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Brief report

Performance on the continuous performance test under parametric increase of working memory load in schizophrenia

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ABSTRACT

We asked 24 schizophrenia patients and 24 healthy comparison subjects to complete a parametric working memory version of the continuous performance test. Patients exhibited a relatively rapid performance decline with increasing working memory demands. We suggest an interaction between sustained attention and working memory abnormalities in schizophrenia.

1. Introduction

Among the most sensitive and specific probes for attentional deficits in schizophrenia is the continuous performance test (CPT) (Cornblatt and Keilp, 1994). Here, we developed a novel parametric working memory CPT (PWM-CPT) to examine the effects of increasing working memory load associated with a CPT, using Sternberg's memory search experiment (Sternberg, 1966). As a baseline test, we utilized the original simple CPT (asking subjects to press a button in response to letter "T"). In two further subtests, subjects were asked to press a button whenever they saw one of two letters ("F" or "S"), or three letters ("Q", "M", or "P"); hence the number of items in working memory (WM) was systematically increased. We hypothesized that there would be a greater effect of WM manipulation in patients with schizophrenia compared with that of healthy volunteers (i.e., a group by task interaction effect). We were particularly interested in administering the PWM-CPT to a group of clinically stable patients with schizophrenia, to ensure that the psychotic state of the patients did not produce a generalized state-dependent performance deficit.

2. Methods

2.1. Subjects

We studied 24 patients with a DSM-IV diagnosis of schizophrenia (17 males and 7 females; mean age of 39.3 years, S.D. = 8.9, range = 23–54; and mean National Adult Reading Test (NART) IQ of 104.2, S.D. = 13.4, range 76–129). The Schedule for the Assessment of Negative Symptoms (SANS) total mean score was 9.5 (S.D. = 4.4). The Schedule for the Assessment of Positive Symptoms (SAPS) total mean score was 4.8 (S.D. = 3.3). We included, as controls, 24 healthy volunteers (18 males and 6 females; mean age of 38.2 years, S.D. = 9.6; range = 21–55; mean NART IQ of 107.3, S.D. = 9.0, range 94–121). The patient group had a mean illness duration of 13.3 years (S.D. = 8.5). They were all clinically stable at the time of assessment as judged by the team responsible for their clinical care. Twenty patients were receiving atypical, and three patents were receiving typical antipsychotics. One patient was not on any medication. The mean daily dose in chlorpromazine equivalents was 361.5 mg, S.D. = 201.6. Of the 24 patients, 14 were residing in the community. This study was approved by the Sheffield Research Ethics Committee.

2.2. The parametric working memory CPT and data analysis

The CPT task was modified from the simple CPT. The number of target items was manipulated in three conditions ("T", "F or S", and "Q, M, or P"). The total number of stimuli in each subtest was 300 consisting of 26 alphabet letters, and target frequency was maintained at 20% across the three subtests. The three subtests were administered in the same order across all subjects (CPT-T to CPT-Q-M-P). Each subtest was preceded by a practice session consisting of 20 stimuli (of which approximately half were targets) to ensure that subjects understood the task instructions. After completion of each subtest, subjects were given a 5-min break, before starting the next test.

Stimuli, presented using a personal computer and monitor, appeared as black letters on a white screen. Stimuli were presented in the middle of the screen at a constant rate of one/s. Each stimulus appeared for the first 50 ms followed by a blank screen for the remaining 950 ms to allow a response to be made to each target. Each letter was approximately 1.5 cm wide and 2 cm high. Subjects sat approximately 50 cm from the computer screen. Responses were collected using a standard PC mouse.

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Table 1
Performance variables in schizophrenia patients and controls (mean with S.D. in parentheses) across the three subtests of the parametric working memory CPT.

	Patients ($n=24$)	Controls ($n=24$)
CPT-T		
Commission errors	5.83 (6.76)	5.13 (6.94)
Omission errors	8.50 (12.28)	6.58 (11.92)
D-prime	3.55 (1.21)	3.77 (1.11)
Reaction time	672.69 (107.09)	564.85 (108.21)
CPT-F-S		
Commission errors	5.25 (5.55)	4.75 (7.04)
Omission errors	7.08 (8.89)	4.25 (7.41)
D-prime	3.54 (0.93)	3.90 (0.97)
Reaction time	702.10 (96.89)	585.61 (104.74)
CPT-Q-M-P		
Commission errors	7.67 (6.86)	5.04 (6.04)
Omission errors	10.63 (9.85)	4.00 (5.73)
D-prime	2.99 (0.83)	3.83 (0.84)
Reaction time	751.28 (100.53)	616.10 (105.67)

Signal detection sensitivity (d') and reaction time (RT) were examined as dependent variables. We obtained d' using the following formula (Snodgrass and Corwin, 1988):

$$d' = Z_{(Truepositives+0.5)/(Total\ number\ of\ targets+1)} - Z_{(Falsepositives+0.5)/(totalnumberoftargets+1)}$$

d' is an estimate of how well subjects are able to respond to targets correctly, whilst also avoiding erroneous responses to non-targets. A higher value of d' indicates a higher ability to discriminate targets from non-targets, irrespective of the criteria adopted by subjects. All statistical test results reported in this experiment were two-sided and statistical significance was set at 0.05.

3. Results

Table 1 presents mean and standard deviations for performance variables across the three subtests. A 2×3 mixed design analysis of variance, with a between-subject variable of group and a within-subject variable of CPT condition, showed a significant group by condition interaction effect on d', $F(2,92)=3.7$, $p<0.05$. As can be seen in Fig. 1A, patients exhibited rapid decline in d' so that their d' for the CPT-Q-M-P was significantly lower than those of the CPT-T ($p<0.01$) and CPT-F-S ($p<0.001$). On the other hand, healthy subjects did not show significant changes in d' across the three subtests. A between-group difference in d' was significant only in the CPT-Q-M-P, $F(1,46)=12.0$, $p<0.001$, whereas no significant group differences were found in the CPT-T, $F(1,46)=0.42$, $p=0.52$, or in the CPT-F-S, $F(1,46)=1.8$, $p=0.19$. The main effect of group for d' did not reach the significance level, $F(1,46)=3.6$, $p=0.07$.

As shown in Fig. 1B, there was no significant group by condition interaction effect on reaction time (RT) for correct trials, $F(2,92)=2.0$, $p=0.15$. There was a significant effect of group on RT, $F(1,42)=17.2$, $p<0.001$, indicating generally slower responses in patients, compared with healthy volunteers.

In patients, the d' drop from the CPT-F-S to CPT-Q-M-P was not significantly correlated with age, IQ, illness duration or symptom severity (SANS or SAPS total scores).

4. Discussion

This study investigated whether schizophrenia patients, relative to healthy control subjects, would show disproportionate performance decline as the number of working memory items held online increased. We found that patients showed a significant decrease in signal detection sensitivity (d') in the CPT-Q-M-P. This finding suggests that patients' ability to detect targets is disproportionately impaired when they are required to maintain and search for additional targets in WM *continuously*. As seen in Fig. 1, there was no significant d' difference between the CPT-T and CPT-F-S tests in patients. It is possible that, in our version of the CPT, there may be a WM threshold that is not surpassed by the CPT-F-S but is surpassed by the CPT-Q-M-P, producing a significant performance decrease. A possible confounding effect might have arisen because we administered the three subtests in the same order across all subjects (CPT-T to CPT-Q-M-P). This might have led to greater fatigue effects in patients during the CPT-Q-M-P, although they were given a 5-min break between tasks. However, we wished to reduce frustration in patients when presented with the hardest version first.

Despite the patient group showing the well-known overall RT delay, RT in correct trials increased in a near-perfect linear pattern across the three subtests in both groups. This finding suggests that neither patients nor healthy control subjects adopted different task

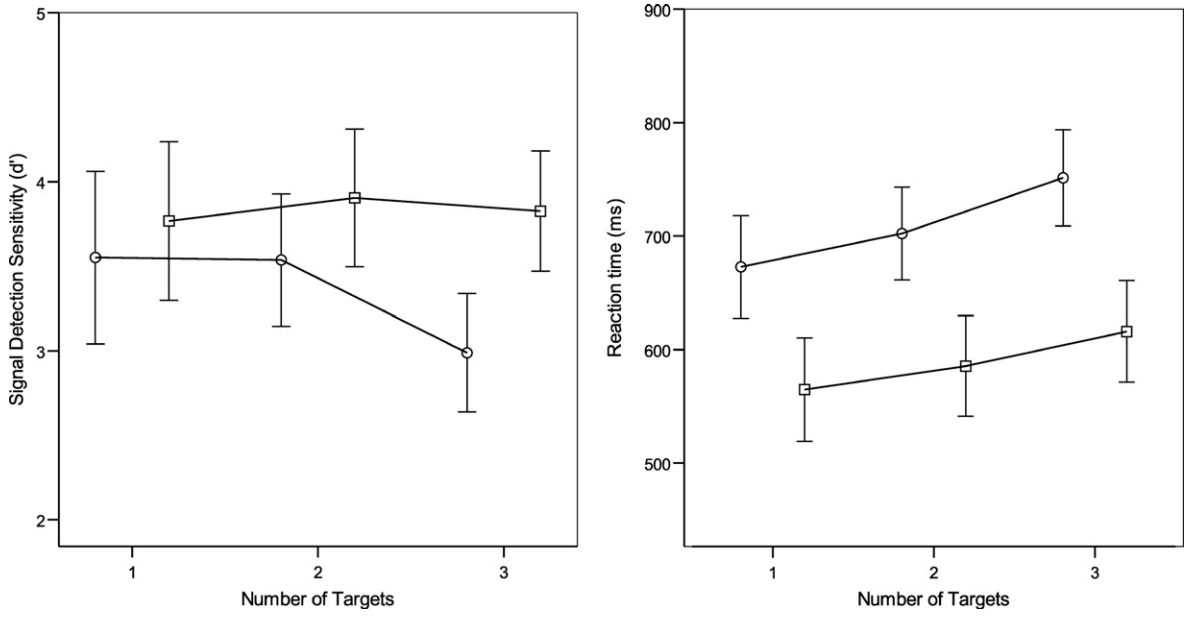

Fig. 1. Patients (circles) show a significant decrease in signal detection sensitivity (d'), as target numbers to be detected increase, whereas healthy volunteers (rectangles) display the same d' across conditions (left panel). By contrast, both groups show a linear increase of reaction time (RT), although the patient group's RT is delayed compared with healthy volunteers (right panel). Error bars show 95% confidence interval of means.

strategies across the three subtests (e.g., speed-accuracy trade-off). More importantly, this linear increase of RT across the three subtests implies that there are no major between-group differences in 1) the execution of WM (i.e., orthographic to phonological recoding and rehearsal of target letters during task by the operation of the phonological loop of WM component as proposed by Baddeley (2003)), nor 2) searching WM content in each trial in order to match the probe item with stored WM items (Sternberg, 1966). Consistent with our observation, Birkett and colleagues found that patients' fastest RTs (1st centile) in a CPT was not significantly different from those of controls (Birkett et al., 2007). Hence, in schizophrenia, the supervisory attention system of the central executive for WM function may often become overloaded when cognitive processing load increases, which suggests that this difficulty may be a trait maker for schizophrenia. According to a recent WM model of Baddeley et al. (2011), the buffer system of the central executive would be responsible for this deficit. As consequences of this overloading, patients might be highly distracted or perseverative, resulting in poor CPT performance such as seen in the present study. We suggest this difficulty may be a trait marker for schizophrenia.

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