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Response suppression deficits in treatment-naïve first-episode patients with schizophrenia, psychotic bipolar disorder and psychotic major depression

Margret S.H. Harris^a, James L. Reilly^a, Michael E. Thase^{c,d}, Matcheri S. Keshavan^{b,c}, and John A. Sweeney^{a,c,*}

^aCenter for Cognitive Medicine, Department of Psychiatry, University of Illinois at Chicago, Chicago, IL, USA

^bDepartment of Psychiatry and Behavioral Neurosciences, Wayne State University, Detroit, MI, USA

^cDepartment of Psychiatry, University of Pittsburgh Medical Center, Pittsburgh, PA, USA

^dDepartment of Psychiatry, University of Pennsylvania, Philadelphia, PA, USA

Abstract

Recent evidence indicates common genetic, neurobiological, and psychopharmacological aspects of schizophrenia and psychotic affective disorders. Some similarities in neurocognitive deficits associated with these disorders have also been reported. We investigated performance on antisaccade and visually-guided saccade tasks in treatment-naïve first-episode psychosis patients (schizophrenia n=59, major depression n=15, bipolar disorder n=9), matched non-psychotic major depression patients (n=40), and matched healthy individuals (n=106). All psychosis groups displayed elevated antisaccade error rates relative to healthy individuals. Antisaccade latencies were elevated in schizophrenia, but no significant error rate or latency differences were observed among psychosis groups. For schizophrenia only, shorter visually-guided saccade latencies were associated with higher antisaccade error rates. Schizophrenia was also the only group without a significant relationship between visually-guided and antisaccade latencies. Reflexive saccades were unimpaired except in psychotic unipolar depression, where saccades were hypometric. As in schizophrenia, antisaccade abnormalities are present in affective psychoses, even early in the course of illness and prior to treatment. Disturbances in frontostriatal systems are believed to occur in both affective psychoses and schizophrenia, potentially causing some similar cognitive abnormalities across psychotic disorders. However, the distinct pattern of dysfunction in schizophrenia across oculomotor paradigms suggests possible unique causes of their observed oculomotor performance deficits.

1. Introduction

Oculomotor paradigms are useful translational tools for profiling neurobehavioral disabilities and have been used to characterize cognitive and sensorimotor deficits in psychiatric disorders (Sweeney et al., 2002). Research with saccadic eye movements has focused primarily on

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*Center for Cognitive Medicine, 912 South Wood Street, MC 913, University of Illinois at Chicago, Chicago, IL 60612, USA, Phone: 312-413-9205, Fax: 312-413-8837, jsweeney@psych.uic.edu.

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schizophrenia. Sensorimotor paradigms such as the visually-guided saccade task have been used to assess the speed of sensorimotor transformation and the precision of motor responses (Fukushima et al., 1990; Reilly et al., 2005). More cognitively demanding paradigms such as the antisaccade task, which assesses the ability to voluntarily suppress saccades to unpredictably appearing targets but instead to execute an eye movement to the exact mirror location in the opposite peripheral field, have been used to evaluate higher executive functions supported by prefrontal systems (Curtis et al., 2001; Harris et al., 2006; Hutton & Ettinger, 2006). Most studies with unaffected family members of schizophrenia probands found increased error rates on antisaccade tasks (McDowell et al., 1999; Calkins et al., 2004); although, a recent study with young patient siblings reported a trend-level increase in error rates only (de Wilde et al., 2008). Further, the paradigm has been used in family genetic investigations (Myles-Worsley et al., 1999; Radant et al., 2007).

The diagnostic specificity of oculomotor abnormalities across psychotic disorders has not been extensively examined. This is an important issue in the context of multiple recent demonstrations of similarities across schizophrenia and psychotic mood disorders (Owen et al., 2007), including responsiveness to antipsychotic medications (Stahl, 2000), postmortem neurochemistry (Woo et al., 2004), MRI morphometry (Coryell et al., 2005), and genetic linkage findings (Detera-Wadleigh & McMahon, 2006). Clarifying these similarities and differences may be helpful for understanding functional disabilities and different pathophysiological mechanisms of these disorders.

Deficits in frontostriatal systems, suggested by some neuroimaging and neuropsychological studies of both schizophrenia and affective psychoses, may be expressed in reduced voluntary control of behavior that can be investigated using the antisaccade task. Previous investigations have reported antisaccade deficits in unmedicated unipolar depression and medicated bipolar disorder in addition to schizophrenia (Sweeney et al., 1998; Gooding & Tallent, 2001). Other results suggest that increases in antisaccade error rates in medicated psychotic depression and psychotic bipolar disorder may be less severe than in schizophrenia (Curtis et al., 2001). However, some studies reported no differences between antisaccade performance in healthy individuals and medication-free as well as medicated mood disorder patients (Crawford et al., 1995; Fukushima et al., 1990). Because neurobiological changes may occur over the course of serious mental illness, and medication effects may confound interpretation of oculomotor data, the comparison of first-episode treatment-naïve samples represents one important approach for studying these patient group differences. The current study aimed to characterize oculomotor performance of schizophrenia, psychotic depression and psychotic bipolar disorder on an antisaccade task and a visually-guided saccade control task in treatment-naïve first-episode psychotic disorders. Both healthy individuals as well as a sample of non-psychotic patients with depression served as comparison groups.

2. Methods

2.1. Participants

123 in- and outpatients meeting DSM-IV criteria for schizophrenia (n=59), major depressive disorder with psychotic features (n=15), bipolar disorder with psychotic features (n=9), and major depressive disorder without psychotic features (n=40) participated in the study. Diagnoses were established using the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID; First et al., 1995) and collateral information reviewed at consensus diagnosis meetings. All patients were experiencing their first lifetime episode of illness and had never been treated with any antipsychotic, antidepressant or mood-stabilizing medications. This latter criterion was important to exclude potential drug effects in the data, but disproportionately excluded mood disorder patients yielding smaller samples of patients with those disorders. Additionally, patients were excluded from the study if they reported exposure at the time of

the study to other medications that may affect oculomotor performance. Diagnoses of psychotic disorders were confirmed at six month follow-up visits as part of the prospective longitudinal study of first-episode psychoses in Pittsburgh. Patients with major depressive disorder without psychosis were included for comparison purposes.

106 healthy individuals from the surrounding community, who did not meet criteria for any present or past Axis I disorder according to SCID interviews, were also recruited via advertisements. This group matched the patient group on gender, age, and IQ (see Table 1). Participants under the age of 18 gave assent, and parental consent was obtained. Adults provided written consent to participate. All study procedures were approved by the Institutional Review Board at the University of Pittsburgh.

All participants met the following criteria: (1) age between 15 and 45 years; (2) no known systemic or neurologic disease; (3) no history of head trauma with loss of consciousness greater than 10 minutes; (4) no lifetime history of substance dependence or substance abuse within 3 months prior to study participation; (5) no benzodiazepines (5 half-lives) prior to testing; (6) no coffee, tea or cigarettes 1 hour prior to testing; and (7) right-handed.

Clinicians without knowledge of eye movement performance completed clinical ratings in parallel with oculomotor testing. Ratings were obtained for the Brief Psychiatric Rating Scale (BPRS; Overall & Gorham, 1962), the Schedule for the Assessment of Positive Symptoms (SAPS; Andreasen, 1984a), the Schedule for the Assessment of Negative Symptoms (SANS; Andreasen, 1984b), and the Hamilton Depression Rating Scale (HAM-D; Hamilton, 1960) (see Table 1).

2.2. Eye movement studies

Participants were tested alone in a darkened black room free from extraneous stimuli. They sat facing a circular black arc with a 1-meter radius and red light-emitting diodes embedded in the horizontal plane at eye level. A chin and forehead rest minimized head movement. A technician blind to diagnostic information provided instructions via intercom in an adjacent room. Electrodes were placed at the lateral and nasal canthi of each eye to obtain electrooculography (EOG) recordings (Grass Neurodata 12 Acquisition System, Astro-Med, Inc.). Blinks were monitored using electrodes placed above and below the left eye.

To minimize potential loss of measurement precision due to baseline drift in EOG recordings over the course of testing, eye position recordings were calibrated for each trial independently using data obtained when participants fixated central and peripheral targets. Recordings digitized at 500 Hz (DI-210 14-bit A/D, DATAQ Instruments) were analyzed using software developed in our laboratory. An algorithm identified saccade initiation when eye velocity rose above 30 deg/s, and saccade termination when eye velocity returned below that level. Anticipatory saccades with latencies less than 70 ms were not included in analyses. Trials were rejected if a blink occurred in the interval between 100 ms prior to presentation of peripheral targets and the end of primary saccades.

2.2.1. Visually-guided saccade task—A visually guided saccade control task was used to assess automatic attention shifting and sensorimotor aspects of saccade control. Participants were instructed to look to visual targets whenever they appeared. Trials began with a center fixation target that remained illuminated for 1.5 to 2.5 seconds before peripheral targets were presented at unpredictable locations 10, 20, or 30 degrees to the left or right of center fixation for 1.5 seconds. Peripheral targets were presented coincident with the termination of the central fixation target. Fifty-four trials were administered. Measures of saccade latency (time from peripheral target presentation to saccade initiation) and saccade gain (percentage of distance

toward new location achieved by the saccade) were obtained. More than 50 of the 54 trials (92.7%) were scorable for all participant groups.

2.2.2. Antisaccade task—Participants fixated a central target for 3 to 5 seconds (pseudo-randomly determined in 200ms steps), after which it was extinguished and a peripheral target appeared immediately at one of six unpredictable locations (8, 16, or 24 degrees to the left or right of center fixation) for 1.5 seconds. Participants were instructed not to look at the peripheral target, but rather to immediately look to the exact mirror location (the same distance from center in the opposite direction). When the peripheral target was extinguished, a light was shown at the mirror location where participants should be looking to provide feedback about performance accuracy. Thirty-six trials were presented, and more than 32 of the 36 trials (89.3%) were scorable for each group.

Participants were first trained using slow presentations of the task during which a technician provided verbal instructions about task demands and appropriate responses. During testing, if participants made consecutive errors on two trials, they were reminded of the task instructions to ensure that performance deficits did not result from confusion about task requirements. Measures of antisaccade error rates (percentage of trials with initial incorrect prosaccades toward the peripheral target) and the latency of correct antisaccade responses were obtained.

2.3. Statistical analyses

Data were averaged across trials with identical target location for each participant prior to statistical analyses. An arcsine transformation was performed on the antisaccade error rate data to render these proportional measures more amenable to parametric statistical analysis.

Because the emphasis of the present study was on group comparisons, data for saccades to the different target locations within each visual field were pooled and are not presented below.

3. Results

3.1. Oculomotor task performance

3.1.1. Gain of visually-guided saccades – Accuracy of sensory-guided eye movements—Analysis of the visually-guided saccade gain data yielded significant effects for laterality [$F(1, 224)=29.60, P<.001$], group [$F(4, 224)=5.60, P<.001$], and laterality by group interaction [$F(4, 224)=3.07, P=.017$]. Saccades were overall more accurate toward targets in the left than the right visual field ($t(228)=-6.17, P<.001$). Saccades of unipolar depressed patients with psychotic features were more hypometric (undershooting) than healthy individuals ($P=.001$) and unipolar depressed patients without psychotic features ($P=.006$) (see Figure 1A). Differences between the psychotic patient groups were not significant. The significant interaction term resulted from a pattern of similar laterality effects (left field advantage) in healthy individuals, the unipolar depressed patients without psychotic features and schizophrenia patients, but a right field advantage in both psychotic mood disorder groups.

3.1.2. Latency of visually-guided saccades—A repeated measures analysis of variance for the visually-guided saccade latency data indicated no significant effects for laterality [$F(1, 224)=.45, ns$], group [$F(4, 224)=.65, ns$], or laterality by group interaction [$F(4, 224)=1.88, ns$]. Thus, there were no differences in the speed with which participant groups shifted attention and gaze to unpredictable visual targets (see Figure 1B). In contrast, results of a previous study on a subset of schizophrenia patients included in these analyses who were followed longitudinally (35 of the current 59 patients; Reilly et al., 2005) showed shorter visually-guided saccade latencies in the schizophrenia group compared to healthy individuals. The differences in these results are due to two patient participants in the current sample (not included in the previous study) who showed particularly long visually-guided saccade latencies, increasing

the group mean by 4 msec and the standard deviation by over 10.5 msec compared to the previous investigation.

3.1.3. Antisaccade error rates - Response suppression failure—The repeated measures analysis of the antisaccade error rate data indicated significant effects for laterality [$F(1, 224)=7.44, P=.007$] and group [$F(4, 224)=25.4, P<.001$], but no significant laterality by group interaction [$F(4, 224)=.78, ns$]. Schizophrenia patients, unipolar depressed patients with psychotic features and bipolar patients made significantly more errors than healthy participants ($P<.001, P<.001$, and $P<.05$ respectively). Schizophrenia patients also made significantly more errors than unipolar depressed patients without psychotic features ($P<.001$). There was a trend for non-psychotic depressed patients to show higher antisaccade error rates than healthy individuals ($P=.075$). Differences among psychotic patient groups were not significant (see Figure 2A). Across all groups, more errors occurred when targets were presented in the right visual field ($t(228)=3.25, P=.001$).

3.1.4. Latency of correct antisaccades—The repeated measures analysis for latencies of correct antisaccades yielded significant effects for group only [$F(4, 224)=5.48, P<.001$]. The effects for laterality [$F(1, 224)=.004, ns$] and the laterality by group interaction [$F(4, 224)=1.85, ns$] were not significant. Schizophrenia patients were slower to initiate correct antisaccades than healthy individuals ($P<.001$) and unipolar depressed patients without psychotic features ($P=.03$). Differences among psychotic patient groups were not significant (see Figure 2B).

3.1.5. Effect size estimates—Because the samples of patient groups were of unequal size, we computed effect size estimates of key measures as a descriptive approach for illustrating the degree of deficit across disorders. Effect size estimates were computed contrasting each patient group separately with the control group as well as other patient groups using Cohen's d procedure (Cohen, 1988). These are presented in Table 2.

3.2. Correlational analyses of oculomotor measures

For healthy individuals, there was a significant association between the latencies of visually-guided saccades and the latencies of correct antisaccades ($r=0.30, P=0.002$). In the unipolar depressed patients without psychotic features and the unipolar psychotic depressed patients the same associations were observed to a somewhat enhanced degree (both $r^2s>0.50$, both $P's\leq.002$). A similar trend-level effect was also observed for the psychotic bipolar patient group ($r=.62, P=0.076$). However, this effect that suggests a general psychomotor speed aspect of response initiation for both visually-guided and antisaccade tasks, was not observed in schizophrenia patients ($r=0.05, P=0.47$) (see Figure 3).

As reported previously in a subset of schizophrenia patients included in these analyses who were followed longitudinally (30 of the current 59 patients; Harris et al., 2006), the schizophrenia group showed a significant inverse association between visually-guided saccade latencies and antisaccade error rates on the antisaccade task ($r=-0.39, P=0.002$). This effect was not seen in other participant groups.

3.3. Relationships of oculomotor task performance with clinical features

Psychotic patient groups did not differ significantly in symptom severity in BPRS, SAPS, SANS, or HAM-D scores (see Table 1). Performance on oculomotor tasks was rarely associated with clinical ratings for patient groups. Increased (i.e. prolonged) latencies on the visually-guided saccade task were associated with increased SANS scores in psychotic unipolar depression ($r=.56, P=0.03$) and increased BPRS scores for psychotic bipolar patients ($r=0.76, P=0.02$). Prolonged latencies on the antisaccade task were associated with increased SANS

scores in psychotic unipolar depression ($r=.56$, $P=0.03$). No other significant associations between oculomotor task performance and clinical ratings were found for other groups.

There was no difference in the duration of prodrome preceding acute psychosis or the duration of untreated psychosis (time from onset of first psychotic symptom to study participation) across psychotic disorders. Performance on oculomotor tasks was not associated with the duration of untreated prodrome or untreated psychosis for any of the psychotic patient groups.

4. Discussion

The present study investigated the diagnostic specificity of antisaccade deficits across psychotic disorders during the first episode of illness before any lifetime treatment with antipsychotic, antidepressant or mood-stabilizing medications. To our knowledge, this is the first study to make these comparisons. Increased error rates on the antisaccade task were not specific to schizophrenia, as rates in both psychotic mood disorder groups were also elevated. Although the patient groups with psychotic mood disorders were not large, which may have limited the ability to detect significant patient group differences, statistical power was sufficient to establish deficits in each group's performance (see Table 2). While there were no statistically significant differences in error rates on trials of the antisaccade task across psychotic disorder groups, the effect size of the abnormality in schizophrenia, relative to healthy subjects, was greatest ($d=1.48$). For psychotic depression patients, the effect size was 78% of that magnitude, and for bipolar patients it was 57%. These descriptive estimates suggest that antisaccade abnormalities, albeit present across psychotic disorders, may be more severe or common in schizophrenia, consistent with a prior report with chronic patients (Curtis et al., 2001). Interestingly, deficits of the unmedicated non-psychotic depression patients were 46% of the effect size of those observed in the schizophrenia sample. These results suggest that antisaccade disturbances may not have a high level of diagnostic specificity for schizophrenia, and thus that disturbances in the frontostriatal systems that support this neurocognitive ability might occur across psychotic disorders – and perhaps to a degree in non-psychotic depression.

4.1. Antisaccade impairments across psychotic patient groups

Abnormalities in prefrontal executive systems are a core cognitive deficit in schizophrenia (Goldberg & Weinberger, 1988). Both functional and anatomic brain imaging data indicate abnormalities in prefrontal cortex in schizophrenia (Buchanan et al., 1998; Keedy et al., 2006). The antisaccade paradigm assesses one prefrontally-mediated neuropsychological function, the ability to voluntarily suppress reflexive prepotent response tendencies (Pierrot-Deseilligny et al., 1991; Sweeney et al., 1996). Several previous studies have reported higher rates of response suppression failure in schizophrenia patients compared to healthy individuals on this task, and frequently prolonged response latencies of correct antisaccade responses (Fukushima et al., 1990; Clementz et al., 1994; Crawford et al., 1995; Nieman et al., 2000; Harris et al., 2006).

In the present study, disturbances in the ability to suppress context-inappropriate behavior on an antisaccade task were observed across psychotic disorders. Hence, as with pursuit eye tracking deficits (Sweeney et al., 1999), high rates of antisaccade errors may not be a neurophysiological abnormality specific to schizophrenia. Because the present findings were observed in groups of untreated first-episode patients, this non-specificity does not appear to be attributable to treatment or disease progression effects.

Results of the current and previous investigations suggest that some neuropsychological deficits occur across psychotic disorders (Hill et al., 2004), and may extend to their non-psychotic relatives (Glahn et al., 2007). Neuropsychological and neuroimaging evidence suggests that alterations in frontostriatal circuitry may cause some of the neurobehavioral

impairments that are shared across disorders. Schizophrenia and mood disorder patients both show deficits on executive function tasks which heavily rely on prefrontal systems (Merriam et al., 1999; Hill et al., 2004). Additionally, neuroimaging studies with affective disorders, paralleling findings in schizophrenia, show abnormalities in regional cerebral blood flow (rCBF) in superior frontal cortex in both psychotic and non-psychotic unipolar depressed patients (Gonul et al., 2004) and dysfunction in prefrontal networks in bipolar disorder (Strakowski et al., 2005). Hence, impairments in some frontostriatal systems may be common to psychotic disorders, regardless of whether the etiology of these effects is similar, and increased response suppression failures on the antisaccade task may be one neurobehavioral manifestation of disturbances in this neural system.

4.2. Visually-guided saccade dysmetria in psychotic unipolar depressed patients

Reduced saccade gain on the visually-guided saccade task was only observed in psychotic unipolar patients (see Figure 1A). We previously reported hypometric visually-guided saccades in an independent sample of unmedicated severely depressed patients of which over one third were psychotic at the time of testing (Sweeney et al., 1998). This finding has not been observed in untreated patients with other psychotic disorders or in non-psychotic depression. One possibility is that this result could be the consequence of a disturbance in the dorsal vermis of the cerebellum, which is known to regulate the accuracy of saccades to visual targets (Scudder et al., 1996). Patients with major depression have been shown to demonstrate volumetric changes in the vermis that might contribute to the saccade dysmetria observed in this patient group (Shah et al., 1992).

Alternatively, saccadic hypometria might be due to disturbances in the midbrain, which is a downstream target of output from the vermis. The pons contains burst cells that drive saccades. During fixation, these cells are inhibited by omnipause cells in the dorsal raphe that are under serotonergic regulation (Schenk et al., 1992). If pause cell firing is not sufficiently disinhibited during saccades, or resumes prematurely, saccades become hypometric (Leigh & Zee, 1999) as were those of psychotically depressed patients in the present study. Given diverse evidence of serotonergic disturbances in depression, it is an intriguing possibility that altered 5HT function of the dorsal raphe in psychotic depression might dysregulate modulation of burst cell firing to cause saccades to undershoot their targets.

4.3. Association of visually-guided and antisaccade task performance

Although univariate group comparisons did not reveal significant differences in antisaccade deficits between schizophrenia and psychotic mood disorders, examination of the correlational structure of eye movement data across the tasks suggests a unique pattern of abnormality in schizophrenia. Healthy individuals and all three mood disorder patient groups (regardless of the presence of psychotic features) displayed significant associations between the latencies of reflexive visually-guided saccades and correct antisaccades, as previously reported in a large sample ($n=115$) of non-clinical participants (Ettinger et al., 2005). This association suggests a shared mechanism involving speed of sensorimotor and attentional processing that determined response latencies in both tasks (Figure 3). Schizophrenia patients did not display this association. This suggests that a factor other than simple attentional processing speed may contribute to deficits in their ability to quickly evaluate contextual information, and to internally generate and initiate behavioral plans in schizophrenia. Alterations in the voluntary control of behavior based on deficits in decision making, or in using cognitive decisions to generate voluntary behavior, may explain this pattern and represent a relatively selective neurocognitive deficit in schizophrenia.

A second difference was the association only seen in schizophrenia patients between faster latencies to initiate reflexive visually-guided saccades and higher antisaccade error rates. We

have previously reported this inverse relationship in a subgroup of the current schizophrenia sample ($n=30$, Harris et al., 2006), and the same association holds for the patients not previously reported on ($n=29$; $r=-.43$, $P=.037$), but no other diagnostic group. This relationship suggests that the difficulty suppressing context-inappropriate behavior in schizophrenia may have unique causes. For example, dysregulation of neocortical attention systems may lead to attention being drawn more quickly and/or compellingly to unpredictably appearing targets, or that there is a difficulty sustaining visual attention at the central fixation cue, that could increase antisaccade error rates (Reilly et al., 2008). The presence of this relationship only in schizophrenia patients suggests that a difficulty suppressing the automatic “visual grasp reflex” may be a somewhat specific cause of increased antisaccade error rates in schizophrenia.

The neural systems controlling antisaccade responses are multifaceted (McDowell et al., 2005; Clementz et al., 2007). Future studies need to determine whether patients with schizophrenia have disturbances initiating voluntary action and/or disinhibiting reflexive shifts of visual attention that are potentially unique causes of their elevated rates of antisaccade errors and slower initiation of antisaccade responses. Such differentiation may provide more specific targets for family genetic research, and a better delineation of frontostriatal disturbances that contribute differentially to impaired antisaccade performance across psychotic disorders.

We recognize that the current study is limited by the relatively small sample sizes of the psychotic mood disorder patient groups. Although 123 treatment-naïve patients were studied, the smaller sizes of some patient groups may have limited power for detecting group differences and also for comparing associations of oculomotor parameters across tasks. However, we did have adequate power to establish deficits in all three groups of psychotic patients, and provide effect size estimates to descriptively characterize the extent of performance deficits in each group. A second limitation is that patients were seen only early during the course of illness. This raises two issues. First, the longitudinal stability of diagnoses is unknown, and some patients meeting criteria for mood disorders may later convert to schizophrenia. Second, while previous studies have reported that antisaccade deficits in schizophrenia are persistent over time (Harris et al., 2006), their stability in mood disorders is less clear. This is important because the degree to which deficits are persistent traits, rather than state-related effects associated with acute illness, may differ across schizophrenia and affective psychoses. The correlations between symptom ratings and eye movement measurements, although rare, occurred all in the psychotic mood disorder groups which suggests that state-related factors may contribute to performance deficits in these patients, and thus that some disturbances in frontostriatal systems may be more state-related in affective psychoses. Longitudinal studies are needed to address this issue.

Antisaccade deficits in 1st degree relatives of psychotic mood disorder patients, to our knowledge, have yet to be systematically investigated. This is a crucial point when considering the implications of our data for the use of the antisaccade task as an intermediate phenotype in family genetic research. It is possible that this deficit is not familial in psychotic mood disorder patients, a possibility that needs to be evaluated in studies of unaffected relatives of these patients.

Findings from the present study indicate that antisaccade abnormalities are present in psychotic affective disorders in addition to schizophrenia - albeit perhaps to a somewhat reduced degree. The presence of frontostriatal system disturbances across psychotic disorders may account for the increased prevalence of this deficit in multiple psychotic disorders. Nonetheless, the pattern of deficits across tasks in schizophrenia patients suggests that the causes of antisaccade performance deficits in this disorder may be somewhat unique. The observation that schizophrenia patients showed a speeded visual grasp reflex that was related to antisaccade error rates potentially implicates the involvement of frontoparietal attentional systems or a

reduced corticofugal frontal regulation of brainstem motor systems. The patients' slowed ability to initiate internally generated behavioral plans might implicate reduced facilitation by thalamocortical drive as a relatively specific cause of altered antisaccade task performance in schizophrenia.

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Figure 1. Visually-guided saccade measures

Mean (SD) for (A) accuracy and (B) latencies of visually-guided saccades for healthy participants, patients with schizophrenia, major depressive disorder with psychotic features, psychotic bipolar disorder, and major depressive disorder without psychotic features. Horizontal lines represent group median values.

Figure 2. Antisaccade measures

Mean (SD) for (A) error rates and (B) latencies of correct antisaccades for healthy participants, patients with schizophrenia, major depressive disorder with psychotic features, psychotic bipolar disorder, and major depressive disorder without psychotic features. Horizontal lines represent group median values.

Figure 3. Association of visually-guided saccade latencies and correct antisaccade latencies
 Scatterplots for latencies of visually-guided saccades and correct antisaccades for healthy participants, patients with major depressive disorder without psychotic features, major depressive disorder with psychotic features, psychotic bipolar disorder, and schizophrenia. Solid lines represent regression lines.

Table 1

Demographic characteristics for all participant groups and clinical ratings for patient groups.^a

	Healthy Participants (n=106)	Schizophrenia (n=59)	Bipolar Disorder (n=9)	MDD w/ Psychosis (n=15)	MDD w/o Psychosis (n=40)	P- value
Gender (M/F)	62/44	32/27	4/5	7/8	13/27	n.s.
Age (yrs)	28.2 (9.4)	27.5 (9.4)	25.4 (10.0)	25.5 (10.8)	29.8 (5.9)	n.s.
IQ	98.6 (5.1)	96.3 (10.3)	97.0 (10.8)	95.0 (11.0)	99.8 (6.7)	n.s.
BPRS	N/A	49.5 (9.5)	46.4 (5.7)	46.9 (11.0)	N/A	n.s.
SANS	N/A	13.3 (3.2)	10.8 (2.9)	12.9 (3.1)	N/A	n.s.
SAPS	N/A	9.5 (3.4)	7.4 (3.0)	6.9 (5.0)	N/A	n.s.
HAM-D	N/A	14.2 (7.5)	13.7 (7.3)	18.7 (6.8)	17.9 (5.4)	n.s.

^aP-value for Gender reflects significance level for χ^2 test. Other p-values reflect significance level for One-way ANOVA.

Mean (SD) are reported for age, IQ (Ammon's Quick Test), and clinical ratings.

MDD = Major Depressive Disorder; BPRS = Brief Psychiatric Rating Scale; SANS = Schedule for the Assessment of Negative Symptoms; SAPS = Schedule for the Assessment of Positive Symptoms; HAM-D = Hamilton Depression Inventory.

Table 2

Absolute effect size estimates^a comparing all participant groups. For visually-guided saccade parameters, effect size estimates above the principal diagonal represent latency measures and data below represent saccade gain measures. For antisaccade parameters, data above the principal diagonal represent latency measures and data below represent error rates.

Visually-guided Saccade Parameters				
	Healthy	MDD w/o Psych	BP w/ Psych	MDD w/ Psych
Healthy				
MDD w/o Psych	0.06	0.27	0.14	0.12
BP w/ Psych	0.14	0.07	0.37	0.05
MDD w/ Psych	1.09	1.04	0.97	0.21
Schizophrenia	0.41	0.36	0.29	0.60
Antisaccade Parameters				
	Healthy	MDD w/o Psych	BP w/ Psych	MDD w/ Psych
Healthy				
MDD w/o Psych	0.68	0.10	0.50	0.60
BP w/ Psych	0.84	0.39	0.34	0.50
MDD w/ Psych	1.16	0.61	0.12	0.27
Schizophrenia	1.48	0.96	0.43	0.34

^a Effect size estimates were computed using Cohen's *d* procedure.