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Impaired action control in schizophrenia: The role of volitional saccade initiation

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Abstract

Schizophrenia patients show prefrontal cortex dysfunctions of neurodevelopmental origin, but the cognitive implications of these dysfunctions are not yet understood. This study used experimental variations of oculomotor tasks to evaluate the relative roles of volitional action initiation and the inhibition of reflexive behavior. Thirty schizophrenia patients and 30 control participants performed standard prosaccades (SP), standard antisaccades (SA), delayed prosaccades (DP), and delayed antisaccades (DA). The delayed tasks allowed separating the inhibition of erroneous prosaccades and the initiation of volitional saccades, which coincide in the SA task. Arrow-cued (AC) saccades were used to evaluate initiation without any inhibitory component. Erroneous prosaccades were less frequent in the delayed tasks than in the SA task. Error rates were generally larger in schizophrenia patients than in control participants, but the deficit was smaller in the delayed tasks than in the SA task. Correct saccade latencies of schizophrenia patients were normal in the SP task, but not on conditions of volitional saccade initiation (all other tasks). Volitional saccade latencies were positively correlated with error rates in the schizophrenia group. These results confirm that schizophrenia patients have a specific deficit in initiating volitional action, which may also contribute to the increased error rates.

Keywords: Saccades; Schizophrenia; Action control; Executive function

1. Introduction

Schizophrenia is a relatively common and often severe mental disorder with a neurodevelopmental origin (Allin & Murray, 2002; Weinberger, 1995). The brain of schizophrenia patients shows volume reductions and grey and white matter abnormalities in the temporal and the prefrontal cortex (Goldstein et al., 1999; Gur et al., 2000; Kubicki, McCarley, & Shenton, 2005; Selemon, Rajkowska, & Goldman-Rakic, 1998). Because the symptoms of schizophrenia are heterogenous and interact with environmental conditions, the functional implications of the brain abnormalities are preferably analyzed using cognitive tasks (Heinrichs, 2005; Pantelis & Maruff, 2002). Performance of schizophrenia patients is in fact reduced in many different neuropsychological standard tests and experimental tasks (Heinrichs, 2005; Heinrichs & Zakzanis, 1998). However, many tasks address multiple cognitive functions, which complicates the interpretation of performance deficits.

Oculomotor tasks address a relatively small range of functions. For example, saccades toward sudden-onset visual stimuli (prosaccades) require sufficient alertness and the transformation of a visual signal into a motor signal. The accuracy and latency of prosaccades is normal in schizophrenia, suggesting integrity of the addressed functions. Deficits occur if action control is demanded. For example, if antisaccades (saccades away from a visual stimulus) are required, schizophrenia patients make markedly more unwanted saccades toward the stimulus (erroneous prosaccades) than healthy subjects (Crawford, Haeger, Kennard, Reveley, & Henderson, 1995a; Fukushima, Fukushima, Morita, & Yamashita, 1990; Hutton, Joyce, Barnes, & Kennard, 2002; Hutton et al., 2004; Karoumi,

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Ventre-Dominey, Vighetto, Dalery, & d'Amato, 1998; Klein, Heinks, Andresen, Berg, & Moritz, 2000; McDowell et al., 2002; McDowell & Clementz, 1997; Reuter, Rakusan, & Kathmann, 2005).

Poor antisaccade performance of schizophrenia patients is likely to indicate prefrontal cortex dysfunctions (Bagary et al., 2004; Klein et al., 2000; McDowell et al., 2002). However, the cognitive implications of this dysfunction are not yet understood (Reuter & Kathmann, 2004). It is difficult to identify the affected cognitive mechanisms because antisaccades appear to demand two processes at the same time, namely inhibiting the erroneous prosaccade and generating the antisaccade. In a previous study, we separated both components by using a delayed antisaccade (DA) task (Reuter et al., 2005). In the DA task, subjects had to continue fixation of a central dot when a peripheral dot appeared, and to generate an antisaccade 500 or 1000 ms later when a tone was presented. Thus, the demand to inhibit an erroneous prosaccade was not simultaneous to the demand to generate a volitional saccade. On this condition, erroneous prosaccades were less frequent than in a standard antisaccade (SA) task, in which inhibition was required simultaneously to generating the antisaccade. Moreover, the deficit of schizophrenia patients was less distinct in the delay condition, suggesting that the failure to inhibit prosaccades is related to the demand to generate the antisaccade.

A relationship between the generation of the antisaccade and the inhibition of an erroneous prosaccade is suggested by models of parallel programming of both saccade types in SA tasks (Hunt, Olk, von Muhlenen, & Kingstone, 2004; Massen, 2004; Reuter et al., 2005; Reuter & Kathmann, 2004). These models propose that the visually triggered prosaccade and the actually required antisaccade compete for execution. Erroneous prosaccades occur if antisaccade generation comes too late (Massen, 2004) or is too weak (Hunt et al., 2004; Reuter & Kathmann, 2004) to override the prosaccade signal. Increased erroneous prosaccades in schizophrenia patients may thus indicate a deficit in the generation of antisaccades.

Impaired antisaccade generation is also suggested by increased latencies of antisaccades in schizophrenia patients (Broerse, Crawford, & den Boer, 2001; Fukushima et al., 1990; Karoumi et al., 1998; Klein et al., 2000; Reuter, Herzog, & Kathmann, 2006). Note that prosaccades, which are triggered by the onset of a visual saccade target, have normal latencies in schizophrenia patients (Broerse et al., 2001). The slowing in antisaccades may hence originate from the need to initiate the saccade volitionally, that is without the sudden-onset of a visual target. However, the latencies of standard antisaccades may also be affected by the response conflict with the prosaccade or the need to compute the target location (Munoz & Everling, 2004; Olk & Kingstone, 2003; Pratt & Trottier, 2005). In delayed antisaccades, the component of volitional saccade initiation is more isolated because competition with the prosaccade and computation of the target position take place during the delay period. In our pilot study, there was yet a trend towards longer latencies of delayed antisaccades in schizophrenia patients compared to control participants. Moreover, the group difference was not smaller than in the standard antisaccade latencies, suggesting that the slowing of schizophrenia patients refers to the common component of volitional saccade initiation in both tasks. However, the general group effect was only marginally significant in that study, probably because of power problems. Therefore, the current study aimed at substantiation in a new and larger sample.

Beyond replicating the previous results, the present study extended the evaluation of volitional saccade initiation in schizophrenia patients by using additional tasks. The DA task was compared to a delayed prosaccade (DP) task (Hutton et al., 2002) where a prosaccade is required after a delay. In both tasks, the required saccades are volitional in that they are not elicited by a sudden target onset. However, the target position of delayed prosaccades is indicated by the dot, whereas the target position of delayed antisaccades must be computed and maintained during the delay. Hence, we could test whether the slowing depends on the need to establish an internal representation of the target location.

Despite the temporal separation of inhibition and saccade generation in both delayed prosaccades and delayed antisaccades, one cannot exclude an influence of the antecedent inhibition on the generation of these types of volitional saccades. Therefore, we applied a third volitional saccade task to further validate the hypothesis of slowed volitional saccade initiation on a condition that was free of any current or prior demand to suppress an erroneous prosaccade. In this task, the requested saccade direction was indicated by a central arrow and a tone signaled when to execute the saccade (*arrow-cued saccades*). Similar to delayed pro- and antisaccades, arrow-cued saccades are not triggered by a visual target. Instead, their initiation is based on a symbolic representation of the saccade direction. The latencies of these and the other volitional saccades were compared to the latencies in a standard prosaccade (SP) task. We hypothesized that saccade latencies of schizophrenia patients are prolonged whenever the saccade is not elicited by the onset of a visual target.

In addition, correlational analyses were used to explore the relationship of volitional saccade latencies and the occurrence of erroneous prosaccades. The proposed dependency of erroneous prosaccades on the efficiency of volitional saccade initiation predicts a positive correlation between volitional saccade latencies and error rates in the SA task. However, volitional saccade latencies do not only reflect volitional saccade initiation but are also influenced by basic perceptual and motor components. To control for the influence of the latter components, we partialed out the standard prosaccade latencies when evaluating the correlations between volitional saccade latencies and error rates.

2. Materials and methods

2.1. Participants

Thirty DSM-IV-diagnosed schizophrenia patients of the Psychiatric Hospital of the Ludwig-Maximilians-Universität, Munich, Germany, and 30 healthy control subjects (11 females and 19 males in each group; matched for age, gender, and educational level, see Table 1) participated in the study. Patients were tested after partial remission of acute psychotic symptoms (not earlier than 2 weeks after admission) and received medication according to clinical requirements (Table 2). Patients with co-morbid axis-1 diagnoses were excluded. Clinical status was rated using the Clinical Global Impression Scale