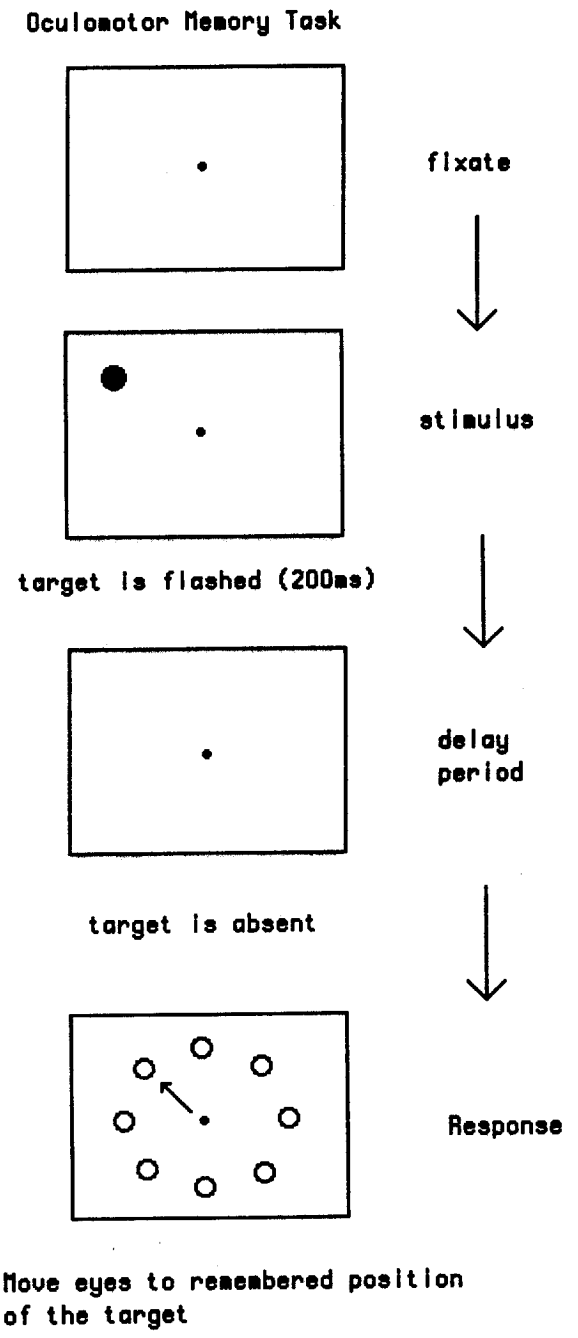

Fig. 1. Oculomotor delayed response task.

3.1. Working memory task

An analysis of variance showed a significant effect of diagnostic group on accuracy of working

Table 2
Results of the working memory task and the WCST

	Working memory	Wisconsin Card Sort Test		
	% correct (S.D.)	No. of errors (S.D.)	No. of perseverative errors (S.D.)	No. of sets achieved (S.D.)
Schizophrenic ($n = 14$)	68.8 (7.5)	16.9 (11.5)	8.6 (5.8)	4.8 (1.2)
Bipolar ($n = 13$)	88.0 (7.8)	4.5 (9.9)	1.1 (1.2)	5.8 (0.8)
Normal ($n = 15$)	86.0 (8.0)	2.9 (1.9)	1.4 (1.4)	6.0 (0.0)

memory ($F_{2,39} = 11.0$, $P < 0.0002$). Schizophrenics were less accurate than the normal controls ($F_{1,27} = 12.2$, $P < 0.002$) and bipolar patients ($F_{1,25} = 13.4$, $P < 0.002$).

3.2. Wisconsin Card Sort Test

There was a significant main effect of diagnostic groups in the number of errors ($F_{2,39} = 10.8$, $P < 0.0002$), the number of perseverative errors ($F_{2,39} = 20.1$, $P < 0.0001$) and the number of sets achieved ($F_{2,39} = 7.8$, $P < 0.0014$). Schizophrenic patients made more errors than bipolar patients ($F_{1,25} = 9.0$, $P < 0.007$) and the normal controls ($F_{1,27} = 21.1$, $P < 0.0001$). Schizophrenic patients also made more perseverative errors than the bipolar patients ($F_{1,25} = 21.0$, $P < 0.0001$) and the normal controls ($F_{1,27} = 21.0$, $P < 0.0001$). Schizophrenic patients achieved fewer sets than the bipolar patients ($F_{1,25} = 5.4$, $P < 0.03$) and the normal controls ($F_{1,27} = 14.4$, $P < 0.0008$). But there were no significant differences between the bipolar patients and the normal controls in any of the above measures.

3.3. Correlations

3.3.1. All subjects ($n = 42$)

There was a significant correlation between the oculomotor memory task and the number of sets achieved ($r = 0.52$, $P < 0.001$), the number of errors on the Wisconsin Card Sort Test ($r = -0.62$, $P < 0.001$) and also the number of perseverative errors ($r = -0.60$, $P < 0.001$).

3.3.2. Schizophrenia patients only ($n = 14$)

There was a significant correlation between the working memory score and the number of sets achieved ($r = -0.61$, $P < 0.05$), the number of errors ($r = -0.78$, $P < 0.001$) and the number of perseverative errors ($r = -0.58$, $P < 0.05$) on the WCST.

4. Discussion

Schizophrenic patients showed deficits on the oculomotor delayed response task and also on the WCST. Spatial working memory and the WCST deficits were significantly associated. This pattern of results supports the hypothesis that the ability to perform the oculomotor delayed response task and the WCST may share some common processes. It is suggested that successful performance on the WCST requires the integrity of working memory, mediated by the dorsolateral prefrontal system.

Acknowledgements

This project was supported by a Young investigator award from NARSAD, a Scottish Rite Schizophrenia Grant, a Human Frontiers of Science grant and a grant from the Swiss National Science Foundation.

References

Andreasen, N.C., Rezai, K., Alliger, R., Swayze, V.W., Flaum, M., Kirchner, P., Cohen, G., O'Leary, D.S., 1992. Hypofrontality in neuroleptic-naive patients and in patients with chronic schizophrenia. Arch. Gen. Psychiatry 49, 943–958.

Berman, K.F., Illowsky, B.P., Weinberger, D.R., 1988. Physiologicdysfunction of dorsolateral prefrontal cortex in schizophrenia. IV. Further evidence for regional and behavioral specificity. Arch. Gen. Psychiatry 45, 616–623.

Freedman, M., Oscar-Berman, M., 1986. Bilateral frontal lobe disease and selective delayed-response deficits in humans. Behav. Neurosci. 100, 337–342.

Funahashi, S., Bruce, C.J., Goldman-Rakic, P.S., 1989. Mnemonic coding of visual cortex in the monkey's dorsolateral prefrontal cortex. J. Neurophysiol. 61 (2), 331–348.

Goldman-Rakic, P.S., 1987. Circuitry of primate prefrontal cortex and regulation of behavior by representational knowledge. In: Plum, F. and Mountcastle, V. (Eds.), Handbook of Physiology — The Nervous System V, American Physiological Society, Bethesda, MD.

Goldman-Rakic, P.S., 1991. Prefrontal cortical dysfunction in schizophrenia: the relevance of working memory. In: B.Carroll (Ed.), Psychopathology and the Brain, Raven Press, New York.

Ingvar, D.H., Franzen, 1974. Abnormalities of cerebral blood flow distribution in patients with chronic schizophrenia. Acta. Psychiatr. Scand. 50, 425–462.

Ingvar, D.H., 1980. Abnormal distribution of cerebral activity in chronic schizophrenia: a neurophysiological interpretation. In: Baxter, C. and Melnechuk, T. (Eds.), Perspectives in Schizophrenia, Raven, New York.

Jacobsen, C.F., 1936. Studies of cerebral functions in primates: I. The functions of the frontal association areas in monkeys. Comp. Psychology Monogr. 13, 3–60.

Kolb, B., Wishaw, I.Q., 1983. Performances of schizophrenic patients on tests sensitive to left orright frontal, temporal, or parietal function in neurological patients. J. Nerv. Ment. Dis. 171 (7), 435–443.

Lezak, M.D., 1983. Neuropsychological Assessment. 2nd edition, Oxford University Press, New York.

Park, S., 1991. The role of prefrontal cortex in spatial working memory deficit of schizophrenic patients. Harvard University Doctoral Thesis.

Park, S., Holzman, P.S., 1992. Schizophrenics show working memory deficits. Arch. Gen. Psychiatry. 49, 975–982.

Park, S., Holzman, P.S., 1993. Association of working memory deficit and eyetracking dysfunction in schizophrenia. Schizophr. Res. 11, 55–61.

Park. S., Holzman, P.S., Lenzenweger, M.F., 1995. Individual differences in working memory in relation to schizotypy. J. Abnorm. Psychol. 104 (2), 355–363.

Pierrot-Deseilligny, C., Rivaud, S., Gaymard, B., Agid, Y., 1991. Cortical control of memory-guided saccades in man. Exp. Brain Res. 83, 617–617.

Sagawa, K., Kawakatsu, S., Shibuya, I., Arata, O., Morinobu, S., Komatani, A., Yazaki, M., Totsuka, S., 1990. Correlation of regional cerebral blood flow with performance on neuropsychological tests in schizophrenic patients. Schizophr. Res. 3, 241–246.

Spitzer, R.L., Williams, J.D.W., 1985. Structured Clinical Interview for DSM III-R, New York State Psychiatric Institute Biomedical Research Division, New York.

Stuss, D.T., Benson, D.F., 1984. Neuropsychological studiesof the frontal lobes. Psychol. Bull. 95 (1), 3–28.

Stuss, D.T., Benson, D.F., 1987. The frontal lobes and control of cognition and memory. In: Perecman, E. (Ed.), The frontal lobes revisited NY. IRBN Press.

Weinberger, D.R., Berman, K.F., Zec, R.F., 1986. Physiologic dysfunction of dorsolateral prefrontal cortex in schizophrenia. I. Regional cerebral blood flow evidence. Arch. Gen. Psychiatry 43, 114–124.

Weinberger, D.R., Berman, K.F., Illowsky, B.P., 1988. Physiologic dysfunction of dorsolateral prefrontal cortex in schizophrenia. III. A new cohort and evidence for monoaminergic mechanism. Arch. Gen. Psychiatry 45, 609–615.

Wolkin, A., Sanfilipo, M., Wolf, A.P., Angrist, B., Brodie, J.D., Rotrosen, J., 1992. Negative symptoms and hypofrontality in chronic schizophrenia. Arch. Gen. Psychiatry 49, 959–966.