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Schizophrenia patients show intact immediate error-related performance adjustments on an antisaccade task

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Abstract

Objective: Schizophrenia patients consistently show impairments on tasks requiring inhibition such as the antisaccade task. Deficits in performance monitoring including the detection of errors and subsequent adjustments to performance may contribute to such impairments. We examined whether immediate error-related performance adjustments during the antisaccade task were intact in schizophrenia.
Method: We compared 21 schizophrenia patients and 14 healthy control subjects on the following measures: 1) error-related, trial-by-trial adjustments in reaction time (pre-error speeding, faster errors and post-error slowing); 2) the speed–accuracy trade-off (SATO) function; and 3) the frequency and type of error self-correction.
Results: Although antisaccade performance in schizophrenia was characterized by increased errors and latency of correct responses, measures of immediate error-related performance adjustments were intact.
Conclusion: Schizophrenia is characterized by intact immediate error–related performance adjustments, even in the context of impaired antisaccade performance. It is possible that deficiencies in other aspects of error processing, indexed by electrophysiological and hemodynamic markers, contribute to antisaccade and other cognitive deficits in schizophrenia.

Keywords: Error processing; Performance monitoring; Inhibition; Post-error slowing; Self-monitoring; Antisaccade task

1. Introduction

Optimal cognitive performance requires an intact performance monitoring system that 1) detects errors, and 2) uses feedback regarding errors to make

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immediate performance adjustments (Holroyd and Coles, 2002). Schizophrenia patients consistently show deficits on the antisaccade task (for reviews see Brownstein et al., 2003; Levy et al., 1998). The antisaccade task requires the inhibition of the prepotent response of looking towards a suddenly appearing target, and the substitution of the novel behavior of looking in the opposite direction. The present study examined whether deficits in immediate error-related performance adjustments contribute to antisaccade deficits in schizophrenia.

Error detection or signaling is thought to involve the anterior cingulate cortex (ACC). Hemodynamic activity in ACC, and an event-related potential generated by the ACC known as the 'error-related negativity' (ERN) (Holroyd and Coles, 2002), are believed to index error detection. Immediate performance adjustments may depend on lateral prefrontal cortex (Garavan et al., 2002; Gehring and Knight, 2000). These adjustments include trial-by-trial changes in performance, such as the speeding up of reaction time (RT) prior to an error (pre-error speeding) (Ridderinkhof et al., 2003), the immediate self-correction of errors (Levy et al., 1998), and the slowing of reaction time (RT) in the subsequent trial (post-error slowing) (Rabbitt, 1966).

The extant literature suggests both intact and impaired performance monitoring functions in schizophrenia. Patients consistently show reduced anterior cingulate cortex (ACC) activity in association with error commission during functional neuroimaging studies (Carter et al., 2001; Laurens et al., 2003), and reduced ERN amplitude following errors during ERP studies (Alain et al., 2002; Kopp and Rist, 1999; Mathalon et al., 2002). This suggests that ACC-based error detection or signaling may be impaired in schizophrenia. In contrast, immediate error-related performance adjustments, such as post-error slowing and error correction, are generally found to be intact in patients (Kopp and Rist, 1994, 1999; Laurens et al., 2003; Levy et al., 1998; Mathalon et al., 2002), although reports of impaired performance adjustments do exist (Carter et al., 2001; Malenka et al., 1982, 1986; Turken et al., 2003). A dissociation between intact performance adjustments versus impaired ACC activity or ERN amplitude is often found within a single study (Kopp and Rist, 1999; Laurens et al., 2003; Mathalon et al., 2002).

Such findings are consistent with the idea that error detection and immediate performance adjustments are the product of different neural systems, and suggest that only one of these systems is impaired in schizophrenia. An alternate possibility is that they are both generated by the same system, but that behavioral adjustments are a less sensitive index of performance monitoring than more direct measures of neural activity. Studies reporting a dissociation between intact immediate performance adjustments and abnormal error-related neural activity have used tasks on which error rates do not differ between patients and controls (Kopp and Rist, 1999; Laurens et al., 2003; Mathalon et al., 2002). Normal error rates in patients might indicate a task that is insensitive to differences in behavioral adjustments.

The present study employed the antisaccade task to assess immediate performance adjustments. This task consistently gives rise to increased error rates in schizophrenia patients relative to controls (see Brownstein et al., 2003 for review), regardless of medication status (Clementz et al., 1994; Crawford et al., 1998; Curtis et al., 2001; Hutton et al., 1998; McDowell et al., 1999; O'Driscoll et al., 1998). We examined whether a task characterized by increased errors would reveal abnormalities in immediate performance adjustments. If so, this would suggest that deficient performance adjustments contribute to impaired antisaccade performance, and that previous studies may have used tasks that were insensitive to performance adjustment failures. If not, this would indicate that antisaccade deficits in schizophrenia do not result from performance adjustment deficits, and would support the notion of different neural systems giving rise to error detection versus performance adjustments, with a selective impairment in the former system in schizophrenia. We have already documented increased antisaccade error rates and latencies for correct antisaccades in the present schizophrenia sample (Manoach et al., 2002). In this study, we investigated whether immediate error-related performance adjustments were intact in the context of deficient antisaccade performance.

We assessed two types of error-related performance adjustments: 1) error-related RT changes and 2) rates of error correction. Error-related RT changes occur in the context of an inverse relationship that exists between speed and accuracy, as described by the

speed–accuracy trade-off function (SATO function) (Fig. 1). Up to a certain point, increasing speed of responding does not impair accuracy. This optimal point occurs when 100% accuracy is achieved at the fastest possible speed. Beyond this point, speed and accuracy are inversely related, with slower trials having a greater probability of being correct than faster trials. Trial-by-trial adjustments in RT are made along this function based on error history. Prior to and during error trials, RT is, on average, faster than during other correct trials (pre-error speeding and faster errors) (Gehring and Knight, 2000; Ridderinkhof et al., 2003). After an error, RT slows down (post-error slowing) and the probability of an error decreases (Rabbit, 1966). Thus, individuals shift to riskier positions on the curve before an error, but following an error, feedback signals cause individuals to shift to a more conservative position on the curve. In this study, we examined three trial-by-trial RT changes: a) *pre-error speeding*; b) *faster errors*; and c) *post-error slowing*. We also examined the actual SATO function between groups.

A second marker of immediate error-related performance adjustments is error correction. We examined error correction rates in the absence of any external feedback. We examined both overall correction rates, and type of error correction, between groups. Saccadic corrections fall into two categories: corrections that occur almost immediately (<130 ms) following an error trial, and corrections that occur more than 130 ms following an error trial. As saccades take approximately 130 ms to be expressed after they have been programmed, a corrective saccade that occurs less than 130 ms after the erroneous saccade is thought to have been programmed prior to the end of the erroneous saccade, and in the absence of any visual feedback about an error. Corrective saccades that occur more than 130 ms after the error saccade are thought to be a response to visual feedback about an error (Fecteau and Munoz, 2003). Short self-corrections are not associated with error awareness, and follow errors that are small in amplitude, while long self-corrections correlate with error awareness, and follow errors that are larger in amplitude (Mokler and Fischer, 1999; Nieuwenhuis et al., 2001). Using RT changes and error correction measures, we examined whether schizophrenia patients would show normal performance adjustments despite significantly impaired performance on the antisaccade task compared to controls.

2. Method

2.1. Subjects

Twenty-three outpatients with schizophrenia were recruited from an urban mental health center. Twenty healthy control subjects, without a history of psychiatric illness, were recruited from the hospital community, and screened to exclude substance abuse or dependence within the past 6 months and any

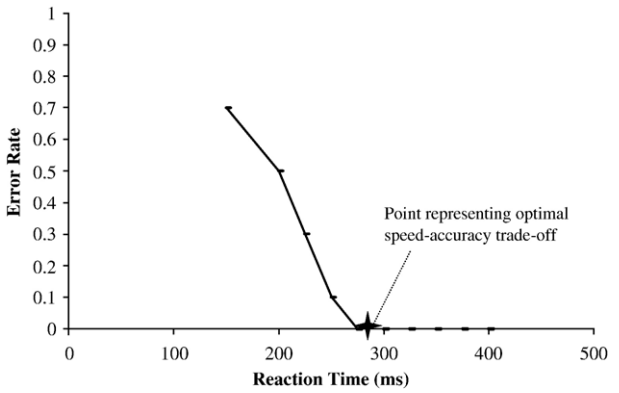

Fig. 1. This is a depiction of a hypothetical speed–accuracy trade off (SATO) function. As reaction time (RT) increases, the error rate decreases. The star represents the optimal point of responding where 100% accuracy is achieved at the fastest possible RT, or the point where speed and accuracy are optimized. Beyond this point, RT and accuracy are inversely related, with faster RT increasing the likelihood of error commission.

medical/neurological conditions that might affect brain function. Two patients and four control subjects did not complete the protocol because they could not tolerate the scleral contact lens. One control subject was excluded due to instrument malfunction. The data were also examined, by group, for outliers using a cutoff of 3 standard deviations from the group mean error rate or latency. This led to the exclusion of one control subject with a 54% error rate. The final sample size was 21 patients and 14 controls. Sample demographics are presented in Table 1. Patients had been maintained on stable doses of antipsychotic medications for at least 6 weeks prior to study, 15 subjects on atypical and 6 on conventional agents. Diagnoses were confirmed with Structured Clinical Interviews for DSM-IV (First et al., 1997). Clinical status was characterized with the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987) and the Brief Psychiatric Rating Scale (BPRS) (Overall and Gorham, 1962). Movement abnormalities were characterized with the Abnormal Involuntary Movement Scale (NIMH and Health, 1974) and the Simpson–Angus Rating Scale (Simpson and Angus, 1970). Seventeen patients and 9 control subjects were strongly right-handed as determined by a laterality score of 70 or above on the modified Edinburgh Handedness Inventory (White and Ashton, 1976). Groups did not differ in age, sex, or handedness. There was a trend for controls to have a higher parental SES as determined by the Hollingshead Index (Hollingshead, 1965) than patients.

2.2. Eye movement apparatus and protocol

We recorded eye movements with a magnetic search coil technique, using a scleral contact lens and a 3-ft field coil (Crist Instruments, Bethesda, MD). The subject's head was secured in a chin rest with the cornea 81 cm away from a tangent screen. Displays were generated by a Power Macintosh 9600/233, using programs written in C^{++} on the Vision Shell platform (www.kagi.com/visionshell), and back-projected with an Eiki LC-7000U LCD-projector. The lens was placed in the left eye. The system was calibrated by having the subject fixate nine targets in a square grid spanning 50°. Twelve data points were collected at each target location, and a regression method was used to find the best linear fit. Eye position was digitized at 500 samples/s. A five-point central difference algorithm (Bahill and McDonald, 1983) was used to derive velocity from eye position.

The initial stimulus presentation display consisted of a dark background with a white fixation ring at center, of 1.0° diameter and luminance of 20 cd/M^2. The fixation ring was flanked by two dots of 0.7° diameter and equal luminance placed 20° right and left of center. These two peripheral dots were visible in each trial until obscured by a target. The subject was required to look at the central fixation point and each trial began when a subject's eye fell within 3° of the fixation point. After a period randomly varying between 1 and 1.5 s, the fixation point was replaced by a blue 'X' spanning 4.5°, which was the prompt for

Table 1
Means, standard deviations and group comparisons of demographic data and rating scale scores

Subject characteristics	Healthy controls ($n=14$)	Schizophrenia patients ($n=21$)	t	p
Age	39.1 ± 8.4	43.7 ± 8.0	−1.63	0.11
Sex	9M/5F	17M/4F	Phi=0.19	0.43
Laterality score (Handedness)	60.0 ± 60.3	71.0 ± 52.6	−0.57	0.57
Parental SES[a]	1.9 ± 1.3	2.8 ± 1.3	$z=-1.86$	0.07
Age of onset		27.7 ± 9.3	Level of severity	
Length of illness (years)		16.1 ± 10.3		
BPRS		17.0 ± 5.6	Minimal	
PANSS positive		11.8 ± 4.0	Minimal to mild	
PANSS negative		19.3 ± 5.7	Mild to moderate	
SANS		41.0 ± 16.6	Minimal to mild	
AIMS		3.0 ± 4.3	None to minimal	
Simpson–Angus		3.8 ± 4.1	None to minimal	

The Phi value is the result of a Fisher's Exact Test. The z value is the result of a nonparametric Mann–Whitney U comparison.
[a] A lower score denotes higher status.

an antisaccade. Prompts lasted 300ms and were then replaced by the white fixation ring. After a mean interval of 2 s the fixation ring disappeared and a similar ring appeared around one of the two peripheral dots, the side randomly determined. The offset of the fixation ring was simultaneous with the appearance of the peripheral ring. This was the cue for the subject to make their saccade as quickly and accurately as possible to the opposite periphery. The white ring remained in the peripheral location until either the subject's eye had fallen within 3° of the desired end position or 10 s had passed, at which time it returned to the central fixation point for the next trial. After practicing the task for 20 trials, each subject performed four blocks of 26 trials of antisaccades for a total of 104 antisaccade trials. Prior to testing, participants were informed that they would receive a monetary bonus for each correct response. This was intended to mitigate potential motivational deficits in the schizophrenia subjects. Antisaccade blocks were counterbalanced with other saccadic blocks as part of larger experimental protocol.

2.3. Scoring of eye movement protocols

We identified saccades as eye movements with velocities exceeding 47°/s. The onset of a saccade was defined as the point at which the velocity of the eye first exceeded 31°/s. For each saccade, we recorded directional accuracy with respect to the required response, latency (the RT from target onset to saccade onset), and amplitude (the distance traveled between the onset and end of a saccade). Trials in which saccadic latency was less than 130 ms were excluded as anticipatory guesses. Trials in which the latency was longer than 800 ms were excluded as too delayed. Trials were also excluded if saccades were less than 15° or greater than 25° in amplitude. Error saccades were scored as self-corrected if the erroneous saccade was followed by a corrective saccade with an overall amplitude of 15° or more; all other errors were considered non-corrected.

2.4. Data analyses

RT analyses were performed using JMP 5.1 software (www.JMPdiscovery.com), SATO function curves were derived using R software (Ihaka and Gentleman, 1996), and error correction rates were analyzed using Statview.

2.4.1. Reaction time changes

To examine changes in RT due to error history, we performed randomized block ANOVAs with group (controls vs. patients) as a between subject factor, trial type as a within subjects factor, and subjects nested within group as the random factor. The only factor that varied between the three following analyses was trial type. Trial type variously refers to whether trials preceded an error (pre-error) or correct (pre-correct) trial in the Pre-error Speeding analysis; whether the response to a current trial was erroneous or correct in the Faster Error analysis; and whether trials followed an error (post-error) or correct (post-correct) trial in the Post-error Slowing analysis.

2.4.1.1. Pre-error speeding. To determine if the mean RT of trials occurring before error responses was significantly faster than the mean RT of trials preceding a correct response, we performed an ANOVA with current response (pre-error vs. pre-correct) as the trial type factor. Only correct saccadic responses were used in this analysis. The last trial of each block was excluded since there was no subsequent trial. Correct trials that followed error trials were also excluded because of the possibility that post-error slowing would counteract the effect of pre-error speeding.

2.4.1.2. Faster errors. To determine if the mean RT for error trials was significantly shorter than the mean RT for correct trials, we performed an ANOVA with current response (error vs. correct) as the trial type factor.

2.4.1.3. Post-error slowing. To determine if the mean RT following an error response was slower than the mean RT following a correct response, we performed an ANOVA with current response (post-error vs. post-correct) as the trial type factor. Only correct trials were used, and the first trial of each block was eliminated as it lacked any immediate historical influence.

2.4.2. The SATO function

We derived a SATO function for each group using performance over repeated trials of the antisaccade

task to plot the probability of a trial being correct given its speed. The slope of the SATO function varies by group, and describes the efficacy of the speed–accuracy trade-off. A steeper slope represents a greater loss in accuracy for the same decrease in speed than a flatter slope. Trial-by-trial changes in RT will only produce equivalent changes in accuracy when the slopes of the SATO functions do not differ between groups. For this reason, it is important to assess if there are differences in the slopes of the SATO functions between groups (Rabbitt, 1966). We derived two group SATO functions (patients, controls) using a method outlined in Rabbitt and Vyas (1970).[1] We converted each subject's trials from raw RT data into z-scores based on each individual's own mean RT and standard deviation (S.D.). We generated frequency histograms for error and correct distributions by binning z-scores by group and across subjects using a 0.05 increment. We then derived the error rate for each z-score bin using the following formula: error rate=(# errors per bin/total # responses per bin). To enhance reliability, for bins that had fewer than 10 total responses, we combined across bins until there were 10 or more data points, and then derived the average z-score and accuracy for the new bin. To ensure that the conversion to z-scores did not mask a group difference in the slope of the SATO function, we re-constituted the z-scores into RT scores by multiplying each z-score by the appropriate group S.D. of RT, and adding the corresponding group RT mean. Using these re-constituted z-scores, we plotted error rate by RT. We plotted and compared SATO functions between groups by using the following model: y=group+linear coefficient+quadratic coefficient+(group×linear coefficient)+(group×quadratic coefficient). A significant linear interaction term would indicate that the *position* of the curve varies by group. A significant quadratic interaction term would indicate that the *slope* of the curve varies by group.

2.4.3. Error correction

Self-corrected errors were divided into long self-corrections (LSCs) and short self-corrections (SSCs) based on time of onset after an erroneous saccade. If the time of onset occurred more than 130 ms following the end of the erroneous saccade, the self-correction was classified as an LSCs. If the time of onset occurred less than 130 ms after the end of the erroneous saccade, the self-correction was classified as a SSC. We calculated several proportion scores: corrected errors (corrected/total errors); uncorrected errors (uncorrected/total errors); SSC (SSC/total corrected errors); and LSC (LSC/total corrected errors). To determine whether error correction was equivalent between groups, both with respect to 1) overall correction rate and 2) type of error correction, which is an indirect marker of error awareness, we performed two repeated measures ANOVAs with group (controls vs. patients) as a between subject factor. The first ANOVA had error correction (corrected vs. uncorrected) as the repeated measure. The second ANOVA had correction type (short saccadic correction vs. long saccadic correction) as the repeated measure. These analyses also examined 1) within-group error correction to determine whether most errors were followed by remedial behavior (i.e. self-correction of errors); and 2) within-group SSCs vs. LSCs to determine whether subjects were more likely than not to make corrections suggesting awareness of their corrective actions.

3. Results

3.1. Antisaccade performance

The mean error rate was significantly greater for schizophrenia patients (28.9%±18.6%) than for healthy controls (5.7%±2.3%), ($t(34)=5.65$ $p=<.0001$). Correct trials were significantly slower in the schizophrenia (364.62±87.75 ms) than in the control group (293.04±48.84 ms) ($t(34)=3.09$, $p=.002$).

3.2. Reaction time changes

3.2.1. Pre-error speeding

Correct responses before error trials were significantly faster than correct responses before correct trials, by about 13 ms ($F(1,34)=3.79$ $p=.05$). There was no significant interaction with group ($F(1,34)=.01$, $p=.92$), indicating that pre-error speeding was present in both patients and controls (Table 2).

[1] Rabbitt and Vyas (1970) used raw RT scores, whereas we used z-scores. However, z-score transformations are linear, and do not affect the shape (skewness, kurtosis) of the underlying distributions.

3.2.2. Faster errors

Error trials were significantly faster than correct trials by about 58 ms ($F(1,34)=98.43$, $p<.0001$). There was also a significant interaction with group ($F(1,34)=17.57$, $p=<.0001$). Follow-up analyses showed that this was due to correct antisaccades being slower in schizophrenia patients than healthy controls ($F(1,34)=9.76$, $p=.002$), whereas the RT for antisaccade errors was not different between groups ($F(1,34)=0.81$, $p=.37$) (Table 2).

3.2.3. Post-error slowing

Correct responses after error trials were significantly slower than correct responses after correct trials ($F(1,34)=4.67$, $p=.03$). There was no significant interaction with group ($F(1,34)=0.31$, $p=.57$), indicating that post-error slowing was present to a similar degree in both groups (Table 2). We also examined whether post-error slowing was proportional to overall mean RT using a linear regression model with mean correct RT, group, and a group by mean correct RT interaction term as the predictor variables, and mean post-error slowing as the criterion variable. We found no relationship between mean post-error slowing and mean correct RT ($F(1,34)=0.007$, $p=.933$), and this relationship was not found to vary by group ($F(1,34)=0.009$, $p=0.926$). Thus, in our data, differences in mean saccadic RT do not significantly contribute to the magnitude of post-error slowing in either group.

3.3. The SATO function

The model accounted for 75% of the variance in saccadic RT ($F(4,128)=97.66$, $p<.001$). The slope of the SATO function was not different in schizophrenia as indicated by a non-significant interaction of group by the quadratic term ($t(127)=0.38$, $p=.54$) (Fig. 2). However, the position of the SATO function differed significantly between groups, reflected in a significant interaction of linear term by group ($t(127)=-6.19$, $p<.001$). In schizophrenia, the SATO function was shifted up and to the right relative to that of the control subjects (Fig. 2). This indicates that patients have a lower baseline accuracy rate (11% less accurate) and a slower baseline speed of responding (by an estimated 116.2 ms) than controls. Thus, the difference between the group SATO functions can be adequately explained by a linear shift (with no rotational component). In other words, the two group SATO curves do not differ significantly from two copies of a single curve, positioned differently because schizophrenia patients tend to make more errors and have longer latencies than controls, but otherwise have similar group SATO behavior. The following equation includes both group curves as special cases: $\text{Error Rate} + a = .5990 - [2.912 \times 10^{-3} \times (\text{RT}+b)] + [3.490 \times 10^{-06} \times (\text{RT}+b)^2]$. For controls, $a=b=0$; for patients, $a=.11$ and $b=116.2$ ms. These values quantify, respectively, the group increases in error rate and latency for patients relative to controls.

3.4. Error correction

Errors were much more likely to be corrected than not ($F(1,34)=378.38$, $p<.0001$), and this did not differ between groups ($F(1,34)=.04$, $p=.84$), indicating that both groups corrected their erroneous behavior most of the time. Self-corrections were equally likely to be short than long ($F(1,34)=0.017$, $p=.90$), and this finding also did not differ

Table 2
Means and standard errors for reaction time changes (in ms) are reported for 'Pre-Error Speeding', 'Faster Errors', and 'Post-Error Slowing', and correction rates (in %) are reported for 'Overall Error Correction' and 'Correction Type' in healthy controls and schizophrenia patients

Effect studied	Trial type	Healthy controls		Schizophrenia patients	
		M	S.E.	*M*	S.E.
Pre-Error Speeding*	Pre-correct	293.87	19.96	365.96	16.46
	Pre-error	280.60	22.47	354.07	17.27
Faster Errors****	Correct	293.06	17.65	364.39	14.48
	Error	259.72	20.24	282.28	14.84
Post-Error Slowing*	Post-correct	291.91	19.94	362.87	16.43
	Post-error	308.86	22.37	372.83	16.94
Overall Error Correction****	Uncorrected	6.85	4.14	5.91	2.42
	Corrected	93.16	4.14	94.09	2.42
Correction Type	Short	55.73	8.52	39.26	6.17
	Long	37.42	9.16	54.83	6.83

*$p<.05$. **$p<.01$. ***$p<.001$. ****$p<.0001$.
"Pre-correct" indicates trials that directly precede a correct trial. "Pre-error" denotes trials that directly precede an error trial. "Post-correct" indicates trials that directly follow a correct trial. "Post-error" denotes trials that directly follow an error. Asterisks indicate *within-group* differences between trial types, and *p*-values are the same for both groups. Means reported for the RT data are least squares means.

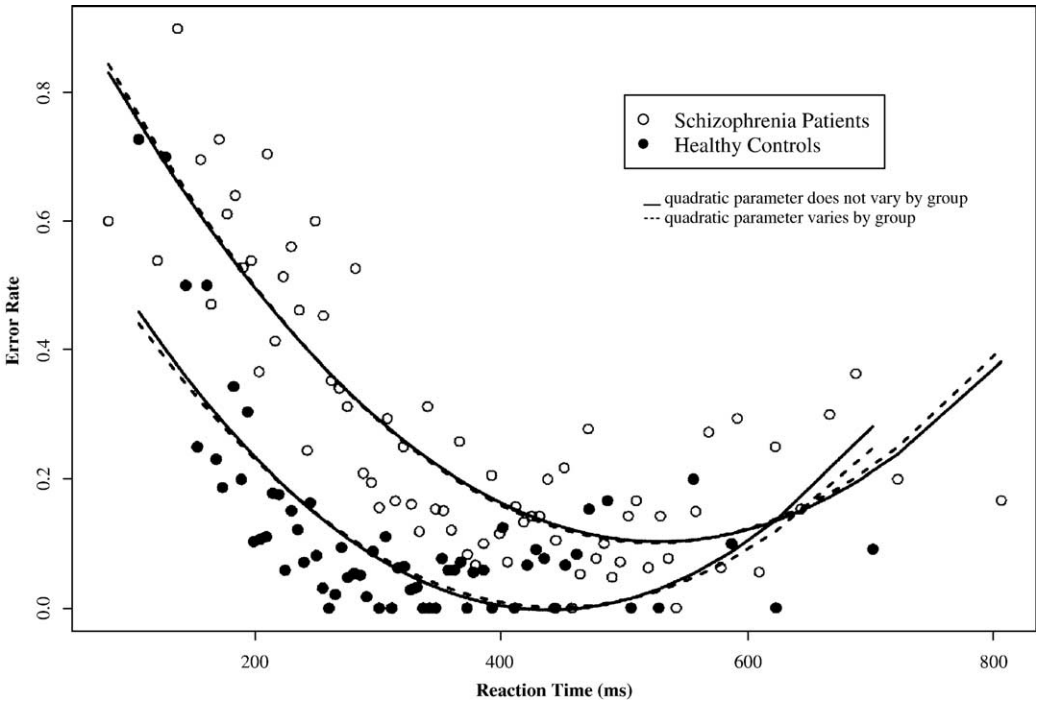

Fig. 2. Schizophrenia patients have a higher baseline error rate than healthy controls, and a longer baseline reaction time. However, the figure illustrates that their trade-off in speed for accuracy is not different from that of controls. The slopes of the SATO functions for both groups are similar, as evidenced by the fact that allowing the shape of the curve (quadratic parameter) to vary by group (represented visually by the dashed line) does not improve the explanatory power of the original curve (represented visually by the solid line).

by group ($F(1,34)=2.60$, $p=.12$), suggesting that corrective actions in both groups were as likely to be reflexive than not (Table 2).

4. Discussion

Our findings provide evidence that immediate error-related performance adjustments are preserved in schizophrenia despite a significantly increased antisaccade error rate. Error-related RT changes of pre-error speeding and post-error slowing were present in both groups and did not differ in magnitude. The slope of the SATO function also did not differ between groups. Finally, the majority of errors were followed by a corrective action, and schizophrenia and healthy subjects showed comparable frequency and types of error self-correction. These findings of intact immediate error-related performance adjustments are consistent with previous reports of normal post-error slowing (Laurens et al., 2003; Mathalon et al., 2002) and error correction (Kopp and Rist, 1994, 1999; Levy et al., 1998) in schizophrenia. The present study extends these findings by demonstrating that other expected error-related RT changes (pre-error speeding), the underlying SATO function, and types of self-correction are intact in schizophrenia. Moreover, we find these preserved immediate performance adjustments on a task producing a significantly increased error rate in schizophrenia. These findings suggest that antisaccade deficits in schizophrenia cannot be attributed to a failure to institute immediate error-related performance adjustments.

Our finding of intact immediate error-related RT changes, while consistent with some previous work (Laurens et al., 2003; Mathalon et al., 2002), contrasts with reports of diminished post-error slowing in schizophrenia (Alain et al., 2002; Carter et al., 2001). These differences may be attributable to methodological factors. For example, the Carter et al. (2001) study imposed a long delay between trials

(20 s). This might have differentially disrupted post-error slowing in schizophrenia on the basis of working memory deficits in schizophrenia (Goldman-Rakic, 1991), which may have resulted in a more rapid decay of the neural activity related to post-error slowing in patients. The Alain et al. (2002) study found intact post-error slowing in schizophrenia in terms of overall change in RT, but found reduced *proportional* post-error slowing (post-error slowing/total RT). Since there is no evidence, including from our own data, to suggest that the magnitude of post-error slowing varies with mean RT, using proportional scores may not be justified.

Our finding of intact self-correction of errors in schizophrenia is also consistent with a subset of studies (Kopp and Rist, 1994, 1999; Levy et al., 1998), while others have found reduced self-correction (Malenka et al., 1982, 1986; Turken et al., 2003). Again, methodological factors, specifically working memory load differences among tasks, may account for these discrepancies. As suggested by Kopp and Rist (1994), on tasks with high working memory load (Carter et al., 2001; Malenka et al., 1982, 1986), patients may have reduced error correction due to an inability to remember what the correct response was. This is in contrast to paradigms with low working memory load (Kopp and Rist, 1994, 1999), including the antisaccade paradigm (Levy et al., 1998), where it is easy for patients to remember the correct response and normal error correction rates are found. Thus, deficient working memory, rather than a failure of performance monitoring, may account for patients' decreased rate of error correction on certain tasks.

We do report one finding that might suggest performance adjustment differences between groups. While the latency of error trials did not differ between groups, the latency of correct trials did, indicating that patients required a greater increase in reaction time to achieve correct performance than did healthy controls. This may be suggestive of an overall SATO difference, since controls require a smaller increase in RT to achieve correct responding than patients do. However, it could also be interpreted as evidence for deficient cognitive control. Antisaccade errors indicate a failure of cognitive control, and reflect the functioning of a reflexive system that is likely intact in schizophrenia given findings of normal accuracy and latency of reflexive saccades. In contrast, schizophrenia is characterized by deficits in cognitive control. As the SATO is a reflection of a system exerting cognitive control, the greater increase in RT from errors to correct responses may reflect their deficits in cognitive control that generally shifts their SATO to the right, but not an abnormality in the shape or slope of their SATO. Therefore, the difference between error and correct RTs may not be an appropriate index of the normality of the SATO since these RTs tap the functioning of different systems.

A potential limitation of our study is that the few number of error trials in healthy controls increased the variability of our estimates, and this may have reduced our power to finding significant between-group differences. Even so, the predicted main effects of trial and correction type were significant, arguing against the study being underpowered. Therefore, while it is never possible to accept the null hypothesis, it can be said that there was only sufficient evidence to reject the null hypothesis for the main effects of performance adjustments, but not the interaction effects of differences in performance adjustments by group.

In summary we have demonstrated intact immediate error-related performance adjustments in the context of deficient antisaccade performance in schizophrenia. It is possible, however, that other aspects of performance monitoring not explicitly assessed in the present study, such as reduced ERN amplitude and ACC hypoactivity, could contribute to deficient antisaccade performance. The ERN, while commonly interpreted to reflect error detection, has recently been reframed as reflecting error-based reinforcement learning which is thought to occur via dopaminergic input to the ACC that reinforces correct responses while suppressing erroneous ones (for a review, see Holroyd and Coles, 2002). This latter interpretation is more consistent with findings of normal performance adjustments in this and other studies (Kopp and Rist, 1994, 1999; Laurens et al., 2003; Levy et al., 1998; Mathalon et al., 2002) suggesting intact error awareness in patients. On the antisaccade task, such learning might involve strengthening the non-dominant response of looking away from the target while weakening the prepotent tendency to look towards it. A failure of such learning in schizophrenia might explain why patients maintain such high error rates despite intact immediate error-related performance adjustments that should improve performance.

Future studies that concurrently assess immediate error-related performance adjustments *and* ACC activity, via electrophysiology or neuroimaging, are needed to address this question. If such studies found increased error rates and reduced ACC activity in the context of intact performance adjustments and associated neural activity, this would support the hypothesis of a selective impairment in ACC-based reinforcement learning in schizophrenia. The present findings provide a foundation for such studies by suggesting that increased antisaccade error rates in patients do not stem from a deficit of immediate error-related performance adjustments.

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References

Alain, C., McNeely, H.E., He, Y., Christensen, B.K., West, R., 2002. Neurophysiological evidence of error-monitoring deficits in patients with schizophrenia. Cereb. Cortex 12, 840–846.

Bahill, A.T., McDonald, J.D., 1983. Frequency limitations and optimal step size for the two-point central difference derivative algorithm with applications to human eye movement data. IEEE Trans. Biomed. Eng. 30, 191–194.

Brownstein, J., Krastoshevsky, O., McCollum, C., et al., 2003. Antisaccade performance is abnormal in schizophrenia patients but not in their biological relatives. Schizophr. Res. 63, 13–25.

Carter, C.S., MacDonald III, A.W., Ross, L.L., Stenger, V.A., 2001. Anterior cingulate cortex activity and impaired self-monitoring of performance in patients with schizophrenia: an event-related fMRI study. Am. J. Psychiatry 158, 1423–1428.

Clementz, B.A., McDowell, J.E., Zisook, S., 1994. Saccadic system functioning among schizophrenia patients and their first-degree biological relatives. J. Abnorm. Psychol. 103, 277–287.

Crawford, T.J., Sharma, T., Puri, B.K., Murray, R.M., Berridge, D.M., Lewis, S.W., 1998. Saccadic eye movements in families multiply affected with schizophrenia: the Maudsley Family Study. Am. J. Psychiatry 155, 1703–1710.

Curtis, C.E., Calkins, M.E., Grove, W.M., Feil, K.J., Iacono, W.G., 2001. Saccadic disinhibition in patients with acute and remitted schizophrenia and their first-degree biological relatives. Am. J. Psychiatry 158, 100–106.

Fecteau, J.H., Munoz, D.P., 2003. Exploring the consequences of the previous trial. Nat. Rev., Neurosci. 4, 435–443.

First, M.B., Spitzer, R.L., Gibbon, M., Williams, J.B.W., 1997. Structured Clinical Interview for DSM-IV Axis I Disorders, Research Version, Patient Edition with Psychotic Screen (SCID-I/P W/PSY SCREEN). Biometrics Research New York State Psychiatric Institute, New York.

Garavan, H., Ross, T.J., Murphy, K., Roche, R.A., Stein, E.A., 2002. Dissociable executive functions in the dynamic control of behavior: inhibition, error detection, and correction. Neuroimage 17, 1820–1829.

Gehring, W.J., Knight, R.T., 2000. Prefrontal–cingulate interactions in action monitoring. Nat. Neurosci. 3, 516–520.

Goldman-Rakic, P.S., 1991. Prefrontal cortical dysfunction in schizophrenia: the relevance of working memory. In: Caroll, B.J., Barrett, J.E. (Eds.), Psychopathology and the Brain. Raven Press, New York, pp. 1–23.

Hollingshead, A.B., 1965. Two Factor Index of Social Position. Yale University Press, New Haven, Conn.

Holroyd, C.B., Coles, M.G., 2002. The neural basis of human error processing: reinforcement learning, dopamine, and the error-related negativity. Psychol. Rev. 109, 679–709.

Hutton, S.B., Crawford, T.J., Puri, B.K., et al., 1998. Smooth pursuit and saccadic abnormalities in first-episode schizophrenia. Psychol. Med. 28, 685–692.

Ihaka, R., Gentleman, R., 1996. R: a language for data analysis and graphics. J. Comput. Graph. Stat. 5, 299–314.

Kay, S.R., Fiszbein, A., Opler, L.A., 1987. The positive and negative syndrome scale (PANSS) for schizophrenia. Schizophr. Bull. 13, 261–276.

Kopp, B., Rist, F., 1994. Error-correcting behavior in schizophrenic patients. Schizophr. Res. 13, 11–22.

Kopp, B., Rist, F., 1999. An event-related brain potential substrate of disturbed response monitoring in paranoid schizophrenic patients. J. Abnorm. Psychol. 108, 337–346.

Laurens, K.R., Ngan, E.T., Bates, A.T., Kiehl, K.A., Liddle, P.F., 2003. Rostral anterior cingulate cortex dysfunction during error processing in schizophrenia. Brain 126, 610–622.

Levy, D.L., Mendell, N.R., LaVancher, C.A., et al., 1998. Disinhibition in antisaccade performance in schizophrenia. In: Lenzenweger, M.F., Dworkin, R.H. (Eds.), Origins and Development of Schizophrenia: Advances in Experimental Psychopathology. American Psychological Association, Washington, DC, pp. 185–210.

Malenka, R.C., Angel, R.W., Hampton, B., Berger, P.A., 1982. Impaired central error-correcting behavior in schizophrenia. Arch. Gen. Psychiatry 39, 101–107.

Malenka, R.C., Angel, R.W., Thiemann, S., Weitz, C.J., Berger, P.A., 1986. Central error-correcting behavior in schizophrenia and depression. Biol. Psychiatry 21, 263–273.

Manoach, D.S., Lindgren, K.A., Cherkasova, M.V., Goff, D.C., Halpern, E.F., Intriligator, J., et al., 2002. Schizophrenic subjects

show deficient inhibition but intact task switching on saccadic tasks. Biol. Psychiatry 51 (10), 816–826.

Mathalon, D.H., Fedor, M., Faustman, W.O., Gray, M., Askari, N., Ford, J.M., 2002. Response-monitoring dysfunction in schizophrenia: an event-related brain potential study. J. Abnorm. Psychol. 111, 22–41.

McDowell, J.E., Myles-Worsley, M., Coon, H., Byerley, W., Clementz, B.A., 1999. Measuring liability for schizophrenia using optimized antisaccade stimulus parameters. Psychophysiology 36, 138–141.

Mokler, A., Fischer, B., 1999. The recognition and correction of involuntary prosaccades in an antisaccade task. Exp. Brain Res. 125, 511–516.

Nieuwenhuis, S., Ridderinkhof, K.R., Blom, J., Band, G.P., Kok, A., 2001. Error-related brain potentials are differentially related to awareness of response errors: evidence from an antisaccade task. Psychophysiology 38, 752–760.

NIMH, Health N.I.o.M., 1974. Abnormal Involuntary Movement Scale (AIMS), US Public Health Service Publication. US Government Printing Office, Washington, DC.

O'Driscoll, G.A., Lenzenweger, M.F., Holzman, P.S., 1998. Antisaccades and smooth pursuit eye tracking and schizotypy. Arch. Gen. Psychiatry 55, 837–843.

Overall, J.E., Gorham, D.R., 1962. The brief psychiatric rating scale. Psychol. Rep. 10, 799–812.

Rabbitt, P.M.A., 1966. Errors and error correction in choice-response tasks. J. Exp. Psychol. 71, 264–272.

Rabbitt, P.M.A., Vyas, S.M., 1970. An elementary preliminary taxonomy for some errors in laboratory choice RT tasks. Acta Psychol. (Amst) 33, 56–76.

Ridderinkhof, K.R., Nieuwenhuis, S., Bashore, T.R., 2003. Errors are foreshadowed in brain potentials associated with action monitoring in cingulate cortex in humans. Neurosci. Lett. 348, 1–4.

Simpson, G.M., Angus, J.W., 1970. A rating scale for extrapyramidal side effects. Acta Psychiatr. Scand., Suppl. 212, 11–19.

Turken, A.U., Vuilleumier, P., Mathalon, D.H., Swick, D., Ford, J.M., 2003. Are impairments of action monitoring and executive control true dissociative dysfunctions in patients with schizophrenia? Am. J. Psychiatry 160, 1881–1883.

White, K., Ashton, R., 1976. Handedness assessment inventory. Neuropsychologia 14, 261–264.