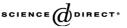


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Saccadic eye movements, schizotypy, and the role of neuroticism

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Abstract

We investigated the relationships of anti- and prosaccades with psychometric schizotypy. One aim was to estimate the role of negative emotionality and general psychopathology (i.e. neuroticism) in this relationship. 115 non-clinical volunteers underwent infrared oculographic assessment of antisaccades and prosaccades. Schizotypy was assessed with the Personality Syndrome Questionnaire (PSQ-80), the Rust Inventory of Schizotypal Cognitions (RISC), and Eysenck Personality Questionnaire-Revised (EPQ-R) Psychoticism. Higher positive schizotypy scores predicted increased antisaccade errors (RISC) and greater prosaccade spatial error (PSQ-80 Unreality). Greater thought disorder (PSQ-80 Activity) predicted shorter prosaccade latencies. EPQ-R Neuroticism was substantially correlated with schizotypy but was not related to saccadic measures and did not account for their relationship with schizotypy. We conclude that saccadic performance patterns in schizotypy are not due to negative emotionality or general psychopathology, but specific to schizophrenia spectrum signs and symptoms. © 2004 Elsevier B.V. All rights reserved.

Keywords: Antisaccade; Prosaccade (reflexive saccade, visually-guided saccade); Oculomotor control; Schizotypal personality traits; Neuroticism; Negative emotionality; Endophenotype; Schizophrenia

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1. Introduction

The antisaccade task requires the initiation of a saccade in the opposite direction to a peripheral target, thereby involving the suppression of a prepotent, or reflexive, response to the target. Performance is primarily measured as the rate of reflexive errors, i.e. glances towards the target, and has been linked to frontal lobe function, in particular the frontal eye fields (FEF), dorsolateral prefrontal cortex (DLPFC), and anterior cingulate, as well as the striatum (Gaymard et al., 1998; Müri et al., 1998; O'Driscoll et al., 1995; Sweeney et al., 1996). People with schizophrenia consistently display increased error rates (Crawford et al., 1995a,b; Curtis et al., 2001; Fukushima et al., 1988).

In contrast to the antisaccade deficit, performance on the prosaccade (or reflexive saccade) task has been argued to be relatively normal in schizophrenia (McDowell and Clementz, 2001). The prosaccade task requires the initiation of a saccade to an abruptly appearing target. Prosaccades share some of the basic saccadic neural circuitry with the antisaccade but do not critically rely on FEF, anterior cingulate, or DLPFC (Gaymard et al., 1998a).

The increased antisaccade error rate has been proposed as a schizophrenia endophenotype (Clementz, 1998; Ettinger and Kumari, 2003). An endophenotype, or intermediate phenotype, is a behavioural or biological marker thought to be a more direct expression of a disease gene than the disease phenotype (Leboyer et al., 1998; Ott, 1991). A useful endophenotype must meet a number of criteria. In addition to its observation in the patient group under study, the marker should also be found in related, or spectrum, populations. In the field of schizophrenia research, the most important spectrum populations are: (1) clinically unaffected first-degree relatives of schizophrenia patients and (2) schizotypal individuals. These groups have been identified on the basis of an increased frequency of schizophrenia-related genotypes (i.e. first-degree relatives) or phenotypes (i.e. schizotypal individuals).

An important methodological advantage of studying these spectrum populations is the relative absence of secondary factors confounding psychological or biological measurement in the patient group, such as antipsychotic treatment, hospitalisation, and variable motivation.

Schizotypy refers to temporally stable signs and symptoms (i.e. traits) that are phenomenologically similar to, but of lesser severity than, the full-blown symptoms of schizophrenia. Although the nature of schizotypy has yet to be fully characterised, it is not thought to be a unitary construct; instead, it is believed to consist of a number of dimensions. The most consistent dimensions that have emerged from factor analytic studies of psychometric schizotypy questionnaires are those of *positive* and *negative* schizotypal features as well as *anxiety-related traits* and *psychoticism* (or nonconformity) (Vollema and van den Bosch, 1995). Positive features include signs and symptoms resembling, albeit in less severe form, the clinical schizophrenic symptoms of delusions and hallucinations (or reality distortion) on the one hand and thought disorder (or disorganisation) on the other hand. Negative features involve a reduced interest in interpersonal interaction, loss of volition, and anhedonia. Psychoticism, or nonconformity (also termed tough-mindedness by Eysenck, 1992) was initially hypothesised to be a predictor of psychotic illness; however, it is now thought to be more indicative of subclinical psychopathy-related traits (Corr, 2000).

There is thought to be a link between schizotypy and schizophrenia not only at a clinical (or phenomenological) level, but also at genetic and neurocognitive levels.

Concerning the hypothesised genetic continuity, individuals with high levels of schizotypy are found with increased frequency amongst the first-degree relatives of schizophrenia patients (Kendler et al., 1995) and have, in turn, an increased prevalence of schizophrenia amongst their first-degree relatives (Kendler and Walsh, 1995). Additionally, levels of schizophrenic symptoms of patients have been shown to be related to levels of schizotypal symptoms of their first-degree relatives (Fanous et al., 2001; Mata et al., 2003). A longitudinal study showed that schizotypal individuals are at increased risk of developing schizophrenia-related pathology (Chapman et al., 1994).

Concerning neurocognitive performance, schizotypal individuals have been shown to display a number of deficits also found in schizophrenia patients (Lenzenweger, 1994).

The hypothesised proximity of schizotypy to schizophrenia provides a powerful platform for assessing the validity of a schizophrenia endophenotype. Indeed, there is evidence linking increased antisaccade error rates to elevated levels of both positive and negative schizotypy in non-clinical samples (Gooding, 1999; Larrison et al., 2000; O'Driscoll et al., 1998; however, see Klein et al., 2000, for a failure to replicate). Increased rates of antisaccade errors were also observed in a subgroup of patients with schizotypal personality disorder (Brenner et al., 2001; Cadenhead et al., 2002) and in first-degree relatives of schizophrenia patients with schizophrenia spectrum symptoms compared to relatives without such symptoms (Thaker et al., 2000).

Concerning the prosaccade task, Gooding (1999) found no association between schizotypy and prosaccade latency. However, Larrison et al. (2000) observed shorter prosaccade latencies in individuals with higher schizotypy levels. Conversely, Iacono and Lykken (1979) observed a relationship between *longer* latency and *higher* psychoticism scores.

One measure that has, to our knowledge, not been examined in relation to psychometric schizotypy is that of spatial accuracy of both antisaccades and prosaccades. On saccade trials one can determine not only the direction and latency of the response but also its spatial accuracy. While prosaccade spatial accuracy is generally thought to be a function of an intact basic saccadic neural circuitry, in particular the cerebellar vermis (Bötzel et al., 1993; Ettinger et al., 2002), spatial accuracy on the antisaccade task has been linked to cognitive processes most likely involving cortical activity. These processes are thought to involve the transformation of visuospatial information into a motor response (Krappmann et al., 1998), possibly relying on fronto-parietal structures (Pierrot-Deseilligny et al., 1995). Given the role of frontal and parietal cortex as well as the cerebellum in the pathophysiology of schizophrenia (Andreasen et al., 1999), saccadic spatial accuracy becomes an important measure to investigate across the schizophrenia spectrum.

Some previous studies have demonstrated reduced antisaccade or prosaccade spatial accuracy in patients with schizophrenia (Crawford et al., 1995a,b; Curtis et al., 2001; Ettinger et al., 2004; Karoumi et al., 1998; McDowell et al., 1999; Schmid-Burgk et al., 1983) and their first-degree relatives (Ettinger et al., 2004; Karoumi et al., 2001; Ross et al., 1998; Schreiber et al., 1997). Consequently, it needs to be clarified whether deficits in saccadic spatial accuracy are observed in individuals with high levels of schizotypy. One aim of the present study is to address this issue.

A second issue that will be addressed here concerns the relationship between schizotypy and negative emotionality. Negative emotionality, or neuroticism, refers to a trait-like, enhanced emotional response to negative stimuli and includes the subclinical signs and symptoms of extensive worrying, psychosomatic complaints, unstable mood, sadness, and anxiety. Clinically, neuroticism may express itself as major depression or anxiety disorder (Claridge and Davis, 2001; Eysenck and Eysenck, 1991).

Interestingly, a number of studies have observed an association between levels of neuroticism and schizotypal traits amongst healthy individuals (Eysenck and Barrett, 1993; Lipp et al., 1994) individuals. Additionally, there is evidence of increased levels of neuroticism in people with a diagnosis of schizophrenia (Berenbaum and Fujita, 1994; Catts et al., 2000).

The reasons for this association are not well understood. One possibility is that increased levels of neuroticism are observed as a consequence of distressing psychosis-like symptoms (Claridge and Broks, 1984). Alternatively, neuroticism may be a non-specific predictor of many different types of psychopathology, not specific to psychosis (Claridge and Davis, 2001). Irrespective of the precise causal relationships, Raine and Lencz (1995) have argued for the need to examine neurocognitive and behavioural deficits for specificity to schizotypy and/or schizophrenia.

This argument has considerable relevance to putative schizophrenia endophenotypes. Previous studies have not conclusively ruled out the existence of antisaccade deficits in people with affective disorder, suggesting perhaps moderate levels of impairments (Curtis et al., 2001; Gooding and Tallent, 2001). A relationship between antisaccade error rate and affective symptoms would indicate that this oculomotor deficit might be an endophenotype not specific to schizophrenia but possibly to a wider class of psychiatric disorders.

Relatedly, Corr et al. (2002) recently observed a relationship between neuroticism and reduced prepulse inhibition (PPI). PPI is an operational measure of sensorimotor gating which has been argued to represent genetic liability to schizophrenia. Another group (Braunstein-Bercovitz, 2000; Braunstein-Bercovitz et al., 2002) demonstrated that the relationship between schizotypy and latent inhibition (LI), the phenomenon of impaired learning of a previously exposed irrelevant stimulus compared to a novel stimulus, can be accounted for by measures of trait anxiety. These studies suggest the need to consider measures of negative trait emotionality in schizotypy research.

Effects of negative emotionality on the association between saccadic impairments and schizotypy have not been explored systematically. O'Driscoll et al. (1998) observed that participants scoring highly on a positive schizotypy scale also had higher scores on measures of *state* anxiety and depression. Additionally, there was a correlation between scores on the depression scale and antisaccade errors. Importantly, neither of these measures fully accounted for the relationship between antisaccade dysfunction and positive schizotypy. O'Driscoll et al.'s (1998) choice of *state* emotionality measures, however, leaves open the question of whether negative *trait* emotionality impacts on the relationship between antisaccade errors and schizotypy.

The aims of this study were, therefore, as follows. First, to replicate the relationship between schizotypy and antisaccade error rate. A selection of schizotypy scales tapping the dimensions of reality distortion, thought disorder, negative symptoms, psychoticism, as well as an overall positive schizotypy scale were employed in order to provide a comprehensive assessment of the various dimensions of this construct. Second, to provide the first investigation, to our knowledge, of the relationship between schizotypy and measures of spatial accuracy of both antisaccades and prosaccades.

Third, to investigate whether any relationships observed between schizotypy and saccadic performance can be accounted for by neuroticism.

2. Method

2.1. Participants

One-hundred and fifteen participants (40 males, 75 females) were recruited from amongst undergraduate and postgraduate students and university staff (age range: 18–44 years; mean = 23.88; S.D. = 5.95). Eighty-four participants were of Caucasian origin (73.0%), 17 participants were of Asian origin (14.8%), nine participants were of Afro-Caribbean origin (7.8%), one was of mixed ethnicity (0.9%), and four participants failed to provide an answer to this item (3.5%). At assessment, the sample had spent an average of 15.17 years in full-time education (S.D. = 2.27). All participants were free of psychosis and neurological disorder by self-report questionnaire. Participants provided written consent after the study details had been fully explained to them. The study had ethical permission (Department of Psychology, Goldsmiths College).

2.2. Eye movement tasks

The tasks were identical to a protocol described previously (Ettinger et al., 2003a,b). A white target of circular shape (approximately 0.3° of visual angle) was presented on a black background using a 17-inch computer monitor. Participants sat in a comfortable chair at a distance of 57 cm from the monitor. Head movements were reduced using a chinrest. Testing took place in a quiet, darkened room. A three-point calibration task ($\pm 12^{\circ}$, 0°) was carried out before each task.

2.2.1. Antisaccade task

A standard (no-gap, non-overlap) antisaccade task was used. A trial began with the target in the central location (0°) for a random duration of 1000–2000 ms. The target then stepped to one of four peripheral target locations ($\pm 6^{\circ}$ and $\pm 12^{\circ}$) where it remained for 1000 ms, before moving back to the centre for the next trial. Each peripheral location was used 15 times, resulting in a total of 60 trials. The sequence of peripheral target presentations was random (sampling without replacement). Four practice trials using each target location once were carried out before the experimental trials; these could be repeated if necessary. Participants were instructed to look at the target while in the central position and to redirect their gaze to the exact mirror image location of the target as soon as it jumped to the periphery. Emphasis was thus placed not only on the inhibition of a reflexive saccade towards the target, but also on the rapid initiation of a spatially accurate saccade in opposite direction. This instruction differs from some protocols (Thaker et al., 2000) simply requiring a saccade in opposite direction but not to an exact location, and thus allows an assessment of spatial accuracy of correct antisaccades.

2.2.2. Prosaccade task

The prosaccade task was administered in a separate block. This task was identical to the antisaccade, except for participants' requirement to follow the target as quickly and accurately as possible. Prosaccade data from five participants was unusable due to recording artefacts.

2.3. Eye movement recording

Eye movements were recorded using infrared oculography (IRIS model 6500; Skalar Medical BV, Delft, The Netherlands). With the IRIS system, horizontal recordings may be made within a range of $\pm 30^{\circ}$. The linearity of the system lies within 3% between $\pm 25^{\circ}$ of horizontal recordings. Further technical specifications of the system can be found in Reulen et al. (1988). Recordings were taken from the left eye. Eye and target position were logged by the eye-tracker. Signals were converted from analogue to digital by a four channel AD converter with 12 bits resolution per channel at 500 Hz sampling frequency. Data were saved onto hard disk for off-line analysis.

2.4. Eye movement analysis

The purpose-written software package EYEMAP Version 2.1 (AMTech GmbH, Weinheim, Germany) was used for analysis of eye movement data. Inter- and intra-rater reliabilities for the analysis of antisaccade and prosaccade variables using EYEMAP in our laboratory are high, ranging from r = 0.91 to r = 0.99.

2.4.1. Antisaccade task

Saccades were automatically detected on the basis of criteria of minimum amplitude (1.5°) , minimum velocity $(30^{\circ}/s)$, and minimum latency (100 ms), and individually categorised by a rater (U.E.). Eye-blink trials and trials including head and/or eye movements before the offset of the fixation point were excluded. Eye-blinks were identified from eye position and velocity charts.

A correct antisaccade trial was counted when the participant performed a primary saccade in the direction opposite to the peripheral target. An antisaccade error was counted when the participant performed a primary saccade towards the peripheral target. A corrective saccade was counted when an error was followed by a saccade in the opposite direction.

The antisaccade error rate reflects the percentage of error trials over the total number of valid trials (excluding, e.g., eye-blink trials). Latency of correct antisaccades was defined as the time (in ms) from target appearance to initiation of correct antisaccades. Spatial accuracy of correct antisaccades was assessed using the measure of spatial error. Spatial error was obtained by calculating, for each saccade, the percentage residual error. Residual error was calculated by subtracting the target amplitude from saccade amplitude and dividing the result by the target amplitude. The absolute value of this term reflects the residual error and was then averaged across all saccades and multiplied by 100. A perfectly accurate saccade thus attracts a spatial error score of 0%; higher scores denote greater spatial error.

Finally, the percentage of corrective saccades (over the total number of error trials) was established as an index of whether participants were able and willing to follow task instruc-

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tions. However, this variable was not analysed for its relationship to schizotypy scales due its extremely skewed distribution (most healthy participants have corrective saccade rates of close to 100%).

2.4.2. Prosaccade task

Prosaccade spatial error (%) and latency (ms) were calculated using above criteria.

2.5. Psychometric assessment

The following questionnaire scales were included in the analyses: the Personality Syndrome Questionnaire (PSQ-80), the Rust Inventory of Schizotypal Cognitions (RISC), and the Psychoticism (P) and Neuroticism (N) scales of the Eysenck Personality Questionnaire—Revised (EPQ-R). Additionally, the Oxford-Liverpool Inventory of Feelings and Experiences (O-LIFE) (Mason et al., 1995) was administered, but was excluded from the current analyses in order to avoid overlap with the remaining scales. O-LIFE data are available on request. Missing data due to administrative errors occurred for EPQ-R (N = 1), RISC (N = 6), and PSQ-80 (N = 7). For all scales, higher scores represent a greater presence of the indicated construct.

2.5.1. Personality Syndrome Questionnaire (PSQ-80)

The Personality Syndrome Questionnaire (PSQ-80) is based on a three-factor model of schizotypy, mirroring hypothesised syndromes of schizophrenia (Gruzelier, 2002). The questionnaire contains 80 items with a two-point response format (yes = 1, no = 0), which yield the Unreality, Withdrawal, and Activity syndromes as well as two validity measures, the Social Desirability and Inattentiveness scales (Croft et al., 2001; Gruzelier and Kaiser, 1996). In addition, two items are presented twice as a measure of response consistency. The *Unreality* syndrome (UR) scale (24 items) is a measure of positive schizotypy, tapping perceptual anomalies and magical ideation. The *Activity* syndrome (AC) scale (18 items) describes increased mental and physical activation, similar to certain aspects of thought disorder observed in schizophrenia and mania. The *Withdrawal* syndrome (WD; 25 items) scale is a measure of negative schizotypy, describing social and emotional withdrawal, constricted affect and social anxiety. The *Social Desirability* (SD; eight items) and *Inattentiveness* (IT; three items) scales provide estimates of the honesty and validity of a participant's responses. The PSQ meets a number of reliability and validity criteria (Croft et al., 2001; Gruzelier, 2002; Gruzelier and Kaiser, 1996).

2.5.2. Rust Inventory of Schizotypal Cognitions (RISC)

The Rust Inventory of Schizotypal Cognitions (RISC) is a 26-item measure of positive schizotypal cognitions, including unusual beliefs and experiences (Rust, 1989). It was constructed to tap the "normal" spectrum by excluding obviously pathological items; consequently, distributions of RISC scores tend to be less skewed than those of other schizotypy questionnaires. The RISC uses a four-point response format (strongly agree = 3, agree = 2, disagree = 1, strongly disagree = 0), thus resulting in a range of possible scores of 0–78. Split-half and test-retest reliabilities were reported to be 0.71 and 0.87, respectively (Rust, 1989).

	Mean	S.D.
Antisaccade error rate (%)	29.23	18.83
Antisaccade latency (ms)	275.48	39.54
Antisaccade spatial error (%)	45.94	18.90
Antisaccade correction rate (%)	96.86	10.59
Prosaccade latency (ms)	173.82	22.84
Prosaccade spatial error (%)	17.76	7.83

Table 1 Descriptive statistics of saccadic variables

2.5.3. Eysenck Personality Questionnaire—Revised (EPQ-R)

The EPQ-R (Eysenck and Eysenck, 1991) is the instrument for the assessment of the Eysenckian personality variables of extraversion (E), neuroticism (N), and psychoticism (P); it also includes a lie (L) scale. Only the P scale was included in the current factor analysis due to its assumed proximity to the schizotypy construct. Additionally, the N scale was used to assess negative trait emotionality. *Psychoticism* (32 items) was proposed as a measure of the liability to the psychosis spectrum (Eysenck and Eysenck, 1976; Eysenck, 1992). However, the spectrum of behaviours described in this scale includes impulsive, antisocial and criminal tendencies, in short psychopathy-related behaviours. Despite a proposed link between psychopathy and psychosis (Corr, 2000), items from the P scale have a somewhat different flavour compared to positive schizotypy scales and correlations tend to be moderate (Chapman et al., 1982; Raine, 1991; Rust, 1989). *Neuroticism* (24 items) is a measure of negative trait emotionality, describing unstable mood, high reactivity to emotional stimuli, anxiety, depression and consequent physical symptoms of sleeplessness, pain sensitivity, and psychosomatic disorders (Claridge and Davis, 2001; Eysenck and Eysenck, 1991). The *Lie* scale (21 items) is a measure of social desirability.

Scale scores reflect summated responses (yes = 1, no = 0). Test-retest and internal reliabilities of all measures are high (>0.76).

2.6. Statistical analysis

Statistical analyses were carried out using the Statistical Package for the Social Sciences (SPSS) Release 10.0.5 (SPSS Inc., Chicago, IL, USA). Prosaccade latency (skewness = 1.09) and spatial error (skewness = 1.12) as well as antisaccade spatial error (skewness = 2.61) were positively skewed. Square root transformation normalised skew for prosaccade latency and spatial error (0.84 and 0.66, respectively) and reduced skew for antisaccade spatial error (1.63). Using transformed instead of untransformed variables did not affect the results in relation to schizotypy. Therefore, and in order to make the results compatible with the descriptive statistics presented in Table 1, untransformed variables were used in all subsequent analyses.

Multivariate analyses of variance (MANOVA) were used comparing males and females on schizotypy questionnaires and saccadic variables. Pearson correlations were run between age and saccadic and psychometric variables.

Multiple regression models were carried out to predict antisaccade and prosaccade variables (DVs) from schizotypy scales (IVs). PSQ-80 Unreality, Activity, and Withdrawal, RISC, and EPQ-R Psychoticism were entered as predictors (IVs) using the Stepwise method

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	Mean	S.D.	Min	Max
PSQ-80 Activity	8.44	3.97	1	16
PSQ-80 Withdrawal	7.86	4.32	0	23
PSQ-80 Unreality	7.66	4.92	0	20
PSQ-80 Social Desirability	1.59	1.30	0	5
PSQ-80 Inattentiveness	0.12	0.35	0	2
RISC	32.20	9.17	10	47
EPQ-R Psychoticism	8.14	3.84	1	20
EPQ-R Neuroticism	11.83	5.92	1	24
EPQ-R Lie scale	6.35	4.05	0	18

Table 2
Descriptive statistics of psychometric questionnaire scales

Note: PSQ-80, Personality Syndrome Questionnaire; RISC, Rust Inventory of Schizotypal Cognitions; EPQ-R, Eysenck Personality Questionnaire—Revised.

(probability to enter set at 0.05). Regression analysis has the advantage over a series of Pearson correlations of reducing the number of analyses carried out, thus decreasing the probability of obtaining false positives (Type I error), and of taking into account inter-correlations between predictor variables.

We then addressed the question of whether individual differences in EPQ-R Neuroticism could account for any significant relationships that might emerge from these analyses. Therefore, further multiple regression models were carried out using saccadic DVs that had been significantly predicted by schizotypy scales. EPQ-R Neuroticism was entered as covariate in the first step (forced entry). Then, in the second step, PSQ-80 Unreality, Activity, and Withdrawal, RISC, and EPQ-R Psychoticism were entered as predictors using the Stepwise method (probability to enter set at 0.05).

Finally, to further evaluate the specificity of any associations obtained between schizotypy scales and saccadic variables, a number of demographic variables (age, sex, years spent in full-time education, ethnicity: Caucasian versus other) and lie and social desirability scales (EPQ-R L, PSQ-80 SD, PSQ-80 IT) as well as the percentage of corrective saccades on the antisaccade task were entered as covariates in separate analyses.

3. Results

Descriptive statistics of oculomotor variables and psychometric questionnaires are given in Tables 1 and 2, respectively. The group means of saccadic variables are comparable to our previous study using identical tasks in a non-clinical university sample (Ettinger et al., 2003a). The group means for schizotypy variables are comparable to previous data from similar age groups (Croft et al., 2001; Eysenck and Eysenck, 1991; Rust, 1989).

3.1. Effects of age and sex

Age was not significantly correlated with any saccadic variables (all P > 0.13). Older individuals tended to have lower scores on PSQ-80 Activity (r = -0.36; P < 0.001), PSQ-80 Unreality (r = -0.26; P = 0.008), and RISC (r = -0.20; P = 0.04).

Females had a slightly higher antisaccade error rate than males (F(1, 110) = 3.67; P = 0.06). Males scored higher on EPQ-R Psychoticism (F(1, 107) = 6.31; P = 0.01) and females scored higher on EPQ-R Neuroticism (F(1, 107) = 3.49; P = 0.06), EPQ-R Lie scale (F(1, 107) = 6.56; P = 0.01), PSQ-80 Unreality syndrome (F(1, 107) = 6.40; P = 0.01) and PSQ-80 Social Desirability (F(1, 107) = 4.80; P = 0.03).

3.2. Relationship between schizotypy scales and saccadic variables

Pearson correlations amongst schizotypy scales, EPQ-R Neuroticism, and saccadic variables are presented in Table 3.

Predicting antisaccade error rate from schizotypy scales yielded RISC as sole predictor with a multiple correlation coefficient of R = 0.27. Adjusted R^2 for the final model was 0.06. The overall model was statistically highly significant, F(1, 106) = 8.02; P = 0.006. Higher antisaccade error rates were associated with higher RISC scores (*Beta* = 0.27).

Predicting prosaccade latency from schizotypy scales yielded PSQ-80 Activity as sole predictor with a multiple correlation coefficient of R = 0.20. Adjusted R^2 for the final model was 0.03. The overall model was statistically significant, F(1, 101) = 4.34; P = 0.04. Shorter prosaccade latencies were associated with higher PSQ-80 Activity scores (*Beta* = -0.20).

Predicting prosaccade spatial error from schizotypy scales yielded PSQ-80 Unreality as sole predictor with a multiple correlation coefficient of R = 0.30. Adjusted R^2 for the final model was 0.06. The overall model was statistically highly significant, F(1, 100) = 9.60; P = 0.003. Greater prosaccade spatial error scores were associated with higher PSQ-80 Unreality scores (*Beta* = 0.30).

No significant predictors were obtained for antisaccade latency and spatial error.

3.3. Effects of neuroticism

Including EPQ-R Neuroticism as covariate in the first step of the regression models did not affect the significant findings reported above: the same schizotypy predictors emerged for antisaccade error rate, prosaccade latency, and prosaccade spatial accuracy, as described above.

3.4. Effects of demographic variables and lie scales

Covarying in separate analyses for age, sex, ethnicity (Caucasian versus other), years spent in full-time education, lie and social desirability scales (EPQ-R L, PSQ-80 SD, PSQ-80 IT), or the percentage of corrective saccades on the antisaccade task did not affect the significant relationships between schizotypy scales and antisaccade error rate as well as prosaccade spatial accuracy. Likewise, including sex, ethnicity, PSQ-80 SD, PSQ-80 IT, or the percentage of corrective saccades as covariate did not affect the results for prosaccade latency. However, including age, full-time education, or EPQ-R L as covariate abolished the significance of the schizotypy predictor of prosaccade latency.

Table 3 Pearson correlations amongst schizotypy questionnaire subscales, neuroticism, and saccadic variables

	PSQ-80 AC	PSQ-80 WD	PSQ-80 UR	RISC	EPQ-R P	EPQ-R N	Anti RefErr	Anti SpatErr	Anti Latency	Pro SpatErr	Pro Latency
PSQ-80 AC	_	0.14	0.55 ^b	0.53 ^b	0.32 ^b	0.39 ^b	0.18	0.12	0.03	0.19	-0.21 ^a
PSQ-80 WD		_	0.08	0.32 ^b	0.13	0.46 ^b	0.19	-0.00	-0.12	0.06	-0.02
PSQ-80 UR			_	0.65 ^b	0.28 ^b	0.44 ^b	0.13	0.12	-0.03	0.30 ^b	-0.10
RISC				_	0.26 ^b	0.48 ^b	0.24 ^a	0.14	-0.03	0.26 ^b	-0.15
EPQ-R P					-	0.04	0.21 ^a	0.11	0.03	0.19 ^a	-0.13
EPQ-R N						-	0.13	-0.03	0.01	0.10	0.00
Anti RefErr							_	0.21 ^a	-0.03	0.16	-0.25^{a}
Anti SpatErr								-	-0.05	0.22 ^a	0.09
Anti Latency									_	0.24 ^a	0.34 ^b
Pro SpatErr										-	0.04
Pro Latency											_

PSQ-80, Personality Syndrome Questionnaire; AC, Activity syndrome; WD, Withdrawal syndrome; UR, Unreality syndrome; SD, Social Desirability; IT, Inattentiveness; RISC, Rust Inventory of Schizotypal Cognitions; EPQ-R, Eysenck Personality Questionnaire-Revised; P, psychoticism; N, neuroticism; L, lie scale. Anti, Antisaccade; RefErr, rate of reflexive errors; SpatErr, spatial error; Pro, prosaccade.

^a Correlation is significant at the level of P < 0.05. ^b Correlation is significant at the level of P < 0.01.

4. Discussion

The findings of this study are as follows. First, antisaccade error rate was predicted by a measure of positive schizotypy. Second, there was no relationship between schizotypy and antisaccade spatial accuracy; however, prosaccade spatial error was predicted by positive schizotypy. Third, prosaccade latency was predicted by a measure of thought disorder. Fourth, these relationships were not accounted for by individual differences in neuroticism.

4.1. Relationship between schizotypy and saccadic eye movements

An increased antisaccade error rate is thought to index liability for schizophrenia, reflecting the action of a disease gene (or several genes) on fronto-striatal function (Clementz, 1998; Ettinger and Kumari, 2003). The present finding of an association between increased error rate and elevated schizotypy scores supports this notion to the extent that variation in schizotypy can be assumed to reflect genetic liability for schizophrenia (Chapman et al., 1994; Fanous et al., 2001; Lenzenweger, 1994). Our finding is compatible with previous studies using measures of positive schizotypy, such as the Perceptual Aberration (Gooding, 1999; O'Driscoll et al., 1998), Magical Ideation (Gooding, 1999), or RISC (Larrison et al., 2000) scales (however, see Klein et al., 2000). The magnitude of the observed relationship, however, is small, suggesting the operation of a number of other sources of variance.

It is important to note in the context of the endophenotype hypothesis that the measures of schizotypy (Croft et al., 2001; Eysenck and Eysenck, 1991; Rust, 1989) and saccadic performance (Ettinger et al., 2003a) employed here have established temporal stability, supporting the trait nature of the behaviours investigated here.

An important methodological point concerns the correction of antisaccade errors. Average correction rate in this sample was very high (96.86%), indicating that participants complied with the task instructions. High error rates in schizotypy high scorers are thus unlikely to be due to failure to comprehend. In addition, the correction rate did not account for the relationships observed between schizotypy and saccadic performance.

The strongest schizotypy predictor of antisaccade errors was the Rust Inventory of Schizotypal Cognitions (RISC). The RISC is an overall measure of positive schizotypy, tapping cognitions and feelings associated with unusual perceptual experiences, magical thinking, delusions, superstition, feelings of unreality, and paranoid ideation. A number of reasons may be invoked to explain this finding. First, it may be that antisaccade error rate is not related to any particular aspects of positive schizotypy and that a global measure of this dimension is most sensitive in detecting the relationship. Second, a feature that positively distinguishes the RISC from other questionnaires used here is its multiple (four-point) response format. A consequence of this is (1) that a greater range of scores is generated, likely exerting a positive influence on correlational analyses, and (2) that participants have greater choice in expressing the true extent of each item, perhaps leading to a more accurate estimation of their true schizotypy scores.

Antisaccade error rate was also correlated with psychoticism, which is thought to reflect psychopathy-related behaviours (Corr, 2000). This finding thus raises the question of whether antisaccade deficits might be observed in populations of clinical psychopaths or personality disordered individuals.

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Negative schizotypy (the Withdrawal syndrome of the PSQ-80) did not significantly predict antisaccade errors, in contrast to a previous study which found both positive and negative schizotypy to be related to antisaccade errors (Gooding, 1999). One explanation for this discrepancy might lie in design differences between the present study, using continuous measures in a non-selected sample, and Gooding's study, using extreme groups pre-selected for schizotypy scores. It is possible that the extreme groups design yields greater statistical power. This suggestion may be consistent with the observation that the Withdrawal syndrome scale was correlated with antisaccade errors at trend level (P = 0.051) in this study (Table 3). It can thus be speculated that a significant relationship may have been detected with a larger sample (and more statistical power). A second reason, however, might be that participants in Gooding's negative schizotypy group also appeared to have elevated positive schizotypy scores relative to low-schizotypy controls, which may have influenced their antisaccade performance.

Another explanation for why positive schizotypy may be a better predictor of antisaccade errors than negative schizotypy might lie in the nature of positive schizotypy. Items from positive schizotypy scales appear more closely related to the pathological features of schizophrenia than those of negative scales, which appear less pathological, relating to introversion, social withdrawal, and hypohedonia. It is, therefore, possible that, in a non-clinical sample, high positive schizotypy scores index greater subclinical abnormality, i.e. proximity to the schizophrenia spectrum, than high negative schizotypy scores.

Measures of antisaccade spatial accuracy and latency were not related to schizotypy. Increased prosaccade spatial error, on the other hand, was predicted by higher positive schizotypy (PSQ-80 Unreality syndrome). This finding might be compatible with evidence of reduced prosaccade accuracy in schizophrenia patients (Curtis et al., 2001; Ettinger et al., 2004; Schmid-Burgk et al., 1983) and their first-degree relatives (Schreiber et al., 1997). It should be noted, however, that these studies used the gain measure of spatial accuracy, our results may still be compatible with these previous findings, as more strongly hypometric saccades (i.e. saccades with lower gain), the pattern observed in previous studies, would also attract greater spatial error scores.

Prosaccade latency was predicted by a positive schizotypal measure of thought disorder (the Activity syndrome scale of the PSQ-80), compatible with a previous observation (Larrison et al., 2000). This finding is of interest, as it represents a divergence of the saccadic performance in schizophrenia and schizotypy. Patients with schizophrenia have mostly normal prosaccade latencies. However, some studies have demonstrated *longer* latencies in this patient group (e.g., Mackert and Flechtner, 1989). The finding of *shorter* latencies in individuals scoring high on the Activity syndrome scale suggests an underlying dimension of impulsivity or hyper-responsiveness. However, this correlation was weak and abolished when covarying for age, education, or the EPQ-R lie scale.

An interesting incidental finding in this context concerns the correlation between prosaccade latency and antisaccade error rate (r = -0.25), suggesting that participants with faster prosaccade latencies tended to commit more antisaccade errors. This finding may be compatible with the suggestion that antisaccade reflexive errors occur during a "horse race" between pro- and antisaccades (Klein et al., 2003). This conceptualisation would predict that the frequency of antisaccade errors is secondary to (or related to) the latency of prosaccades, as demonstrated in this study.

4.2. Effects of neuroticism

The relationships between schizotypy and saccadic performance were then tested for the influence of negative trait emotionality (i.e. neuroticism). Neuroticism failed to predict saccadic performance, and covarying for neuroticism did not significantly reduce the predictive power of schizotypy. It is, therefore, concluded that individual differences in schizotypy, in this sample, significantly predicted saccadic performance over and above the contribution of negative emotionality and general psychopathology.

This finding is noteworthy given the established relationship between neuroticism and schizotypy. Previous studies have shown that these measures are correlated and that patients with schizophrenia display increased neuroticism. Replicating these findings, neuroticism was substantially correlated with positive (RISC, PSQ-80 Unreality, PSQ-80 Activity) and negative (PSQ-80 Withdrawal) schizotypy in our sample (but not with EPQ-R Psychoticism). It is, therefore, suggested that saccadic performance and neuroticism tap different aspects of schizotypy. Schizotypy, which is in itself an indicator of liability for schizophrenia, may thus comprise a component indexed by neurocognitive deficits such as antisaccade errors (e.g., fronto-striatal dysfunction) and a component consisting of emotional instability, perhaps related to limbic function (Eysenck and Eysenck, 1991).

The importance of our finding of an independent relationship between schizotypy and antisaccade error rate lies in the assumed specificity of this deficit to the schizophrenia spectrum. As noted above, neuroticism is a potent indicator of not only emotional instability but of general psychopathology and associated somatic complaints. Therefore, a strong influence of this variable on antisaccade error rate would have undermined the claim that this oculomotor deficit is a specific schizophrenia spectrum endophenotype. This observation is in accord with O'Driscoll et al.'s (1998) finding of a lack of a significant effect of *state* emotionality on the relationship between antisaccade error rate and schizotypy.

The absence of an association between neuroticism and saccadic performance positively distinguishes these measures from other neurocognitive markers studied in schizophrenia spectrum populations. Both PPI and LI appear to be associated with negative emotionality (Braunstein-Bercovitz, 2000; Braunstein-Bercovitz et al., 2002; Corr et al., 2002). A preliminary comparison of these measures thus indicates that the antisaccade error rate might possess greater specificity to schizotypy. While the current finding suggests that antisaccade error rate might tap (genetic) variance independent of affective disturbance, this assumption must be tested further. Given evidence suggestive of an overlap between schizophrenia and affective disorder at not only a clinical but also genetic level (Maier et al., 1999) and the observation of subtle antisaccade deficits in patients with affective disorder (Curtis et al., 2001; Gooding and Tallent, 2001), the current evidence of specificity to schizotypy should be considered preliminary.

The Eysencks' neuroticism scale is a general measure of negative trait emotionality, encompassing the two related but dissociable components of anxiety and depression. Future research should extend the present design by using separate trait measures of anxiety and depression.

Future research might also extend the investigation into the specificity of the current markers by applying them to a sample of first-degree relatives of patients with known antisaccade deficits, such as patients with attention deficit/hyperactivity disorder (ADHD), dyslexia, or bipolar affective disorder. Such a design would allow one to address the question of whether antisaccade deficits observed in these patient groups are due to the influence of the disease process, due to a genetic liability to the disease, or both (see, e.g., Kathmann et al., 2003, for an investigation of smooth pursuit eye movements in first-degree relatives of affective disorder patients).

Finally, while the schizotypy and saccadic measures used here have established reliability, it might be of interest to investigate the temporal stability of their relationships.

4.3. Limitations

The present findings should be viewed within the context of a number of limitations.

First, participants were not screened for a family history of psychosis, which may be associated with saccadic performance scores. Given that it has been suggested that relationships between schizotypy and putative endophenotypes may be different for first-degree relatives of schizophrenia patients and non-relatives (Thaker et al., 2000), future studies should use samples of healthy individuals without a family history of schizophrenia.

Second, in order to retain the maximum number of trials, the present study did not investigate target characteristics such as eccentricity in relation to schizotypy.

Third, the minimum amplitude used for the detection of saccades (1.5°) was somewhat larger than that used by other researchers. It is possible, therefore, that some low-amplitude saccades were missed in our analyses. It remains to be investigated whether the degree of antisaccade impairments in schizotypal individuals (or indeed in other schizophrenia spectrum populations) is associated with the amplitude of error saccades, i.e. whether greater impairments are detected when error saccades of smaller amplitudes are included.

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