



The impact of context processing deficits on task-switching performance in schizophrenia

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ABSTRACT

The prefrontal cortex (PFC) has been described as important for maintaining and implementing contextual information in the service of goal-oriented behavior. Accordingly, impairments in context processing are thought to underlie cognitive deficits associated with schizophrenia, a clinical disorder that has been linked to PFC dysfunction (Servan-Schreiber et al., 1996). However, task switching, a cognitive ability linked to PFC function, has not been consistently impaired in schizophrenia. In this experiment, we assessed whether task-switching performance would be selectively impaired for patients when context demands were high. In the rule-switching condition, a switch required the updating of the relevant task response rules whereas perceptual switching did not entail a switching of contextual information. Instead, a perceptual switch entailed a shift of visuospatial attention to the relevant feature. A second goal was to determine whether potential deficits in context switching would be observed in schizophrenia even in situations when these patients do not need to overcome a prepotent response. Studies of context processing have typically required patients with schizophrenia to use contextual rules to overcome prepotent response tendencies whereas our switching paradigm did not require the inhibition of a competing response. Patients were much slower to switch tasks than controls when contextual rules switched from one trial to the next whereas their performance was intact when the switch occurred between different feature sets and contextual demands were low. Our results demonstrate that context processing deficits are observable in schizophrenia even when there is no prepotent response tendency to inhibit. Moreover, our results suggest that PFC impairments influence performance primarily when patients are required to switch the application of one explicit rule to another.

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1. Introduction

Goal-directed behavior relies on the ability to represent, maintain, and implement contextually-relevant information such as rules, goals, and intentions. Miller and Cohen (2001) argue that the prefrontal cortex (PFC) is critical in achieving goals. The PFC is thought to represent goals and rules and in doing so bias cognitive processes in posterior regions. The

ability to derive and maintain contextual information is necessary for the successful performance of many tasks; however, context processing has been tested in only a few paradigms. One ability that may rely on PFC-mediated context processing is task switching; that is, task switching may require knowledge about which task is appropriate in the current situation and the ability to implement this contextual information. The goal of this study is to assess whether deficits in context processing could underlie task-switching impairments in patients with schizophrenia, an illness associated with abnormal PFC functioning (Andreasen et al., 1992; Liddle, 1995).

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Studies assessing the task-switching abilities of schizophrenia patients have been scarce and those that have been conducted report inconsistent results across paradigms. Several studies of task switching have used the discrimination-learning paradigm subsets of the Cambridge Neuropsychological Test Assessment Battery (CANTAB) (Pantelis et al., 1999) which imposes high demands on contextual processing. In this test, participants must determine which of the two stimuli (e.g., shapes) is a target by deriving the rules for correct responding based on feedback. On occasion, a different stimulus becomes the target causing participants to have to switch their rules for responding. Patients with schizophrenia perform poorly in this paradigm (Hutton et al., 1998; Pantelis et al., 2004) and they take longer than controls to learn which stimulus is the target even before shifting is required (Pantelis et al., 1999).

In contrast, Meiran et al. (2000) reported that task switching was intact among patients with schizophrenia in a design that placed relatively few demands on contextual processing. Participants were asked to switch between classifying a stimulus on the vertical dimension (“up” or “down”) and the horizontal dimension (“left” or “right”). Task-relevant information (e.g., response rules) did not change from trial to trial as the keys were spatially congruent with the stimulus location. Accordingly, patients’ shifting speed and accuracy were equivalent to controls except at the very shortest cue-to-target interval (132 ms).

Based on these previous findings, we hypothesized that patients with schizophrenia show impairments only when task switching involves the active use of contextual information; that is, when a task switch involves updating the rules or goals of the situation. In contrast, we predicted that patients should have no difficulty task switching when rules remain relatively static. In support of this view, we have shown in a previous work that the dorsolateral prefrontal cortex (DLPFC), a region that is associated with functional and structural abnormalities in schizophrenia, is more active when contextual information (i.e., the appropriate set of stimulus-response mappings) switches than when this information stays the same from trial to trial (Ravizza and Carter, 2008), and was less engaged by shifts of purely perceptual information. Instead, this latter type of switch engaged the parietal cortex. These results suggest that task switching is not a unitary phenomenon but that switches of perceptual and contextual information reflect dissociable cognitive processes.

In this experiment, we assessed whether patients were impaired when contextual information switched compared to when switching did not involve changes of context using the procedure from Ravizza and Carter (Ravizza and Carter, 2008). In the *perceptual-switching* condition, a task switch requires participants to reorient visuospatial attention from one set of externally-based features to another while the rule information remained relatively static. We predict that patients with schizophrenia would switch tasks normally in this condition. In a separate condition, the task switch involves retrieving and instantiating the appropriate set of stimulus-response mappings (*rule switching*). In this condition, we predict that patients will have difficulty. If an impairment of contextual processing underlies task-switching deficits in schizophrenia, patients should be impaired only when contextual information changes.

2. Method

2.1. Participants

Eighteen patients who were diagnosed with schizophrenia and seventeen healthy controls were paid for their participation. All participants gave their informed consent and this study was approved by the Institutional Review Board at UC Davis. Patients and controls were matched in age (32.06, 33.12 years), parental education (average of mother and father: 14.38, 14.07),¹ and sex (12 males in each group, 5 female controls, 6 female patients). All schizophrenia patients were clinically stable (in the judgment of their treating clinician) and on stable doses of medications for at least 2 months prior to testing. All patients met the criteria for schizophrenia or schizoaffective disorder according to the DSM IV. The Structured Clinical Interview for DSM IV (SCID, First et al., 1996) was administered to both patients and controls (NP version for controls). Patient diagnoses were established by consensus in a panel including psychiatrists, clinicians, and masters-level research assistants based on the SCID and a review of medical records. In the same week that the patients were tested, a masters-level research assistant assessed severity of past-week symptoms (see Table 1) using the Scale for the Assessment of Negative Symptoms (SANS; Andreasen, 1983) and the Brief Psychiatric Rating Scale (BPRS; Overall and Gorham, 1962). Inter-rater reliability for these measures was maintained at monthly reliability rounds at a level of intra-class correlation co-efficient (ICC) of 0.8.

General exclusion criteria were substance abuse or dependence in the previous six months, a history of significant head injury, seizure disorder, ECT, or an untreated mood disorder. None of the controls had any lifetime Axis I disorder or a first degree relative with an Axis I disorder. All but three patients were screened for drug usage using a urine sample on the day of testing, and all came back negative. One control participant did not undergo drug tests for technical reasons. The results were the same when these participants were and were not included in the analyses.

2.2. Materials and procedure

Four letters (b, i, n, and v) and four shapes (cross, hexagon, parallelogram, and triangle) comprised the stimulus set in the perceptual-switching condition. A different set of letters and shapes was used in the contextual switching task (o, s, t, x; circle, diamond, pentagon, and square).

Participants performed an odd-man-out (OMO) task in which the target was either a letter or a shape (see Fig. 1). A switch occurred when the OMO changed from a letter to a shape or vice versa. In all conditions, the task was to determine which stimulus did not match the others (Fig. 1); three of the four stimuli were identical. Stimuli were presented until the participant responded; responses were followed by a 500 ms interval and then the next trial began. In all conditions, a row of keys on the computer keyboard was used to collect responses. The probability of a switch in target feature was 0.5.

¹ One patient and two controls were unable to provide years of parental education.

Table 1
Ratings of symptom severity for each patient and their medications.

Patient	Disorganization ^a	Positive ^b	Negative ^c	BPRS total	Name current Rx
1	1	5	5	40	Risperidol (1 mg)
2	2	8	3	49	Niaspan (500 mg), Clozapine (300 mg)
3	0	1	9	34	Risperdal (2 mg × 1 day), Geodone(nr), Abilify(nr)
4	1	0	5	30	Zyprexa (25 mg), Pamalon (100 mg)
5	2	8	12	53	Prozac (40 mg), Zeprexa (20 mg), "sleeping pills" (50 mg)
6	0	4	0	37	Geodon (20 mg + 80 mg), Abilify (30 mg)
7	1	0	1	25	Abilify (5 mg), Effoxer (225 mg)
8	5	0	13	38	Clozapine (100 + 200 mg), Effexor xr (150gd), Perphenazine (16 + 32 mg), Desmopressin-DDAVP (0.4qd), Famotidine (20qd), Metformin (1000 + 500), Xanax (nr)
9	1	0	10	30	Abilify (10 mg), Wellbutrin (75 mg), Nephasolone (50 mg), Ambian (15 mg), Lutera (nr)
10	2	5	13	35.5	Abilify (20 mg) and Zoloft (50 mg)
11	5	7	8.5	43	no rx reported
12	4	7	12	53	Paxil (40 mg), Remeron (nr), Seroquil (nr)
13	3	4	6	31	Zyprexa (10 mg), Abilify (nr), Risperdal (nr)
14	2	5	11	42	Clozapine (100 + 200), Effexor XR (150qd), Perphenazine (16 + 32), Desmopressin (DDAVP) (0.4qd), Famotidine (20qd), Metformin (1000 + 500), Xanax (nr)
15	1	4	10	34	Risperdal, Metformin, HCTZ, thorazine, Lantis (4–8 mg reported only)
16	0	0	6	39	Abilify (15 mg), Zyprexa (15 mg), Klonopin (1.5 mg), Cymbalta (60 mg)
17	3	5	9	39	Abilify (20 mg), Lomictoll (200 mg), Risperdol (1 mg) and Proponolol (10 mg)
18	1	5	5	40	Abilify, Zyprexa, Wellbutrin, Haldol, Cogentin
AVG	1.94	3.71	7.85	38.38	

^a Disorganization was calculated by summing the global scores of for formal thought disorder and bizarre behavior from the Schedule for the Assessment of Positive Symptoms (SAPS) and the score for attention from the Schedule for the Assessment of Negative Symptoms (SANS).

^b Sum of the global scores for hallucinations and delusions from the SAPS.

^c Sum of the global scores for poverty of speech, flat affect, anhedonia/asociality, and amotivation from the SANS.

In the rule-switching condition, a change in the target feature meant a change in the relevant set of stimulus-response mappings. There was one set of response rules for shapes and another for letters. When a switch occurred,

participants had to retrieve and implement the appropriate response rule associated with the stimulus. There were few demands on perceptual switching in this condition. The alternate feature set was not present and so participants did not have to move attention between one type of feature

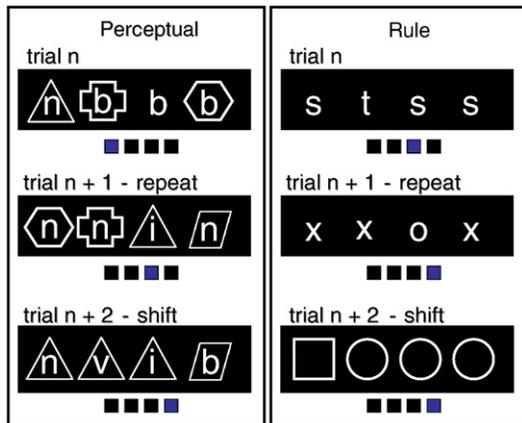


Fig. 1. Examples of 3 trials in the perceptual (left side) and rule (right side) conditions of Experiment 1. In both tasks, the participant is asked to find the odd-man-out. The four boxes under each display of letters and shapes indicate the appropriate key press for that trial. In the perceptual condition, participants respond by pressing a button that is spatially congruent to the odd-man-out. In the rule condition, participants had to implement the correct response rule (e.g., if the odd-man-out is a "t", press the key under your ring finger). In this example, the second trial in each condition is a repeat trial (letter to letter) and the third trial is a shift trial (letter to shape). Note that this sequence is used for illustrative purposes and that shift and repeat trials were randomized within each block of trials.

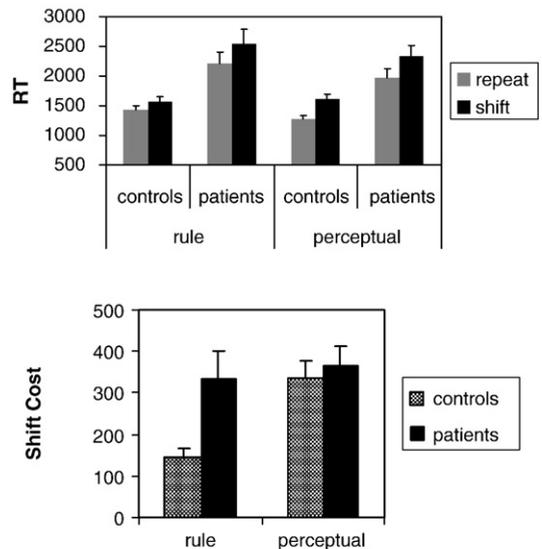


Fig. 2. Reaction time (top) and shift cost (bottom) in each condition of Experiment 1. Solid bars represent patients with schizophrenia and textured bars represent control participants.

and/or location to another. Once participants identified the stimulus that did not match the others, they pressed a button on the computer keyboard that had been previously memorized for that particular OMO. For example, if the stimuli were “x”, “x”, “s”, and “x”, participants would have to *recall the response rule* that was associated with an “s” rather than pressing the location of the target. The second through fifth fingers of the right hand were mapped to the letters “s”, “x”, “t”, “o” and circle, diamond, pentagon, square, respectively.

In the perceptual-switching condition, both letters and shapes were presented. This required participants to disengage attention from the previously relevant feature and reorient their attention to the alternate set of features. Contextual information, the stimulus-response rules, remained static in this condition; participants responded in the same way regardless of whether the OMO was a letter or a shape and the goal was always the same (i.e., find the OMO).

If the OMO was a letter, then all the shapes were different and vice versa when the OMO was a shape. A shift occurred when the OMO switched from one feature set (e.g., letters) to another (e.g., shapes) in consecutive trials. When participants found the odd letter or shape, they responded by pressing the button that corresponded to the spatial location of the OMO.

Participants completed one block of trials in each condition; block sequence was administered at random. Instructions appeared at the beginning of each block and informed participants as to the task that they were to perform. The rule- and perceptual-switching conditions contained 256 trials; this ensured that each combination of target dimension (2), target stimulus (4), target location (4), and distractor stimulus (4) was presented at least once.

Immediately preceding the rule-switching condition, participants received a practice session of 80 trials in which they memorized the stimulus-response mappings. In these practice trials, one stimulus, either a letter or a shape, was presented and participants had to produce the correct response mapping for that stimulus. All participants achieved over 75% correct before they received trials in the contextual-switching condition.

3. Results

Only RTs for correct trials were analyzed. Trials were discarded if RTs were above or below 3 standard deviations from the participant’s mean RT or above an absolute value of 8s. A minimum of 70 trials remained in each cell of our 2 (repeat/switch) × 2 (perceptual/rule) design. We per-

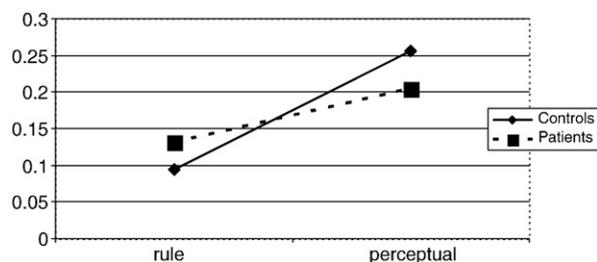


Fig. 3. Shift cost adjusted for overall RT in Experiment 1. The solid line represents control participants and the hatched line represents patients with schizophrenia.

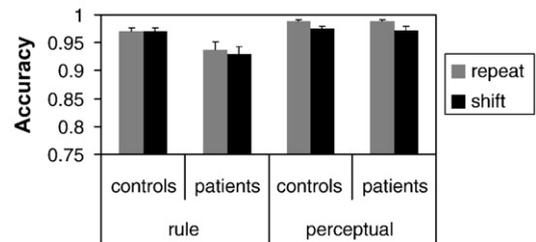


Fig. 4. Accuracy scores for control participants and schizophrenia patients in each condition in Experiment 1.

formed a mixed factor ANOVA with switch and task as within-subject factors and group as a between-subject factor (Fig. 2). Main effects of shift ($F(1, 33) = 102.93, p < .05$) and group ($F(1, 33) = 15.32, p < .05$) were obtained. Shift trials were slower than repeat trials and patients were slower than controls. The interaction of shift × task was also significant ($F(1, 33) = 8.56, p < .05$). Switching was more difficult in the perceptual condition than in the rule condition. Note, however, that significant shift costs (shift RT – repeat RT) were obtained in both the perceptual ($t(34) = 10.97, p < .05$) and the rule ($t(34) = 6.02, p < .05$) conditions. The three-way interaction of group, shift, and task was also significant ($F(1, 33) = 4.38, p < .05$). Independent-sample t-tests confirmed that patients had higher shift costs than controls in the rule-switching condition ($t(33) = 2.61, p < .05$), but not in the perceptual condition ($t(33) = .5, p = .62$).

Patients were slower overall than controls; thus, we ran a separate analysis using the proportion shift cost ($[\text{shift RT} - \text{repeat RT}] / \text{repeat RT}$) calculated separately for each task (rule, perceptual) and each participant (Meiran et al., 2000). This adjusted shift cost was subjected to a 2 (task) × 2 (group) mixed factor ANOVA (Fig. 3). This analysis produced a main effect of task ($F(1, 33) = 31.98, p < .05$) and a significant interaction of group by task ($F(1, 33) = 5.42, p < .05$). Adjusted shift costs were greater in the perceptual condition than in the rule condition, confirming that participants had greater difficulty in the former than in the latter condition. The significant interaction term confirmed that patients and controls exhibited different patterns of performance based on the type of switch required. Patients had greater rule shift costs and smaller perceptual shift costs than controls; however, neither of these simple effects was significant.

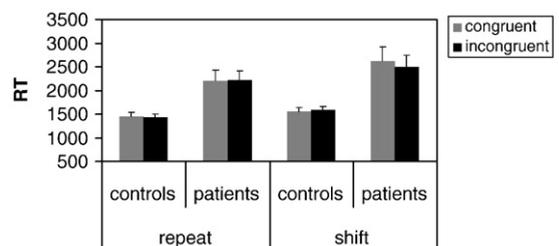


Fig. 5. RT in the rule condition for repeat and shift trials when the rule for responding to the odd-man-out was congruent with its spatial location. An example of a congruent trial is when the odd-man-out is the letter “s” and it is presented in the left-most location. This is because the response rule for an “s” is to press the left-most response key. An incongruent trial would occur if the “s” was the odd-man-out and was located in either the 2nd, 3rd, or 4th location from the left.

Both patients and controls were quite accurate, achieving scores above 93% in each condition (Fig. 4). Errors were analyzed with a 2 (shift) \times 2 (task) \times 2 (group) ANOVA. This analysis produced main effects of shift ($F(1, 33) = 13.28, p < .05$), task ($F(1, 33) = 15.41, p < .05$), and group ($F(1, 33) = 5.29, p < .05$) as well as an interaction between task and group ($F(1, 33) = 5.99, p < .05$). Both patients and controls were less accurate in the rule condition (regardless of switching) than in the perceptual condition (controls: $t(16) = 3.04, p < .05$; patients: $t(17) = 3.42, p < .05$), but this was especially true for patients. Patients were significantly less accurate in the rule condition ($t(33) = 2.51, p < .05$) than controls, whereas we found no group difference in the perceptual condition ($t(33) = .3, p = .76$). No interaction involving group and switching was significant. Severity of disorganization, positive, and negative symptoms were not significantly related to performance.

4. Discussion

The contextual processing theory of PFC function has been useful in characterizing how this region orchestrates thought and action in the pursuit of everyday objectives. We found contextual impairments among schizophrenia patients when participants had to apply different response rules across trials. Patients were not impaired when perceptual features switched across trials, but the response rules remained the same; that is, they were unimpaired when selecting the appropriate response when it involved only shifting visual attention to the newly relevant feature.

Indeed, patients were able to reorient attention to the correct target feature even in the presence of stimulus interference from the alternate set of features.

Note that the shift cost in the rule-switching condition was lower than in the perceptual-switching condition indicating that, in general, rule switching was less effortful than perceptual switching. Given that patients were impaired in the less effortful switching condition, our results suggest that schizophrenia is associated with a selective deficit in rule switching rather than a generalized impairment that increases with task difficulty. These results demonstrate the far-reaching effects of context processing deficits in a domain such as task switching and suggest that difficulty in the maintenance and implementation of rule representations is linked to cognitive disorders in schizophrenia.

Importantly, we found these effects despite the fact that there was no need to overcome a prepotent response. Although many studies have reported contextual processing deficits in schizophrenia, the tasks used in these experiments placed high demands on response inhibition, for example, color naming in the Stroop Task (Barch et al., 2003, 2001; Chambon et al., 2008; Cohen et al., 1999; Servan-Schreiber et al., 1996). Yet, the notion of contextually-appropriate processing is broader than that involved in overcoming prepotent responding. In this study, we tried to minimize such demands to assess whether response inhibition is a necessary requirement for observing contextual deficits in schizophrenia. Although stimulus interference was high in the perceptual-switching condition because the alternate feature set was present, the interfering set did not suggest a potential response. There was no OMO target in the competing feature set. Crucial for our hypothesis is whether participants needed to overcome a prepotent res-

ponse tendency in the rule-switching condition. One could argue that participants were biased to respond to the location of the OMO rather than responding via arbitrary response key assignments; that is, participants may have had to overcome a tendency to press the key that corresponded to the OMO location. We assessed this idea by observing whether performance was faster when the correct response and the location of the OMO matched (congruency) in the rule-switching condition. A 2 (shift) \times 2 (congruency) \times 2 (group) ANOVA showed no main effects or interactions involving congruency ($ps > .1$). In fact, patients tended to be a little slower in the congruent than the incongruent condition (see Fig. 5). This result argues for minimal response inhibition demands in the rule-switching condition and that contextual processing deficits can be observed in schizophrenia patients even when there is no prepotent response tendency.

Switching between sets of response rules requires the ability to instantiate the correct rule and load it into working memory. One might argue that the crucial difference between the rule and perceptual conditions is that the former places more demands on working memory than the latter. Indeed, patients were less accurate overall in the rule-switching condition, suggesting that they experienced difficulty remembering each set of stimulus-response mappings. Often, rule-guided behavior relies on updating the contents of working memory and may represent a specific form of working memory (Kerns et al., 2004). In other words, selection and maintenance of context-appropriate responses are two reflections of the same underlying neural mechanism (Barch et al., 2001).

In summary, this study helps to illuminate the nature of cognitive deficits in schizophrenia. These results suggest that problems with contextual processing are not restricted to situations in which a prepotent response must be overcome. Thus, we have provided evidence that schizophrenia is associated with an impairment in applying task-relevant information regardless of response inhibition. We hypothesize that this impairment is due to the PFC abnormalities associated with the disease. When switching from one set of response rules to another, PFC functioning is important for responding flexibly (Ravizza and Carter, 2008). When task switching is more parietally-mediated, such as in perceptual switching (Ravizza and Carter, 2008), patients are intact. An fMRI study of schizophrenia patients comparing frontal and parietal activity in rule and perceptual switching would be helpful in confirming these hypotheses.

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Contributors

Dr. Ravizza supervised the project, designed and programmed the experiments, analyzed the data, interpreted the results, and wrote the paper.

Ms. Moua recruited and tested participants, integrated the data files, and analyzed the data.

Dr. Long helped design the experiment, interpreted the results, and helped write the manuscript.

Dr. Carter advised Dr. Ravizza on experimental design and clinical assessments, provided testing space and patient access, interpreted the results, and helped write the manuscript.

Conflict of interest

All authors declare that they have no conflicts of interest.

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