BRIEF REPORT

Spatial Working Memory: Absence of Gender Differences in Schizophrenia Patients and Healthy Control Subjects

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Background: *Spatial working memory dysfunction has been suggested to be a cardinal feature of schizophrenia. But schizophrenia is heterogeneous in its clinical profile, course, and outcome. One fundamental contributor to this heterogeneity may be gender. No report has yet addressed gender differences in spatial working memory, as measured by the delayed-response task (DRT).*

Methods: *We aggregated data from three previously published studies of spatial working memory in schizophrenia and also collected DRT data from a new sample of subjects in order to examine potential gender differences in DRT performance.*

Results: *As previously reported, schizophrenia patients (*n *= 71) showed deficits in spatial working memory relative to normal control subjects (*n *= 213), however, no within-group or between-group gender differences were present.*

Conclusions: *These findings provide evidence for the absence of gender differences in spatial working memory function.* Biol Psychiatry 1999;46:1003–1005 © *1999 Society of Biological Psychiatry*

Key Words: Working memory, schizophrenia, sex differences, frontal lobe, delayed response task, gender differences

Introduction

Relative to their male counterparts, female schizophrenia patients tend to experience a more benign course of illness, as demonstrated by fewer neuroanatomic abnormalities, later onset, superior premorbid adjustment, better outcome, longer periods of remission, and fewer readmissions (Andreasen et al 1990; Angermeyer et al 1990; Goldstein et al 1998; Lewine 1988). Given such gender differences in the course of illness, it is possible that female schizophrenia patients may also manifest superior neurocognitive functioning relative to males. To date, no definitive pattern of gender differences in the neurocognitive profile of schizophrenia has been established (Goldstein et al 1998; Haas et al 1990; Hoff et al 1992; Walker et al 1992).

However, recent studies suggest that gender differences in neuropsychological performance may be attributable to sexual dimorphism of the brain (e.g., Seidman et al 1997). Pathophysiology of schizophrenia includes local gray matter reduction in the frontal heteromodal association cortex (e.g., Pearlson et al 1996; Schlaepfer et al 1995). Healthy female brains have increased gray matter volume in the dorsolateral prefrontal cortex (DLPFC) relative to male brains (Schlaepfer et al 1995).

The DLPFC is essential in mediating working memory (WM) processes (see Goldman-Rakic 1991; Jonides et al 1993). Lesions in the DLPFC result in profound deficits in WM, as assessed by the DRT (Freedman and Oscar-Berman 1986; Funahashi et al 1993). Schizophrenia patients also show similar deficits (Carter et al 1996; Keefe et al, 1995; Park and Holzman 1992, 1993). Spatial WM, as assessed by the DRT, is associated with WCST scores (Park 1997; Park et al 1995). These results suggest that the DRT, mediated by the DLPFC, taps WM, and is associated with WCST. But the DRT offers advantages over traditional neuropsychological tests (e.g., WCST) because the neurobiologic basis of the DRT is well described and understood (see Goldman-Rakic 1991).

Although gender differences in WCST have been reported and interpreted as providing evidence for sexual dimorphism of DLPFC (Seidman et al 1997), gender differences in DRT performance have not been examined. Since the DRT is a much more circumscribed test of assessing the DLPFC, we examined the potential gender differences in spatial WM (and therefore, DLPFC function) by aggregating data from three previously published studies and by collecting additional DRT data from a new set of subjects.

Methods and Materials

Participants

Data from three previous studies of were aggregated (see the following papers for descriptions of participants, sampling procedures, and methods: Park and Holzman 1992, 1993; Park et al 1999). New subjects were recruited and tested on the same DRT.

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Received July 28, 1998; revised April 19, 1999; accepted June 1, 1999.

0006-3223/99/$20.00
PII S0006-3223(98)00149-3

Table 1. Demographic Characteristics of Schizophrenia Versus Control Groups

	n	Age[a]	Education[a]	Duration of illness[a]	Age of onset[a]
Control subjects	213	27.3 (9.2)	13.8 (1.6)		
Females	106	27.7 (10.6)	13.9 (1.7)	N/A	N/A
Males	107	26.9 (7.8)	13.6 (1.4)	N/A	N/A
Patients	71	35.5 (9.2)	12.8 (1.8)	11.9 (7.5)	23.6 (8.2)
Females	26	37.3 (12.1)	13.1 (1.8)	10.6 (8.5)	26.7 (11.5)
Males	45	34.4 (6.9)	12.6 (1.8)	12.6 (6.8)	21.5 (4.6)

[a]Mean (SD).

This resulted in a sample of 71 schizophrenia patients who met the DSM criteria (26 females) and 213 normal control subjects (106 females). Subjects had no brain damage, were under 50 years old, and were not mentally retarded. All control subjects were screened for history of mental illness. For each study, the patients and the control subjects were matched for age, education, and handedness (see Table 1 for demographics).

Delayed-Response Task (DRT)

For details of the procedure, please refer to the previous work (Park and Holzman 1992, 1993; Park et al 1999). Participants looked at the central fixation dot on a screen. Then, a target was flashed for 200 msec in the periphery, followed by a delay period during which subjects performed an intervening task to prevent rehearsal. After the delay, subjects selected the remembered position of the target (see Figure 1 for procedure). The percentage of correct scores (%) were calculated.

Results

Within the schizophrenic group, there were no significant gender differences in age [t (69) = 1.28; p = .20], education [t (69) = 1.16; p = .25], or illness duration [t (69) = −1.10; p = .27]. There was a significant gender difference in age of onset [t (69) = 2.5; p = .01]; women had later onset. Within the control group, there were no significant gender differences in age [t (211) = 0.58; p = .56] or education [t (211) = 1.82, p = .07].

A two-way (group × sex) ANOVA was performed on the DRT accuracy (Table 2). There was a main effect of group [F (1,280) = 129.7; $p < .001$] but there was no main effect of gender [F (1,280) = 0.003; $p > .96$] or a group × gender interaction [F (1,280) = 0.08; $p > .78$]. Corresponding effect sizes were 0.93 for the main effect of diagnosis, 0.003 for gender, and 0.02 for group × sex interaction. DRT performance was not associated with age (r = −.01, patients; r = −.11, controls), education (r = −.07, patients; r = −.10, controls), duration of illness (r = −.12), or age of onset (r = .09).

Discussion

We examined gender differences in spatial WM (as assessed by the DRT), mediated by the DLPFC, because recent neuroanatomic and neuropsychological data suggested gender differences in DLPFC structure and function (Schlaepfer et al 1995; Seidman et al 1997). Seidman and colleagues (1997) found that male schizophrenic subjects perform significantly worse on the WCST than the female patients. They interpreted the results in the context of the sexual dimorphism of the DLPFC. Others, however, reported no gender differences in WCST performance (Lewine et al 1996).

WCST performance is associated with the DRT accuracy (Park 1997; Park et al 1995) but the neural correlates of the DRT are much more circumscribed and better described. The DRT, therefore, may be one of the best noninvasive tasks for probing the DLPFC function. We found no gender differences in spatial working memory, as assessed by DRT, among schizophrenic or control subjects.

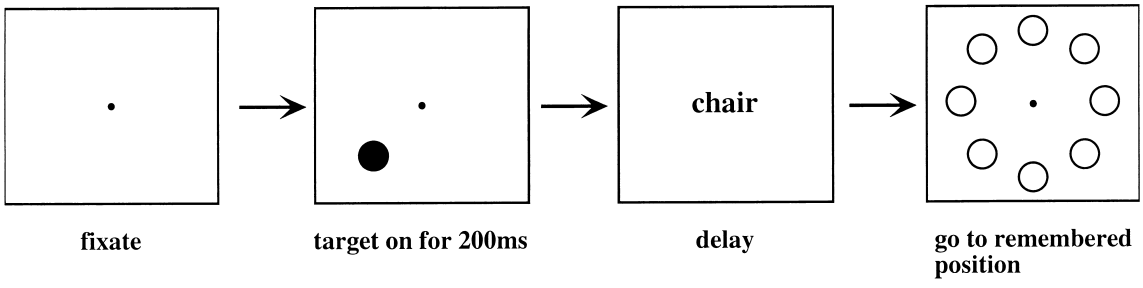

Figure 1. Spatial working memory task.

Table 2. Mean Accuracy (Percent Correct) On the Spatial Delayed Response Task for Schizophrenic Patients and Healthy Control Participants

	n	Mean accuracy (%)	Standard deviation	Standard error	99% Confidence interval
Control subjects	213	94.2	7.44	0.50	(93.19, 95.20)
Females	106	94.0	7.21	0.70	(92.56, 95.33)
Males	107	94.4	7.68	0.74	(92.93, 95.91)
Patients	71	76.9	17.22	2.04	(72.79, 80.94)
Females	26	77.1	15.72	3.08	(70.73, 83.43)
Males	45	76.4	18.20	2.71	(71.28, 82.21)

Although our analysis has sufficient statistical power, owing to the post-hoc nature of our investigation, it necessarily has limitations. Schizophrenia is reportedly less severe in women during the first decade of illness (Goldstein 1988; Salokongas and Stengard 1990) and gender differences have been reported to disappear as early as 5 years after the onset (Häfner 1987). The patients in this study tended to be chronic, which might limit the probability of finding gender differences. Although the DRT performance was not correlated with duration of illness, large scale future studies are needed to rule out possible gender differences in recent-onset or first-episode patients in relation to their WM functioning.

This project was funded by the NIMH, NARSAD, and the Scottish Rite Schizophrenia Research Program.

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