Clinical correlates of saccadic eye movement in antipsychotic-naïve schizophrenia

Aditi Subramaniam\textsuperscript{a,b,1,2}, Vijay Danivas\textsuperscript{a,b,1,2}, Sri Mahavir Agarwal\textsuperscript{a,b,1,2}, Sunil Kalmady\textsuperscript{a,b,1,2}, Venkataram Shivakumar\textsuperscript{a,b,1,2}, Anekal C. Amaresh\textsuperscript{a,b,1,2}, Anushree Bose\textsuperscript{a,b,1,2}, Janardhanan C. Narayanawamy\textsuperscript{a,b,1,2}, Shivrama Varambally\textsuperscript{a,b,1,2}, Samuel B. Hutton\textsuperscript{c}, Ganesan Venkata\textsuperscript{a,b,1,2}, 1,2

\textsuperscript{a} InSTAR Program, The Schizophrenia Clinic, Department of Psychiatry, National Institute of Mental Health and Neurosciences, Bangalore, India
\textsuperscript{b} Translational Psychiatry Laboratory, Neurobiology Research Centre, National Institute of Mental Health and Neurosciences, Bangalore, India
\textsuperscript{c} University of Sussex, Brighton, United Kingdom

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ABSTRACT

Some aspects of saccadic performance have been found to be abnormal in chronic schizophrenia. The majority of this research has, however, been performed on patients treated with long-term antipsychotic medication. Very few studies have examined saccadic performance in antipsychotic-naïve/free patients. There are also very few studies describing the relationship between saccadic performance and clinical symptoms, particularly in antipsychotic free patients. In this study, we compared pro and antisaccade performance in a large sample of antipsychotic-naïve/free schizophrenia patients (N = 45) with healthy controls (N = 57). Clinical symptoms were assessed using Scale for Assessment of Positive Symptoms (SAPS) and Negative Symptoms (SANS). In the antisaccade task, patients made significantly more errors, and their correct antisaccades had smaller amplitudes in comparison to healthy controls. Higher error rates were associated with increased severity of hallucinations. In the prosaccade task, patients had less accurate final eye positions, and made saccades with slower latency and reduced amplitude compared to the healthy controls. These observations in schizophrenia patients without the potential confounds of antipsychotic treatment suggest intrinsic link between saccadic deficits and schizophrenia pathogenesis. The relationship between antisaccade errors and hallucination severity supports the potential link between hallucinations and deficits in inhibitory control.

1. Introduction

Oculomotor abnormalities such as increased antisaccade error rate and reduced smooth pursuit velocity gain have been consistently observed in schizophrenia patients (Hutton and Ettinger, 2006; O’Driscoll and Callahan, 2008), and it has been argued that the study of eye movements offers a valuable paradigm for elucidating the neurophysiological basis of schizophrenia. The neurological circuitry underlying eye movements has been well established in primates (Goldberg and Colby, 1992), and their corresponding human counterparts have also been identified using functional imaging. Importantly, the key neural circuits involved in oculomotor control share brain regions that are implicated in schizophrenia pathogenesis (O’Driscoll et al., 2000). Moreover, eye movements provide a non-invasive yet precise and accessible means of investigating psychomotor functioning as well as neural mechanisms of higher-order cognitive processes (Gooding and Basso, 2008).

Saccades are ballistic, conjugate eye movements that alter the point of fixation of the fovea. Visually guided saccades or prosaccades are generated towards a particular target in the visual field, and rely on simple sensorimotor transformations for optimal performance. Volitional saccades, such as those performed in the antisaccade task, involve higher level cognitive processes such as goal activation and spatial memory, requiring the participant to inhibit a pre-potent response of looking at a visual target, and instead generate an endogenously driven saccade to the mirror image location of the target (Hutton and Ettinger, 2006).

Many studies have shown that prosaccade performance in...
Since performance in antisaccade task relates with a second generation antipsychotic (Reilly et al., 2005). Volitional saccades (such as required in the antisaccade task) are more cognitively complex than visually guided saccades. Numerous studies have shown that patients with schizophrenia make significantly more antisaccade errors than matched comparison subjects (Hutton et al., 1998; Radant et al., 2007; Reuter et al., 2005; Water et al., 2009; Zanelli et al., 2005). Increased errors in the antisaccade task are generally interpreted as reflecting impaired inhibitory control mediated by dysfunctional prefrontal cortex in schizophrenia (Clementz, 1998).

There is sparse literature on the relationship between antisaccade error rates and specific measures of psychopathology in schizophrenia. It is also worth noting that, in most antisaccade studies, psychopathological rating scales are administered to patients, but only a minority of papers report correlational analyses between these measures and antisaccade performance (Hutton and Ettinger, 2006). An earlier study examining schizophrenia patients reported that the internally guided saccade performance recruits a fronto-parieto-subcortical network, primarily involving frontal eye fields (FEF), supplementary eye field, dorsolateral prefrontal cortex (DLPFC), anterior cingulate, posterior parietal cortex, thalamus and striatum (O’Driscol et al., 1995; Sweeney et al., 1996).

Healthy controls (N = 57; age = 26.8 ± 3.2 years; 35 men), who volunteered for study, were screened to rule out any psychiatric diagnosis using the MINI Plus (Sheehan et al., 1998) as well as a comprehensive mental status examination. None of the controls had family history of psychiatric disorder in first-degree relatives.

Only those subjects that were right-handed (as ascertained by Edinburgh Handedness Inventory (Oldfield, 1971)), were examined in this study. None of the participants had clinically significant ophthalmological problems or uncorrected refractory errors. Patients and controls did not have features suggestive of alcohol abuse / dependence. None used stimulant or opiate drug. None had history or clinical feature suggestive of neurological/medical disorder. None had abnormal movements as assessed by Abnormal Involuntary Movements Scale. Clinical assessments and eye tracking experiments were performed on the same day before starting antipsychotics. After complete description of study to the subjects, written informed consent was obtained. The research protocol was reviewed and approved by the National Institute of Mental Health and Neurosciences (NIMHANS) ethics committee.

2.1. Eye tracking methodology

Eye movement recordings were conducted in a room with controlled illumination. Before the eye tracking experiments, the ocular dominance was assessed using the hole-in-the-card-test (Dolman method) (Cheng et al., 2004). In this test, the participant was instructed to hold a piece of cardboard with a central circular hole through which they had to view a target at about 6 m away with both eyes open. Subsequently, each eye was occluded in turn. The target would not be seen through the hole when the dominant eye was covered; on the contrary, the target persisted to be seen when the non-dominant eye was covered since the dominant eye would continue to fix the target. In this forced-choice test of dominance, there was only one result for dominance (left or right). The eye movement data of the subject was recorded using the dominant eye to avoid potential confounding effect of differential dominance on eye tracking measures (Vergilino-Perez et al., 2012).

Stimuli were displayed on a 22-in. flat screen monitor (Fuzilicon, Vieswonic, 120 Hz) placed 74.3 cm in front of the subject. Eye tracking data were collected using an EyeLink 1000 eye tracker (SR Research, Canada) sampling at 1000 Hz. Head movements were constrained using chin rest and forehead abutments. The saccadic task was based on the principles and procedures as described earlier (Taylor and Hutton, 2009). All subjects were explained about the task in detail and it was ensured that they understood the task.

Each participant performed a total of 24 prosaccade trials in one block followed by 48 antisaccade trials in the subsequent block. We chose to have lesser number of prosaccade trials since they were relatively easier for the patients to learn and perform; since we examined schizophrenia patients that were antipsychotic-naive, lesser number of prosaccade trials ensured that the total duration of the eye tracking
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