

# Schizophrenia patients show impaired response switching in saccade tasks

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## Abstract

Action control deficits of schizophrenia patients result from frontostriatal brain abnormalities and presumably reflect an impairment of selective cognitive processes. This study aimed at dissociating two different levels of action control in saccades toward and away from visual stimuli (pro- and antisaccades). Results of previous studies suggested that task switch effects (between pro- and antisaccades) reflect the persistence of a task-specific production rule and refer to the level of task selection, whereas response switch effects (between leftward and rightward saccades) point to the persistence of a specific response program, referring to the level of response selection. In the present study, task switching and response switching were investigated in 20 schizophrenia patients and 20 control subjects. Groups did not differ concerning task switch effects. In contrast, response switching entailed a stronger enhancement of error rates in patients, suggesting a specific deficit on the level of response selection in schizophrenia. The deficit was associated with spatial working memory capacities, confirming and specifying existing hypotheses on a relationship between working memory and action control.

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## 1. Introduction

Schizophrenia patients show structural and functional brain abnormalities in frontal and temporal cortex (Goldstein et al., 1999; Gur et al., 2000; Kubicki et al., 2005; Selemon et al., 1998). A frontostriatal dysfunction is assumed to account for the frequently reported deficits in the performance of antisaccades (saccades to the opposite side of a sudden-onset peripheral visual stimulus) in schizophrenia (Crawford et al., 1995; Nakashima et al., 1994; Raemaekers et al., 2002). The dorsolateral prefrontal cortex (DLPFC), which is essential for correct antisaccade performance (Ploner et al., 2005), was shown to be less activated in schizophrenia patients compared to healthy subjects during antisaccade performance (McDowell et al., 2002). However, the cognitive implications of this dysfunction are not yet fully understood, and experimental analyses are needed to further elucidate them (Hutton and Ettinger, 2006; Reuter and Kathmann, 2004).

The performance of antisaccades requires the suppression of a reflexive saccade toward the stimulus and the generation of a volitional saccade to the opposite side (Munoz and Everling, 2004; Pratt and Trottier, 2005; Unsworth et al., 2004). Thus, it involves action control in terms of actively selected rather than reflexive reactions to stimuli. In contrast, prosaccades (saccades toward a sudden-onset peripheral visual stimulus) are relatively automatic responses and performed normally by schizophrenia patients (Broerse et al., 2001; Brownstein et al., 2003; Fukushima et al., 1990; Karoumi et al., 1998). Hence, poor antisaccade performance points to action control deficits in schizophrenia.

Presumably, antisaccade deficits in schizophrenia patients reflect an impairment on selective levels of action control. As pointed out by Manoach et al. (2002), saccade tasks address a relatively small range of cognitive functions and thus allow the investigation of single components of action control which was often impeded by the use of neuropsychological instruments that require multiple cognitive functions for successful performance. Analyzing task switch effects on saccade performance, Manoach et al. (2002) showed that the ability to flexibly switch between pro- and antisaccades is normal in

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schizophrenia. Pro- and antisaccade instructions were presented in a randomly mixed order. Thus, pro- and antisaccades were either repeated (i.e., prosaccade after prosaccade and antisaccade after antisaccade) or switched (i.e., prosaccades after antisaccades and antisaccades after prosaccades). Switching from pro- to antisaccades and from anti- to prosaccades enhanced error rates both in schizophrenia patients and in healthy subjects, suggesting that both groups similarly activate task-specific production rules that may persist in the subsequent trial and entail errors if a new task has to be performed.

In addition to task switch effects, recent studies investigated effects of switching the response direction on error rates in pro- and antisaccades (Barton et al., 2006; Fecteau et al., 2004; Reuter et al., 2006). For instance, Reuter et al. (2006) analyzed the performance of leftward and rightward pro- and antisaccades that were randomly mixed across task repetition and task switch conditions in healthy subjects. Thus, the required response direction was either repeated (i.e., rightward saccade after rightward saccade and leftward saccade after leftward saccade) or switched (i.e., rightward saccade after leftward saccade and vice versa). The results showed that not only task switching but also response switching enhanced error rates, suggesting that the specific response program of a previous saccade can persist in the subsequent trial, entailing errors if a new response direction is required (Reuter et al., 2006). However, pro- and antisaccades were differently affected by response switching. Only antisaccades following antisaccades showed enhanced error rates in response switch trials compared to response repetition trials. This points to different modes of response generation in pro- and antisaccades (Reuter et al., 2006). Antisaccades require the volitional activation of a response program involving information on the demanded saccade direction. Prosaccades are more automatic because the visual stimulus is directly transformed into a motor signal (Munoz and Everling, 2004; Pratt and Trottier, 2005). The specific response switch effect in repeated antisaccades thus suggests that only volitionally selected responses persist in subsequent trials and are affected by a persisting response program from a previous saccade (Reuter et al., 2006). Hence, response switching complicates the generation of volitional saccades if a volitionally selected response was performed in the prior trial. Previous studies provided evidence for deficits in the generation of volitional saccades in schizophrenia patients (Reuter et al., 2005, 2007). Schizophrenia patients might thus show enhanced response switch effects in repeated antisaccades.

Yet, reanalyses of the data of Manoach et al. (2002) showed response switch deficits of schizophrenia patients not only in repeated antisaccades but also in prosaccades following antisaccades (Barton et al., 2006; Barton et al., 2005). Hence, prosaccades of schizophrenia patients were not fully unaffected by response switching. Interestingly, in that study also the control subjects did not show response switch effects specific to repeated antisaccades as reported by Reuter et al. (2006). The design used by Reuter et al. (2006) contained task switches after every second trial whereas in the study of Manoach et al. (2002), task switches were unpredictable. It is conceivable that

the difference in the mode of response generation in pro- and antisaccades is more pronounced in a procedure with predictable than with unpredictable task switches.

In the current study, we applied the design of Reuter et al. (2006) in a slowed version to schizophrenia patients. Thus, two levels of action control were analyzed in a design with regularly alternating pro- and antisaccades. Effects of task switching, reflecting the persistence of a specific task rule, refer to the level of task selection. Effects of response switching, reflecting the persistence of a specific response program, refer to the level of response selection. With reference to Manoach et al. (2002), schizophrenia patients and healthy controls were expected to show a similar enhancement of error rates in task switch compared to task repetition trials. As regards response switching, we expected to replicate the specific response switch effect (enhanced error rates in response switch compared to response repetition trials in repeated antisaccades) for healthy subjects reported by Reuter et al. (2006) and to find this effect to be particularly pronounced in schizophrenia.

A second aim of the study was to analyze the relationship between working memory capacities on the one hand and overall antisaccade error rates and experimental effects on antisaccade error rates on the other hand. As to overall antisaccade performance, subjects with high working memory capacity were reported to commit less antisaccade errors than subjects with low working memory capacity (Kane et al., 2001; Unsworth et al., 2004). Furthermore, two previous studies found significant correlations between spatial working memory scores and antisaccade performance in schizophrenia patients but not in control participants (Gooding and Tallent, 2001; Hutton et al., 2004), suggesting a functional relationship between reduced working memory capacities and deficient action control in schizophrenia. We expected to replicate the correlation between working memory and antisaccade performance in schizophrenia patients.

Furthermore, we conducted an exploratory analysis of correlations between working memory scores and task switch and response switch effects on error rates in antisaccades. Working memory capacities determine the ability to maintain an action goal (Kane et al., 2001; Kane and Engle, 2003; Unsworth et al., 2004). Reduced working memory capacities lead to a higher susceptibility to goal neglect (Kane et al., 2001), affecting action in situations of strong internal interference (Unsworth et al., 2004). However, it is unclear whether the goal neglect refers to specific levels of action control. More insight was expected from correlations between working memory scores and experimental effects that differentially reflect the levels of task and response selection.

## 2. Methods

### 2.1. Participants

Twenty DSM-IV-diagnosed schizophrenia patients (6 female, 14 male) from the Department of Psychiatry and Psychotherapy of the Charité Universitätsmedizin Berlin, Germany, and 20 healthy control subjects (6 female, 14 male, matched for age and educational level) participated in the study. Patients were tested after partial remission of acute psychotic symptoms (but not earlier than

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