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Trajectory estimation in schizophrenia

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Abstract

Two experiments were conducted to investigate the ability of schizophrenia patients to maintain internal representation over time and space. It has been hypothesized that the ability to guide behavior by internal representation, mediated by the dorsolateral prefrontal cortex (DLPFC), is impaired in schizophrenia [e.g. Goldman-Rakic, P.S., 1996. The functional parcellation of dorsolateral prefrontal cortex and the heterogeneous facets of schizophrenia. In: Matthysse, S., Levy, D.L. (Eds.), Psychopathology: Evolution of a New Science. Cambridge University Press, Cambridge]. In Experiment 1, subjects observed a target, which traveled behind an opaque wall during a part of its trajectory. The task was to accurately assess the speed of the target by predicting when the target would re-emerge on the other side of the wall. In Experiment 2, subjects were asked to estimate the spatial trajectory of an established target path when it was partially occluded from view by another object. Schizophrenia patients were impaired in estimating the speed of a moving target and in estimating the spatial trajectory, without showing deficits in the control tasks. These results suggest that schizophrenia patients may not be able to accurately maintain the internal representation of a target over time and space. Such deficits may have deleterious consequences in goal-directed behavior.

Keywords: Cognitive estimation; Frontal cortex; Mental representation; Schizophrenia; Speed estimation; Trajectory estimation

1. Introduction

Schizophrenia patients show deficits in representational guidance of behavior, mediated by the dorsolateral prefrontal cortex (e.g. Goldman-Rakic, 1987, 1996; Park and Holzman, 1992, 1993; Cohen et al., 1997; Carter et al., 1998). The ability to maintain internal representation to guide action is absolutely crucial in all aspects of our behavior. Strong support for the evidence of abnormalities in the functioning of internal representation of behavior in schizophrenia patients exists (e.g. Park and Holzman, 1992). There are cells in the DLPFC that increase activity specifically during the delay period of the delayed response task, maintaining the internal representation of the invisible target (e.g. Funahashi et al., 1989, 1990, 1991; Funahashi and Kubota, 1994). Furthermore, neuroimaging studies consistently report that tasks requiring an 'on-line' mental representation of the stimulus are accompanied by an increased activation of the DLPFC (Jonides et al., 1993; Braver et al., 1997; Cohen et al., 1997).

Abnormalities of DLPFC may result in profound deficits in all behaviors that require maintenance of representation over time, including the ability to track a smoothly moving target in space. The majority of schizophrenia patients and about

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40% of their healthy relatives show a smooth pursuit eye movement (SPEM) deficit, which has been suggested to be a potential biological marker for schizophrenia (e.g. Holzman and Matthysse, 1990). Schizophrenia patients are unable to match their eye velocity with the target velocity, and, in addition, numerous saccadic intrusions are present during smooth pursuit tracking. These observations, in addition to neurophysiological data from non-human primates, suggest that the prefrontal cortex is crucial for SPEM (Levin, 1984; Lynch, 1987; Goldman-Rakic, 1996). In humans, SPEM deficits correlate with neuropsychological tests of frontal lobe functioning, but not with the performances on the tasks tapping other cortical regions (Katsanis and Iacono, 1991). Recent studies looking for the cause of SPEM deficits in schizophrenia suggest that motion perception is impaired in schizophrenics (Chen et al., 1999a) and that deficient processing of velocity contributes to problems in the initiation and maintenance of SPEM in schizophrenia patients (Chen et al., 1999b). Schizophrenia patients are impaired in maintaining internal representation of the target and therefore may not be able to discern velocities of moving targets accurately.

In the present study, we directly investigated the ability of schizophrenia patients to maintain representation over time and space. The ability to predict the trajectory of a moving target has been associated with frontal lobe development (Diamond, 1988; Diamond and Doar, 1989) and is related to the emergence of the 'object permanence' [see Bower (1974)]. Infants, before they achieve 'objective permanence', do not expect a target that disappeared behind a wall to reappear; hence, for young children as well as monkeys with lesions in the DLPFC, 'out of sight' is equivalent to 'out of mind' (Diamond, 1988; Diamond and Doar, 1989; Goldman-Rakic, 1996). The use of internal representation to predict future events, such as the trajectory of a moving object, should be difficult for those with frontal lobe deficits, including schizophrenia patients. A recent study found that schizophrenia patients indeed have deficits in trajectory perception (O'Donnell et al., 1996).

Deficient maintenance and manipulation of internal representation may be manifested in any behavior that requires using information from the immediate past in order to estimate and predict future events. For example, following a moving target with one's eyes requires very rapid estimation of the target position, velocity and acceleration in space, in addition to executing and maintaining motor commands to set the eyes in motion. Therefore, the possible components of successful SPEM include intact motion perception, maintenance of internal representation and execution of motor commands from the internal representation. A recent study has shown that schizophrenia patients have deficits in discerning small velocity differences in the absence of deficits in contrast sensitivity or orientation discrimination and that the deficits in motion processing are implicated in SPEM dysfunction (Chen et al., 1999a,b). However, other factors are likely to be involved in SPEM deficits. Controlling the eye velocity to match the target velocity in a SPEM task requires intact motion perception and the internal representation of the trajectory of the target, based on the motion processing signals which are continuously updated.

We hypothesized that schizophrenia patients would show deficits in estimating the speed of the moving target as well as in projecting the imaginary spatial path of a trajectory. We conducted two experiments to test the ability of schizophrenia patients to estimate the speed and spatial trajectory of visual targets. In Experiment 1, subjects were asked to estimate the speed of the moving object that had disappeared behind an opaque wall for a part of its trajectory. Experiment 2 was a spatial estimation task in which subjects were asked to use available information to project the trajectory of the path of the target.

2. Experiment 1: Speed estimation of visual targets

We hypothesized that the schizophrenia patient would be impaired in representing the trajectory of a moving target and therefore would be less likely to accurately estimate its speed. Furthermore, because a slower target speed requires the subject to maintain stimulus representation for a

longer period of time for a given distance, schizophrenics should be worse when the target speed is slow.

2.1. Methods

2.1.1. Subjects

Twenty-nine schizophrenia patients (12 women) were recruited from a private psychiatric residential care facility, and 34 age- and education-matched normal control subjects (14 women) were recruited from the same urban area. Patients met the DSM IV criteria for schizophrenia as determined by a structured interview (SCID). All patients were receiving antipsychotic medication. Subjects were excluded if they had any history of brain injury, tardive dyskinesia or current substance abuse. Normal control subjects were medication-free, clinically unaffected and had no personal or family history of mental illness of substance abuse. The mean age of the schizophrenia patients was 37.2 years (s.d. = 8.5) and that of the normal controls was 33.4 years (s.d. = 10.1). The mean years of education were 13.2 (s.d. = 2.6) for the patients and 14.0 (s.d. = 2.1) for the controls. The mean duration of illness for the patients was 16.3 (s.d. = 8.2) years. There was no significant difference between normal controls and schizophrenia patients in age [$F(1,61) = 1.3$, $p > 0.10$] or education [$F(1,61) = 1.05$, $p > 0.10$].

2.1.2. Procedure

Subjects sat 46 cm from the computer screen, and a head-rest was used to minimize their head movement. Subjects pressed a spacebar to see the target (a black circle, 0.5 cm in diameter) move across within a frame on computer screen at a constant velocity. The horizontal width of the frame was 16 cm so the target always traveled 16 cm from left to right. Subjects were allowed to see the target move across the screen at the same speed 10 times to become familiar with the paradigm. They were asked to follow the target with their eyes from one end of the screen to the other.

Subjects were then told that the same target would travel across the screen at the same speed but that a part of its trajectory would be obscured by a 'wall'. The wall was then shown. This occupied the middle part of the screen (8 cm wide). The target appeared on the extreme left side of the screen and traveled at a constant velocity for 4 cm before arriving at the wall. Then, it was not visible while traveling between the left edge of the wall to the right side (8 cm). During practice trials, the target re-emerged on the right edge of the wall and traveled further for 4 cm towards the extreme right border of the frame. Subjects were asked to follow the target as it moved behind the left edge of the wall, imagine it moving behind the wall at the same speed and press the labeled key when they thought the target would reappear at the right edge of the wall. They were given 10 practice trials in which they could practice estimating the re-emergence of the target and pressing the key. During the practice trials, the participants received feedback on their accuracy because the target always re-appeared on the other side of the wall. The same wall was presented for all trials. The practice trials were followed by 10 test trials. The test trials were different from the practice trials in one aspect. When the target moved behind the wall, subjects estimated the point of re-emergence and pressed the key when they thought the target would re-emerge, but it was programmed such that the target never re-appeared. Therefore, there was no feedback on the performance. A schematic diagram of the procedure is shown in Fig. 1.

There were two different speed conditions. In the fast condition, the target speed was always 10 cm per second. In the slow condition, the speed was always 5 cm per second. In the fast condition, the perfect representation of the speed of the target behind the wall should have resulted in the key press, exactly 800 ms after the target disappeared from view. In the slow condition, a perfect response would be 1600 ms. The wall was always 8 cm wide.

To summarize, subjects were asked to estimate the time it takes for the target to travel from the point of its disappearance to its expected re-emergence at the end of the wall. Each session began with 10 observation only trials (no wall), followed by 10 practice trials (wall with feedback) and 10 test trials. The order of presentation of the

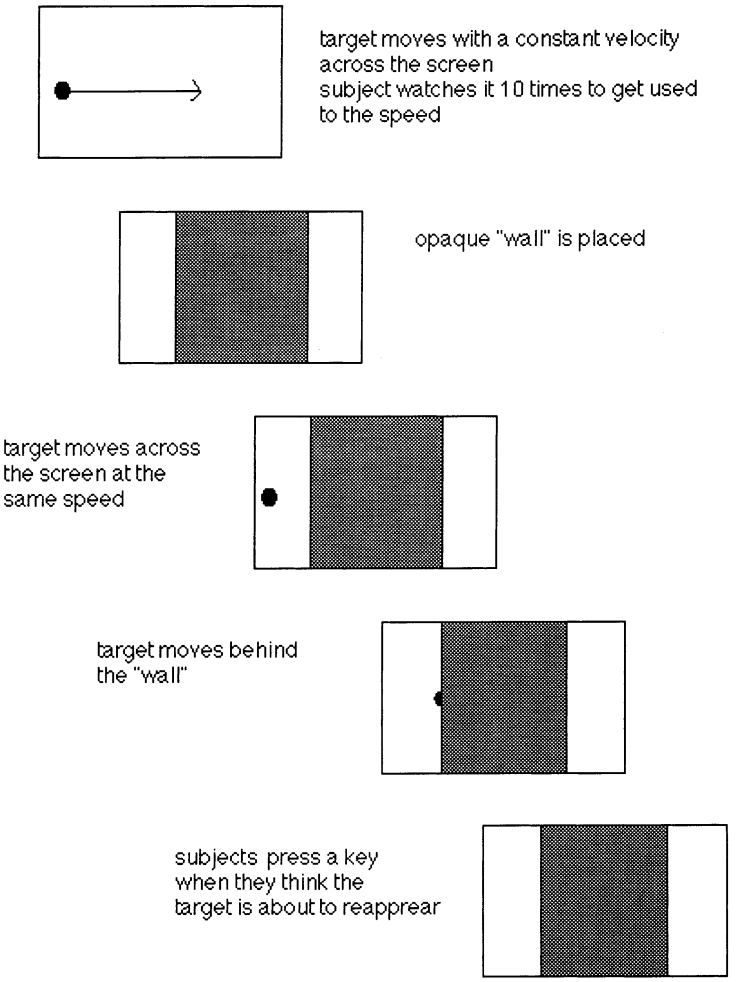

Fig. 1. Procedure of speed estimation task. This task measures the ability of subjects to estimate speed of the target and also the time taken for the target to travel from one end of the wall to the other end.

fast and slow conditions was counterbalanced across subjects.

2.1.3. Results

We conducted two main analyses of the speed estimation data. We first calculated the mean speed estimation time (SET) for each subject. The purpose of this analysis was to ensure that schizophrenia patients were not simply exhibiting a slower response time overall. The ideal response time for the 'fast' condition was 800 ms and that for the 'slow' condition was 1600 ms, so a perfect response on the fast and the slow conditions would yield the speed estimation time (SET) of 800 and 1600 ms, respectively.

Repeated-measures ANOVA showed that there was no main effect of the diagnosis on SET [$F(1,61)=1.32$, $p>0.25$]. In other words, schizophrenia patients were not consistently slower (or faster) in their response times as compared to normal control participants. As expected, we did find a main effect of the speed condition [$F(1,61)=146.3$, $p<0.0001$], but there was no interaction between diagnosis and target speed [$F(1,61)=0.13$, $p>0.71$]. This suggests that both subject groups had a longer speed estimation time for the

slow condition, and schizophrenia patients did not show any pattern of response that was significantly different from normal controls in either speed condition.

We also found that the frequency of underestimating and overestimating the speed of the target was equally distributed among schizophrenics and controls. About half the subjects underestimated. From the SET data, we divided the subjects into those who overestimated and those who underestimated. We found that there was no difference in the distribution of those who tend to anticipate and those who wait too long before they press the key ($\chi^2=0.7$, $p>0.78$ for slow condition and $\chi^2=1.6$, $p>0.21$ for the fast condition).

We then computed a mean 'Absolute Difference Score' (ADS). This score was calculated by taking the average of the absolute difference between the estimated and ideal response times for each trial (i.e. |ideal time − estimated time|). For example, in the fast condition, an ideal response time would be 800 ms, so a subject who estimates the target's re-emergence from behind the wall 700 ms after it disappeared would have an ADS of 100 for that trial ($|800-700|=100$). A subject who estimated the speed at 900 ms would also have an ADS of 100 ($|800-900|=100$). Thus, the ADS provides information about the magnitude of inaccuracy for each response.

Repeated-measures ANOVA showed that there was a main effect of diagnosis on the ADS [$F(1,61)=14.4$, $p<0.001$]. Schizophrenia patients were less accurate in estimating the speed than normal controls. There was a main effect of speed [$F(1,61)=9.2$, $p<0.05$] showing that all subjects were less accurate in estimating the correct speed in the slow condition than in the fast condition. The interaction between diagnosis and speed condition was in the predicted direction; schizophrenia patients had more difficulty estimating speed in the slow condition, but it was not significant [$F(1,61)=2.0$, $p>0.10$]. Please see Table 1 for means and standard deviations and Fig. 2 for a graph of results.

Table 1
Mean (standard deviation) of absolute difference scores in milliseconds

Subject	Fast condition	Slow condition
Schizophrenic	388.7 (427.6)	614.1 (604.7)
Normal control	164.8 (66.3)	252.0 (135.7)

2.1.4. Discussion

Schizophrenia patients were less accurate than normal controls in estimating the speed of the moving target regardless of how fast the target traveled. This difference is not likely to be the result of schizophrenia patients being slower than normal controls on any reaction-time-based tasks, because these patients were not consistently slower than the target. Instead, they were inconsistent; they were faster than the target about half the time and slower than the target the rest of the time. We used predictable trajectories with a constant target speed to make the task as easy as possible, but schizophrenic patients were less accurate than normal controls in estimating the constant velocity of a hidden target moving along a familiar, linear trajectory. The results do not support our hypothesis that a speed estimation deficit would be exacerbated in the slow condition for the patients but not for the normal controls. In fact, both groups were worse at estimating the speed when the target was slow.

Overall, our finding suggests that schizophrenia patients may not be able to internally generate the target speed accurately. A recent study reported that the schizophrenia patients have stable deficits in motion perception and that this deficit is related to both initiation and maintenance of SPEM (Chen

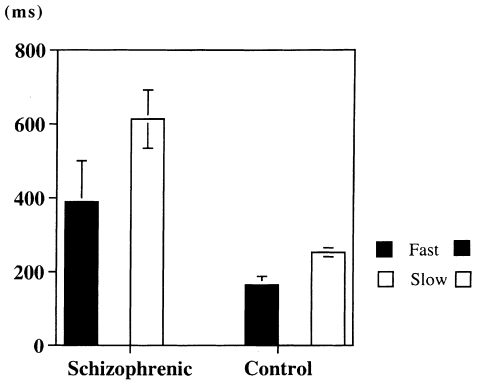

Fig. 2. Mean absolute deviation from the target speed.

et al., 1999b). In addition to motion perception deficits, an inability to estimate or project the target trajectory in time and space may be a factor in SPEM dysfunction, but this possibility remains to be tested. Results from the present study suggest that schizophrenia patients are impaired in estimating the speed of a predictable target. The next question is whether schizophrenia patients are able to predict the spatial path of a target when they are not required to estimate speed. In Experiment 2, we examined schizophrenia patients' ability to continue an established (stationary), visual trajectory when it is partly occluded from view.

3. Experiment 2: Spatial path estimation

Experiment 2 examined the ability of schizophrenia patients to project the spatial path of a target without the involvement of speed estimation. The question is whether schizophrenia patients are able to project the spatial path of the target accurately, given a partial trajectory. In contrast to Experiment 1, the path of the trajectory was in full view while the subjects were asked to 'continue' the representation of that trajectory as it would appear behind the occluding object. The spatial path estimation paradigm was developed to address several unanswered questions from Experiment 1. The spatial path estimation paradigm does not have a memory component, but it does require the ability to generate or internally project the representation of the stimulus path. We measured whether or not subjects were able to project the correct estimated path of the target and, if they were able to estimate the path, how far they were able to maintain it. We hypothesized that schizophrenia patients' representation of the exact trajectory pathway would be less accurate than that of normal controls and also that they would maintain the trajectory path for a shorter distance than the normal controls.

3.1. Method

3.1.1. Subjects

Fifteen schizophrenia patients (four women) and 12 normal controls (two women) from Experiment 1 were recruited at random to participate in Experiment 2. The average ages of schizophrenia patients and normal controls were 39.3 (7.2) and 33.9 (10.0) years, respectively. The mean education level was 11.8 (2.5) years for the schizophrenia patients and 13.8 (1.8) years for the normal controls. Schizophrenia patients had an average duration of illness of 9.5 years (8.7). The age and the years of education did not differ between the two subject groups.

3.1.2. Procedure

The spatial estimation experiment was administered as a paper and pencil task. Participants were given a packet of 20 line drawings that served as the stimuli. Each stimulus was presented on an 8.5×11 sheet of paper. A 'path' was drawn from one end of the paper and extended to establish the pattern of the trajectory. The path was then occluded from view by an object or objects. Participants were asked to draw the 'path' as it would continue behind the object or objects, to assume that, if there was an established pattern of the trajectory, this pattern would continue, and to draw the path as it would continue all the way across the stimulus page. There were four practice trials, two control trials and 14 test trials. The purpose of the practice trials was to ensure that all subjects understood the task. If they did not understand the task, the instructions were repeated and explained. No feedback on accuracy was given during the practice trials. The control trials consisted of a straight line obscured from view by an opaque wall in the middle of the page. Participants successfully completed the control task if they could draw a straight line within a 0.5 inch (1.3 cm) boundary on either side of the ideal path of the target. This task was included to ensure that any motor problems due to tremors would not confound the results.

There were three measures of spatial estimation: accuracy, pattern and the extent of completion. These responses were scored by blind raters by a 'yes' or 'no' judgment. Participants received a 'yes' score in the accuracy measure, if they were able to project and recreate the established path of the trajectory within 0.5 inch from the ideal pathway of the target, all the way across the page.

Participants received a 'yes' score in the pattern measure if they were able to illustrate the correct pattern of the trajectory, even if it was not within the 0.5 inch boundary of accuracy. Participants were given a 'yes' on completion if they continued a trajectory path (even if it was not accurate) until the boundary of the stimulus page. Completion and pattern scores are independent but a 'yes' score on accuracy resulted in a 'yes' score on both pattern and completion. For example, a subject could receive a 'yes' for the pattern measure if they illustrated understanding of the pattern of the trajectory path. However, they could still receive a 'no' for completion if they did not continue the path all the way across the page and a 'no' for accuracy if the pattern did not continue to follow the accurate trajectory to its completion. Please refer to Fig. 3 for examples of stimuli items and patient responses.

We developed these three scores for each item in order to assess several different ways that the failure to maintain internal representation may affect performance. In addition, the three scores attempted to address the wide range of performance for both normals and patients. In particular, we were concerned that a measure that would be challenging for patients would be too easy for normal participants and, conversely, that a measure tapping the upper range for normals would prove to be too difficult for patients.

3.1.3. Results

Percentage correct scores were calculated for each measure from the number of 'yes' scores. All subjects were able to successfully complete the control trials. Performances on all three measures were significantly correlated. Repeated measures ANOVA showed significant group differences in all measures of the spatial estimation task. There was a main effect of the diagnostic group [$F(1,24)=24.97$, $p<0.0001$] and a main effect of measure [$F(2,48)=102.5$, $p<0.0001$]. There was no interaction between group and measure [$F(2,48)=0.009$, $p>0.61$]. Schizophrenia patients were significantly worse at recreating the established trajectory with exact accuracy [$F(1,24)=15.7$, $p<0.0005$]; recognizing and recreating the general pattern of the trajectory [$F(1,24)=17.3$, $p<0.0003$]; and completing the entire path of the trajectory [$F(1,24)=10.1$, $p<0.004$]. The three measures differed significantly from one another regardless of diagnostic membership. Please see Table 2 for performance scores on each measure and Fig. 4 for a graph of the results.

The measures of pattern and completion resulted in almost perfect scores for normal controls, whereas the measure of accuracy resulted in a wider range of scores for normal participants and was difficult for the patients. All three measures of the spatial path estimation indicate that schizophrenia patients were unable to project the representation of the stimulus trajectory and that they had difficulty extrapolating stimulus cues from the information concurrently available to them. However, they were able to do the control task, which suggests that possible motor problems cannot explain the observed deficit.

3.1.4. Discussion

Schizophrenia patients have deficits in estimating or predicting where the target path would continue. There was no time constraint or speed factor for the task. Thus, in addition to deficits in temporal, speed estimation, schizophrenia patients have deficits in spatial estimation. Not only do they have difficulty estimating when a predictable target event would occur, but they also have problems in guessing where the target would end up, given the past trajectory of the target. These results suggest that schizophrenia patients may be unable to use internal representation of the target to predict future stimulus events or perhaps to image 'what would happen next'.

It is interesting that 'carrying' the trajectory over the space of the page was a problem specific to patients. However, the reason for this poor performance requires further examination. Although participants were given detailed instructions to carry the trajectory to the end of the stimulus page and were reminded, if necessary, of this requirement during practice trials, patients had a very difficult time completing whatever trajectory they had established.

The initial study using a spatial estimation task provides intriguing results but, clearly, more work needs to be done. We decided to score the spatial

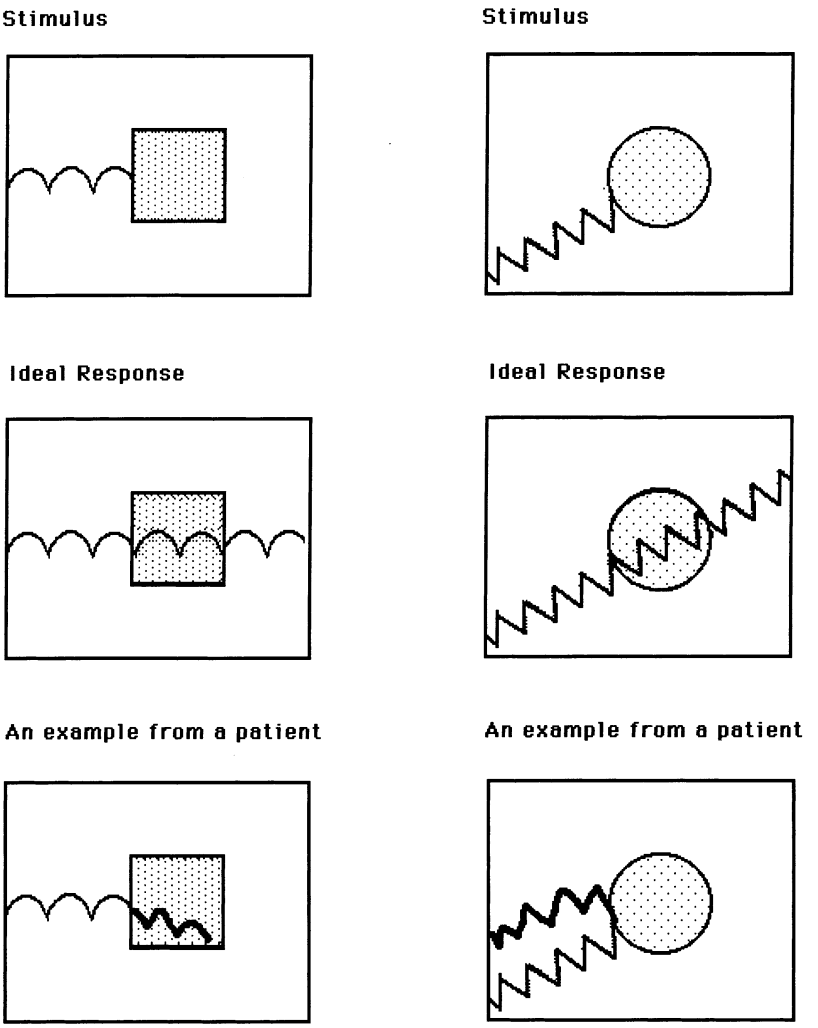

Fig. 3. Spatial estimation task.

estimation data categorically (yes or no), but the responses can also be scored in a continuous, metric way. Our dichotomous scoring scheme has several problems. For example, on the accuracy measure, the response is scored 'no' if the response line lies more than 0.5 inch away from the ideal path, but the score does not state how far off the subject was. A quantitative, metric scoring scheme would be able to capture the range of responses elicited by the subjects. Additionally, future studies

Table 2
Mean (standard deviation) percentage correct scores for each spatial measure

Participant	Accuracy	Pattern	Completion	Control
Schizophrenic	24 (15)	75 (16)	73 (25)	100 (0)
Normal control	52 (22)	96 (6)	97 (6)	100 (0)

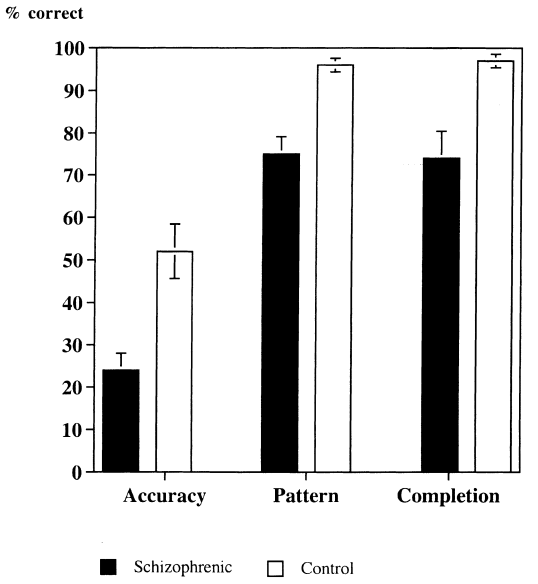

Fig. 4. Spatial path estimation.

could systematically manipulate the number of occluding objects and the type of trajectory pattern that is established.

4. General discussion

Both experiments of trajectory estimation support the hypothesis that schizophrenia patients have difficulty in projecting and maintaining the internal representation of a target in order to predict the next probable stimulus event. The ability to guide behavior by internal representation has been shown to be dependent on the integrity of the DLPFC, and there is converging evidence that this area of the cortex is dysfunctional in schizophrenia patients (Goldman-Rakic, 1996; Cohen et al., 1997).

Our results suggest that working with internal representation (hypothesized to be mediated by the DLPFC) may affect cognitive estimation. Both the speed estimation and the spatial path estimation tasks require the subject to use internal representation of the stimulus to predict its probable next step (i.e. when and where the next stimulus event will be, given its past trajectory). Thus, in a larger context, predicting the future from a present or past experience seems to pose a great difficulty for the schizophrenia patients.

Estimation or prediction from internal representation is problematic for patients with frontal-lobe lesions. Frontal-lobe patients perform poorly on a wide range of cognitive estimation tasks such as estimating the height of a building, the age of the oldest person in the country, and the length of an average man's spine (Shallice and Evans, 1978; Smith and Milner, 1984; Taylor and O'Carroll, 1995). These tasks require the development of an internal representation and the extrapolation of information from that representation in order to make an assessment. Since the ability to maintain the stimulus representation appears to be dependent on DLPFC structures, problems with cognitive estimation of all types may be dependent on the DLPFC as well. However, we do not have the direct evidence for the hypothesis that schizophrenia patients performed poorly on trajectory estimation as a result of DLPFC dysfunction.

One important caveat concerns the possibility of a generalized deficit in schizophrenia (Chapman and Chapman, 1978). Schizophrenia patients tend to perform poorly on a variety of cognitive tasks. We matched the two subject groups on education and included a control task, but it is possible that the control task was 'easier' than the trajectory task. Therefore, we cannot eliminate the possibility that the deficits in speed and spatial estimation may reflect a generalized cognitive deficit. However, deficits in DLPFC lead to a wide range of cognitive, social and affective deficits, which may then appear as if the subject has a generalized deficit. In the latter case, the subject's performance should be intact when no internal representation is needed. If no internal representation is required to perform a task, schizophrenia patients have been shown to perform well (Park and Holzman, 1992; Park et al., 1999).

In designing the present study, we tried to create a series of tasks that may isolate the cognitive function of maintaining an internal representation of a stimulus. Our study suggests that schizophrenia patients have great difficulty maintaining the internal representation of a trajectory path in both spatial and temporal paradigms. Future studies using functional brain imaging techniques

will begin to reveal the extent of the DLPFC involvement in internal representation in general and trajectory estimation. Future behavioral studies will also begin to ascertain the specificity of this deficit in comparison to general cognitive performance.

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References

Bower, T.G.R., 1974. Development in Infancy. Freeman, San Francisco, CA.

Braver, T.S., Cohen, J.D., Nystrom, L.E., Jonides, J., Smith, E.E., Noll, D.C., 1997. A parametric study of prefrontal cortext involvement in human working memory. Neuroimage 5 (1), 49–62.

Carter, C.S., Perlstein, W., Ganguli, R., Brar, J., Mintun, M., Cohen, J.D., 1998. Functional hypofrontality and working memory dysfunction in schizophrenia. Am. J. Psychiatry 155 (9), 1285–1287.

Chapman, L.J., Chapman, J.P., 1978. The measurement of differential deficit. J. Psychiatr. Res. 14, 303–311.

Chen, Y., Palafox, G.P., Nakayama, K., Levy, D.L., Matthysse, S., Holzman, P., 1999a. Motion perception in schizophrenia. Arch. Gen. Psychiatry 56 (2), 149–154.

Chen, Y., Levy, D.L., Nakayama, K., Mattysse, S., Palafox, G., Holzman, P.S., 1999b. Dependence of impaired eye tracking on deficient velocity discrimination in schizophrenia. Arch. Gen. Psychiatry 56 (2), 155–161.

Cohen, J.D., Perlstein, W.M., Braver, T.S., Nystrom, L.E., Noll, D.C., Jonides, J., Smith, E.E., 1997. Temporal dynamics of brain activation during a working memory task. Nature 386 (6625), 604–608.

Diamond, A., 1988. Abilities and neural mechanisms underlying AB performance. Child Dev. 59, 523–527.

Diamond, A., Doar, B., 1989. The performance of human infants on a measure of frontal cortex function, the delayed response task. Dev. Psychobiol. 22 (3), 271–294.

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, 331–348.

Funahashi, S., Bruce, C.J., Goldman-Rakic, P.S., 1990. Visuospatial coding in primate prefrontal neurons revealed by oculomotor paradigms. J. Neurophysiol. 61, 814–831.

Funahashi, S., Bruce, C.J., Goldman-Rakic, P.S., 1991. Neuronal activity related to saccadic eye movements in the monkey's dorsolateral prefrontal cortex. J. Neurophysiol. 65 (6), 164–183.

Funahashi, S., Kubota, K., 1994. Working memory and prefrontal cortex. Neurosci. Res. 21 (1), 1–11.

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

Goldman-Rakic, P.S., 1996. The functional parcellation of dorsolateral prefrontal cortex and the heterogeneous facets of schizophrenia. In: Matthysse, S., Levy, D.L. (Eds.), Psychopathology: Evolution of a New Science. Cambridge University Press, Cambridge.

Holzman, P.S., Matthysse, S., 1990. The genetics of schizophrenia: A review. Psychol. Sci. 1 (5), 279–286.

Jonides, J., Smith, E.E., Koeppe, R.A., Awh, E., Minoshima, S., Mintun, M.A., 1993. Spatial working memory in humans as revealed by PET. Nature 363 (6430), 583–584.

Katsanis, J., Iacono, W.G., 1991. Clinical, neuropsychological and brain structural correlates of smooth pursuit eye tracking performance in chronic schizophrenia. J. Abnorm. Psychol. 100, 526–534.

Levin, S., 1984. Frontal lobe dysfunctions in schizophrenia: I. Eye movement impairments. J. Psychiatr. Res. 18 (1), 27–55.

Lynch, J.C., 1987. Frontal eye field lesions in monkeys disrupt visual pursuit. Exp. Brain Res. 68, 437–441.

O'Donnell, B.F., Swearer, J.M., Smith, L.T., Nestor, P.G., Shenton, M.E., McCarley, R.W., 1996. Selective visual deficits in visual perception and recognition in schizophrenia. Am. J. Psychiatry 153, 687–692.

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

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

Park, S., Puschel, J., Sauter, B., Rentsch, M., Hell, D., 1999. Spatial working memory deficits and clinical symptoms in schizophrenia: A 4-month follow-up study. Biol. Psychiatry 46 (3), 392–400.

Shallice, T., Evans, M., 1978. The involvement of the frontal lobes in cognitive estimation. Cortex 14, 294–303.

Smith, M.L., Milner, B., 1984. Differential effects of frontal lobe lesions on cognitive estimation and spatial memory. Neuropsychologia 22, 697–705.

Taylor, R., O'Carroll, R., 1995. Cognitive estimation in neurological disorders. Br. J. Clin. Psychol. 34, 233–238.