Smooth-Pursuit Eye Movement Dysfunction and Liability for Schizophrenia: Implications for Genetic Modeling

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Forty-one nonpsychiatric subjects, 38 probands with schizophrenia, and 99 of their relatives were studied. Oculomotor functioning was bimodally distributed for probands and relatives. Oculomotor dysfunction was not present in all families with a schizophrenic proband. In those families in which it was present, there were significant phenotypic correlations between oculomotor functioning and schizophrenia-related characteristics. The patterns of familial resemblance in the families in whom oculomotor dysfunction was present were consistent with nonadditive genetic variance contributing both to oculomotor dysfunction and to the relationship between oculomotor dysfunction and clinical symptoms. These results suggest that schizophrenia may be etiologically heterogeneous and that oculomotor dysfunction may help to identify nonadditive genetic variance for this disorder.

Family, twin, and adoption studies demonstrate that schizophrenia is a genetically influenced disorder (Gottesman, Shields, & Hanson, 1982). Attempts to determine the most likely mode of inheritance for the psychiatric diagnosis of schizophrenia have consistently demonstrated that a generalized single locus model cannot adequately account for the epidemiological relative-risk data (McGue & Gottesman, 1989; Risch, 1990a). Nevertheless, Gottesman and McGue (in press), in an elegant simulation study, have demonstrated that a moderately common single gene (q = .097) of relatively low penetrance (10%) working in concert with a polygenic background could account for the observed risks. Risch (1990a) has also demonstrated that, when combined with polygenes, two or three genes that work epistatically can also account for the same data.

One potentially serious complication for genetic studies, however, may be the fact that a psychiatric definition of affection does not identify all carriers of a genetic predisposition for schizophrenia (Gottesman & Bertelsen, 1989). It appears, then, that a substantial number of false negatives could occur in pedigree analyses when the psychiatric diagnosis of schizophrenia or related disorders is used as the sole means of defining the phenotype. The untoward consequences for linkage studies when only a few such cases are included have recently been demonstrated in a study (Kelsoe et al., 1989) on bipolar affective disorder, in which a linkage finding became nonsignificant when two members of a large pedigree changed from unaffected to affected status on follow-up.

The inability of schizophrenia or related diagnoses to sufficiently identify gene carriers does not necessarily suggest that we simply need a better psychiatric definition. Clearly, the psychiatric diagnosis of schizophrenia is not what is inherited (see Meehl, 1990); rather, some parameter(s) related to the central nervous system that can lead to such a diagnosis is(are) transmitted within family lines. Thus, more fundamentally, the suggestion is that we need a different means for identifying potential gene carriers.

Meehl (1989) has described how schizophrenia’s symptomatic diversity could reasonably lead one to conjecture a ubiquitous quantitative aberration in single cell function that affects the entire central nervous system. This hypothetical aberration may manifest itself as soft neurological and/or psychophysiological signs, either of which may provide alternatives to the use of clinical interview diagnoses alone for defining affected cases and eliminating nongenetic cases. The presence of even a few of the latter cases could substantially reduce the probability of detecting single gene influences on genetic characters.

One psychophysiological variable that may detect Meehl’s (1989) ubiquitous quantitative aberration (called hypokinesia) is smooth-pursuit eye movement (SPEM) dysfunction (for recent reviews of the SPEM literature, see Clementz & Sweeney, 1990; Iacono, 1988). SPEM dysfunction has a low base rate in samples of psychiatrically normal persons and their relatives (Iacono, Moreau, Beiser, Fleming, & Lin, 1992), is temporally stable (Iacono & Lykken, 1981), and is specifically related to patients...
Table 5
Regression of Offspring's Mean Scores on Their Single-Parent Values for the Families in Whom Smooth-Pursuit Eye Movement Dysfunction Was Present

<table>
<thead>
<tr>
<th>Offspring</th>
<th>Parent</th>
<th>Gain</th>
<th>RMS error</th>
<th>Social only</th>
<th>Cognitive only</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RMS error-defined families</td>
<td>0.07</td>
<td>0.00</td>
<td>0.14</td>
<td>0.09</td>
</tr>
<tr>
<td>Gain</td>
<td>RMS error</td>
<td>0.09</td>
<td>0.04</td>
<td>0.07</td>
<td>0.13</td>
</tr>
<tr>
<td>Social only</td>
<td>RMS error</td>
<td>0.20</td>
<td>0.24</td>
<td>0.24</td>
<td>0.25</td>
</tr>
<tr>
<td>Cognitive only</td>
<td>RMS error</td>
<td>0.18</td>
<td>0.22</td>
<td>0.23</td>
<td>0.24</td>
</tr>
</tbody>
</table>

| Gain-defined families | Gain  | 0.10  | 0.01       | 0.07        | 0.05          |
| Social only          | 0.07  | 0.03  | 0.06       | 0.14          |
| Cognitive only       | 0.15  | 0.22  | 0.19       | 0.20          |

Note. For the upper half of the table, 32 pairs of scores from 21 families in whom smooth-pursuit dysfunction was defined by RMS error were used; for the lower half, 30 pairs of scores from 19 families in whom smooth-pursuit dysfunction was defined by oculomotor gain were used. The regressions on the diagonals (in bold) estimate half the additive genetic variance for those traits. Gain = oculomotor gain; RMS error = root mean square error; social only = social-interpersonal characteristics of schizophrenia; and cognitive only = cognitive-perceptual characteristics of schizophrenia.

were significantly greater than the offspring-parent regressions for oculomotor gain alone, z = 1.79, one-tailed p < .05; RMS error alone, z = 1.87, one-tailed p < .05; social-interpersonal features and oculomotor gain, z = 2.45, one-tailed p < .05; social-interpersonal features and RMS error, z = 1.71, one-tailed p < .05; cognitive-perceptual features and oculomotor gain, z = 1.94, one-tailed p < .05; and social-interpersonal features and cognitive-perceptual features, z = 2.97, one-tailed p < .05. In addition, the cross-trait correlations between oculomotor gain and RMS error (ICC = 0.93) suggest that, within families, these two measures were essentially identical measures of oculomotor dysfunction.

Discussion

The present results are consistent with major gene hypotheses about the etiology of oculomotor dysfunction in schizophrenia. Oculomotor functioning was bimodally distributed in the present sample of probands with schizophrenia and their first-degree relatives. This result replicates the finding of Iacono et al. (1992) for RMS error and extends it to oculomotor gain. Documentation of bimodality using three samples from geographically diverse regions of North America suggests that this may be a general characteristic of schizophrenic probands and their relatives. Neither AS frequency nor S/N demonstrated admixture in the proband and relative samples. The distributional characteristics of the AS measure were such that it was not suited to the more sophisticated types of analyses carried out in the present study (although it still may be of some value in the pursuit of specific forms of oculomotor functioning in schizophrenic individuals and their relatives; see Clementz et al., 1990).

The patterns of phenotypic correlations and familial resemblance also suggest that SPEM dysfunction may be an informative variable in a subsample (up to 58% in this study) of families ascertained via a schizophrenic proband. There were significant and substantial phenotypic correlations between both oculomotor gain and social-interpersonal features and RMS error and these features in the total relative samples. Neither AS frequency nor S/N demonstrated significant correlations with the schizotypy measures. When families were divided for heuristic purposes into those in which SPEM dysfunction was present and those in which it was absent, only the former relatives demonstrated significant correlations between SPEM scores and schizophrenia-related features. Oculomotor dysfunction accounted for up to 24% of the social-interpersonal phenotypic variance and up to 56% of the schizophrenia spectrum diagnosis variance in the families in whom SPEM dysfunction was present.

Siblings, but not offspring and parents, share nonadditive genetic variance (one fourth of the dominance variance, on average). Furthermore, both sibling and offspring-parent pairings share the same proportion of additive genetic variance (one half). A pattern of results in which the sibling–sibling correla-

Table 6
Sibling-Sibling Intraclass Correlations for Oculomotor Dysfunction and Schizophrenia-Related Characteristics for Families in Whom Smooth-Pursuit Eye Movement Was Present

<table>
<thead>
<tr>
<th>Variable</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>RMS error-defined families</td>
<td>0.55**</td>
<td>0.45*</td>
<td>0.70***</td>
<td>0.63**</td>
</tr>
<tr>
<td>SPEM measure</td>
<td>1. Gain</td>
<td>0.93***</td>
<td>0.46*</td>
<td>0.95***</td>
</tr>
<tr>
<td>2. RMS error</td>
<td>0.66***</td>
<td>0.56**</td>
<td>0.75***</td>
<td>0.54**</td>
</tr>
<tr>
<td>Schizophrenia characteristic</td>
<td>0.66***</td>
<td>0.56**</td>
<td>0.75***</td>
<td>0.54**</td>
</tr>
<tr>
<td>3. Social only</td>
<td>0.46*</td>
<td>0.70***</td>
<td>0.63**</td>
<td>0.54**</td>
</tr>
<tr>
<td>4. Cognitive only</td>
<td>0.70***</td>
<td>0.63**</td>
<td>0.54**</td>
<td>0.70***</td>
</tr>
</tbody>
</table>

Gain-defined families

| SPEM measure   | 0.66*** | 0.56** | 0.75*** | 0.54** |
| 1. Gain | 0.93*** | 0.46* | 0.95*** |
| 2. RMS error   | 0.66*** | 0.56** | 0.75*** | 0.54** |
| Schizophrenia characteristic | 0.66*** | 0.56** | 0.75*** | 0.54** |
| 3. Social only | 0.46* | 0.70*** | 0.63** | 0.54** |
| 4. Cognitive only | 0.70*** | 0.63** | 0.54** | 0.70*** |

Note. For the upper half of the table, 46 siblings from 22 families in whom smooth-pursuit dysfunction was defined by RMS error were used; for the lower half, 43 siblings from 21 families in whom smooth-pursuit dysfunction was defined by oculomotor gain were used. The correlations on the diagonals (in bold) estimate a lower bound on half the broad-sense heritability and, therefore, must be doubled to estimate heritability (i.e., the proportion of phenotypic variance due to genetic [additive + nonadditive] effects). The off-diagonal coefficients are the cross-trait genetic correlations that estimate the degree to which pairs of traits share genes in common. SPEM = smooth-pursuit eye movement; gain = oculomotor gain; RMS error = root mean square error; social only = social-interpersonal characteristics of schizophrenia; and cognitive only = cognitive-perceptual characteristics of schizophrenia.

* p < .05, ** p < .01, *** p < .001.
tions are substantially higher than the offspring–parent regressions is consistent, therefore, ceteris paribus, with the hypothesis that nonadditive genetic variance effects contribute to the relationship between two variables (Falconer, 1989). In the families in whom SPEM dysfunction was present, this pattern of results emerged for oculomotor gain, RMS error, and the relationships between schizophrenia-related characteristics (especially social–interpersonal features) and both oculomotor gain and RMS error.

**SPEM Dysfunction and the Matthysse-Holzman Hypothesis**

Matthysse et al. (1986) and Holzman et al. (1988) suggested that SPEM dysfunction and the clinical diagnosis of schizophrenia (in combination) can be accounted for by a nearly completely dominant autosomal gene. Given the gene, an individual can manifest SPEM dysfunction, schizophrenia, or both (pleiotropy). As Matthysse et al. and Holzman et al. pointed out, their model was a heuristic that provided only a mathematical fit to their data; alternative models were not tested (see also Matthysse & Holzman, 1989). It is, therefore, unclear at present whether their hypothesis provides the most defensible explanation for even the data on which it was developed.

Holzman et al. (1988) stated that, using dichotomous ratings based on visual inspection of eye-tracking tracings, 8% of the normal populations, “51% to 85% of schizophrenic patients [and] about 45% of [schizophrenic subjects’] clinically non-schizophrenic parents and siblings” (p. 641) had deviant eye tracking. The findings from both the present study and Iacono et al. (1992), in which an empirically derived cutoff score was used, suggest much lower prevalence estimates for all groups. The SPEM dysfunction prevalence ranged between 20% and 37% in the probands, 19% and 22% in the relatives, and 4% and 7% in the normal subjects, depending on whether oculomotor gain or RMS error was used to define dysfunctional pursuit tracking.

The reasons for the difference between the findings of Holzman et al. (1988) and both the present results and those of Iacono et al. (1992) are unclear. There are, however, some factors that could have significant bearing on this issue. First, as Clementz and Sweeney (1990) pointed out, quantitative ratings such as those of Holzman et al. have yielded highly variable rates of SPEM dysfunction even within normal groups across laboratories. Using a qualitative rating may also result in an artificial inflation of “abnormal” cases given a tendency by raters to use extreme scores (see Murphy, 1964). Furthermore, both the present data and those of Iacono et al. demonstrate that SPEM dysfunction is not a manifestly dichotomous measure, but one with great variability that is evident when quantitative measures such as RMS error and oculomotor gain are used to characterize performance.

Second, Matthysse et al. (1986) also stated that “schizophrenics with good tracking tend to have relatives with bad tracking even when those relatives are not schizophrenic” (p. 58, italics in the original). This would be remarkable for a characteristic that ostensibly assesses genetic liability for developing schizophrenia. Although Iacono et al. (1992) identified schizophrenic subjects with deviant pursuit who had relatives with deviant pursuit, they also found that probands with normal pursuit had relatives with oculomotor dysfunction. Those results were extended by the present investigation: 5 probands from families in whom oculomotor dysfunction was present had normal pursuit. There was also, however, a significant correlation among siblings for oculomotor functioning. Hence, it is not the case that there is no relationship between the eye-tracking performance of schizophrenic subjects and their relatives; nor is it the case, as Matthysse et al.’s statement implies, that there is a negative relationship between the eye tracking of probands and that of other members of their families. The present results also suggest that oculomotor dysfunction may be an informative variable for assessing schizophrenia risk in only a subset of the families ascertained via an affected proband. Sizable SPEM-dysfunction-absent families (like we found here) would not be expected to occur, even assuming pleiotropic effects, given the Matthysse-Holzman model's parameter values.

What implications might these findings have for the Matthysse-Holzman results? The higher percentages of oculomotor abnormalities reported by Holzman et al. (1988) and Matthysse et al.’s (1986) finding that oculomotor dysfunction is seemingly not specific to particular schizophrenic families suggest at least one possibility. The present results and those of Iacono et al. (1992) may indicate that the qualitative rating is an overinclusive measure of oculomotor abnormality in schizophrenic subjects and their relatives. (Matthysse-Holzman’s higher abnormality rates and nonspecificity to particular families may have been the result of their subjects’ being spuriously labeled “bad” trackers on the basis of qualitative ratings.) Such a factor could have substantial influence on the outcome of complex segregation analyses (cf. Morton, 1990), like those of Matthysse et al. and Holzman et al. Further research, of course, is needed to address this important issue.

Consistent with Holzman’s (Holzman, Kringlen, Levy, & Haberman, 1980; Holzman et al., 1977; Holzman et al., 1984) findings, however, there were probands in both Iacono et al.’s (1992) study and the present study with normal eye tracking who had relatives with deviant pursuit (using the distribution-based cutoff scores). This suggests at least four possibilities: (a) SPEM dysfunction (or the cutoff score), as currently defined, imperfectly assesses a genetic predisposition for schizophrenia in these families. (b) SPEM dysfunction is one manifestation of a gene with pleiotropic effects. (c) The genetic factor responsible for SPEM dysfunction is neither necessary nor sufficient for developing the clinical phenotype, but when present exerts considerable influence (Meehl, 1977). (d) SPEM dysfunction may be the result of a recessive gene in strong linkage disequilibrium with another gene that exerts considerable influence over the eventual development of schizophrenia.

To address the first possibility, researchers could use an alternative, perhaps more powerful, means of measuring oculomotor functioning. Levin et al. (1988), for instance, have found that using a ramp-tracking task with unpredictable target direction and velocity increased the separation between patients with schizophrenia and normal control subjects from approximately 1.0 to more than 2.0-t units. Such a stimulus presentation technique may help to more accurately detect SPEM abnormalities than measures that rely on predictably repeating waveforms.
It is also possible that SPEM dysfunction is one manifestation of a major gene with pleiotropic effects, as the Matthysse-Holzman model proposes. Because the schizophrenia phenotype might be genetically heterogeneous, researchers might consider using other potential marker variables (see Erlemeier-Kimling, 1987; Freedman et al., 1987) rather than the clinical diagnosis of schizophrenia (Holzman et al., 1988; Matthysse et al., 1986) as alternative manifestations of the hypothetical predisposing gene. Various authors (Gottesman et al., 1982; Meehl, 1989; Ott, 1990; Risch, 1990b) have suggested that biological variables may provide a more useful means of identifying gene carriers and thus may eliminate considerable error variance from genetic studies of schizophrenia (Iacono et al., 1988). Using multiple such variables in family studies (e.g., Grove et al., 1991) may also provide a means of clarifying schizophrenia's conjectured etiological heterogeneity.

Conclusions

SPEM dysfunction appears to be a highly informative indicator of liability for schizophrenia in a substantial proportion of families ascertained through a schizophrenic proband. The finding that SPEM dysfunction was not present in all such families, however, supports the often made conjecture that the clinical diagnosis of schizophrenia is etiologically heterogeneous. Using a clinical diagnosis alone to define the phenotype in genetic studies, therefore, may provide misleading results. The use and further development of multiple biological marker variables may prove important to the future success of genetic studies of this complex disorder.

References


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with schizophrenia and their first-degree relatives (Holzman, Solomon, Levin, & Waternaux, 1984; Iacono et al., 1992; Levy et al., 1983). SPEM dysfunction is also related to syndromal and subsyndromal manifestations of schizophrenia-related characteristics in the first-degree relatives of affected probands (Clementz, Sweeney, Hirt, & Haas, 1990). Furthermore, Iacono, Bassett, and Jones (1988) studied the eye movements of Bassett, McGillivray, Jones, and Pantzer's (1988) trisomy-5 family and discovered that two of the schizophrenic, partially trisomic members had SPEM dysfunction whereas the three non schizophrenic, nontrisomic members did not. This was the first study to suggest an association between SPEM dysfunction and a genetic abnormality conjecturally related to schizophrenia risk.

Thus SPEM dysfunction appears to be a promising means, beyond clinical diagnosis alone, for identifying potential gene carriers. A “simpler” phenotype (like SPEM dysfunction) that may be useful for identifying single gene influences on a more complex phenotype (like schizophrenia) should ideally possess at least two important features. First, the simpler phenotype should have characteristics that suggest that dominance genetic variance significantly contributes to its manifestation. Matthysse, Holzman, and Lange (1986) and Holzman et al. (1988) have recently proposed a pleiotropy model to account for the joint transmission of schizophrenia and SPEM dysfunction in families. The maximum likelihood parameter estimates for their model suggested that a nearly completely dominant gene with essentially no phenocopies can account for their data. Furthermore, Iacono et al. (1992) have demonstrated that ocularmotor functioning is significantly bimodally distributed in such a sample, a finding consistent with, but not dispositive for, a discontinuous (e.g., single gene) cause (cf. Falconer, 1989; Murphy, 1964). The present study replicates this finding in an independent sample and extends it by investigating the pattern of familial correlations in probands with schizophrenia and their first-degree relatives.

Second, the simpler phenotype should account for some substantial proportion of the more complex trait's phenotypic variance, which includes definite cases plus schizophrenia spectrum disorders, such as schizotypal personality. Clementz et al. (1990) have demonstrated that SPEM dysfunction is more frequent in spectrum versus nonspectrum first-degree relatives of schizophrenic probands. The present study extends this finding with an enlarged sample of relatives.

### Method

#### Subjects

The subjects were drawn from two samples collected independently in New York City (Clementz et al., 1990) and Minneapolis (Grove et al., 1991). Proband and relatives were clinically identified and evaluated in highly similar fashion using both the Structured Clinical Interview for DSM-III-R (revised 3rd edition of the Diagnostic and Statistical Manual of Mental Disorders: American Psychiatric Association, 1987) diagnoses (SCID: Spitzer, Williams, & Gibbon, 1987) and the Schedule for Schizotypal Personalities (SSP: Baron, Asna, & Gruen, 1981).

Table 1 provides the demographic characteristics for the subject samples. All subjects were in good physical health and provided informed consent. No subject reported drinking alcohol on the day of testing.

<table>
<thead>
<tr>
<th>Subject Group</th>
<th>n</th>
<th>% Female</th>
<th>M</th>
<th>SD</th>
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<tr>
<td>New York sample</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonpsychiatric controls</td>
<td>23</td>
<td>30.4</td>
<td>37.0</td>
<td>9.9</td>
</tr>
<tr>
<td>Probands</td>
<td>24</td>
<td>41.7</td>
<td>26.8</td>
<td>6.8</td>
</tr>
<tr>
<td>Relatives</td>
<td>53</td>
<td>56.6</td>
<td>44.5</td>
<td>16.0</td>
</tr>
<tr>
<td>Minneapolis sample</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonpsychiatric controls</td>
<td>18</td>
<td>50.0</td>
<td>42.3</td>
<td>13.3</td>
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<tr>
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<td>14</td>
<td>28.6</td>
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<tr>
<td>Relatives</td>
<td>46</td>
<td>50.0</td>
<td>40.7</td>
<td>14.5</td>
</tr>
</tbody>
</table>

More detailed descriptions of the subject samples have been provided by Clementz et al. (1990) and Grove et al. (1991).

**Proband** The probands (n = 38) from both samples were ascertained through consecutive admissions to inpatient units of large university-based teaching hospitals. The New York sample consisted of 24 probands with DSM-III-R schizophrenia, and the Minneapolis sample consisted of 14 probands with DSM-III-R schizophrenia. All probands were hospitalized and receiving neuroleptic medication at the time of the evaluation. Oculomotor recordings were obtained only after the patients were relatively stabilized on medications (at least 10 days after their admission date).

**Relatives** Fifty-three and 46 first-degree biological relatives were contributed by the New York and Minneapolis samples, respectively. The combined participation rate from the available first-degree relatives was approximately 77%. These relatives were all interviewed with the SSP and the SCID. Seventeen of the 99 relatives (17.2%) were afflicted with either schizophrenia (n = 4) or a schizophrenia-related personality disorder (n = 13), a figure that approximates previously published prevalence estimates (Fleming, Kendler, and Gruenberg, 1988) called a “highly screened” control group.

#### Procedure

**New York sample** Oculomotor recordings were obtained in a quiet, darkened room. Eye movements were measured using a Gulf and Western infrared (IR) monitor mounted on modified eyeglass frames. A Gulf and Western chin and head restraint was used to limit head movement during recording. A Princeton HX-12 color monitor located 51 cm from the subject's eyes was used to present stimuli. Eye movement recordings were digitized at 250 Hz using a Tectra Labmaster A-to-D board in an IBM AT computer for disk storage.

Subjects were asked to sit in front of the video monitor and place their head in the chin and head restraint. They were told to keep their eyes on an X as it moved sinusoidally for 12 cycles at 0.4 Hz through ±10° of visual angle while trying not to blink. Although four pursuit tasks were actually presented, only the first was used here to make the results comparable to those of the Minneapolis sample. Further details about recording and measurement have been provided by Clementz et al. (1990).

**Minneapolis sample** Subjects were seated in an acoustically and
electrically isolated room with their heads placed in an occipital head rest. Electrooculographic (EOG) recordings were obtained using 1-cm silver/silver chloride electrodes filled with Redux paste attached with adhesive collars to the outer canthi of both eyes and above and below the right eye (to monitor blink artifact). Patient ground was a Grass gold clip on the right earlobe. Eye movements and target motion were recorded on FM tape and by a Beckman Type R Dynograph, and were conditioned by Type 9806A AC couplers modified to provide a 3-s time constant. FM-recorded data were digitized off-line at a sampling rate of 258 Hz using a Data Translation DT2821 A-to-D converter in an IBM-compatible computer. A dark cross centered in a bright spot projected onto a white screen 50 cm from the subject's eyes served as the stimulus. Subjects were told to relax, refrain from blinking, and keep their heads still while visually tracking a 0.4-Hz sinusoidal target subtending $\approx 10^\circ$ of visual angle. All subjects completed 12 cycles of sinusoidal pursuit. For further details about recording and measurement of eye movements, see Grove et al. (1991).

**Variable Scoring**

**Schizotypy ratings.** It has previously been suggested that "social-interpersonal," as opposed to "cognitive-perceptual," schizophrenia-related characteristics are more closely related to a genetic predisposition for schizophrenia (Grove et al., 1991; Gunderson & Siever, 1985). Furthermore, because it has recently been demonstrated that SPEM may be more closely related to social-interpersonal than to cognitive-perceptual features (Clementz, Sweezy, Hirt, & Haas, in press; Siever et al., 1989), the SSP was subdivided accordingly for the present study.

The SSP consists of 40 items, each of which is rated on a 4-point scale from not at all (1) to severe (4). These subscales are unevenly divided among 10 scales, 5 of which are cognitive-perceptual in nature (Illusions, Ideas of Reference, Depersonalization/Derealization, Magical Thinking, and Delusions/Hallucinations), and 5 of which are social-interpersonal (Suspiciousness/Paranoid Ideation, Inadequate Rapport, Odd Communication, Social Isolation, and Undue Social Anxiety or Hypersensitivity to Real or Imagined Criticism). There are 19 cognitive-perceptual and 21 social-interpersonal subscales. By adding the ratings for the separate subscales, subjects were given total as well as cognitive-perceptual and social-interpersonal SSP scores.

**Eye movement analyses.** All eye movements were scored and analyzed without knowledge of subject status. EOG and IR eye-tracking measurements have been found to be highly correlated (Iacono & Lykken, 1981); nevertheless, to further ensure similarity across samples, we filtered all oculomotor recordings with a low-pass 30-Hz Blackman filter. This technique preserved the actual eye movements from both EOG and IR but reduced the biopotential and other extraneous noise found in the former. Waveforms were then displayed using ASYST (Version 3.1; Asyst Software Technologies, Inc) interactive waveform analysis software. Segments containing blinks were identified by visual inspection and edited by removing the blink segment and substituting an interpolated line approximating as closely as possible the target movement for that segment. Subsequently, four measures of oculomotor function were obtained: ocular movement gain, anticipatory saccadic (AS) frequency, root-mean-square (rms) error, and signal-to-noise (S/N) ratio.

Oculomotor gain, which estimates the degree to which the subject's eye tracking reproduces the target waveform and amplitude, was calculated in the frequency domain using Fourier analysis (Yee et al., 1987).

The calibrated ocular movement and target waveforms were first scaled to 20 points using a linear interpolation program. Both waveforms were then fast Fourier transformed (FFT) using ASYST, and the magnitude component of the complex conjugate was extracted. For each subject, there was a recognizable peak in the magnitude distribution at the fundamental target frequency (0.4 Hz). The extent to which a subject's performance could be described by the target waveform was calculated as a ratio of eye to target waveform magnitudes at 0.4 Hz. Scores close to 1.0 indicated more accurate gain. Gain calculated in similar fashion has been found to closely approximate bioengineering models for smooth-pursuit system functioning (cf. Bahill, Iandolo, & Troost, 1980).

Anticipatory saccades were defined as large-amplitude (greater than 5°) saccadic movements in the direction of target motion (Abel & Ziegler, 1988; Whicker, Abel, & Dell'Ossio, 1985). During the intersaccadic interval there is a significant reduction in pursuit velocity contemporary with the initial saccade. Either the eyes await the target before resuming pursuit or another saccade is generated that accurately refocuses the target. The intersaccadic interval is at least 250 ms.

The root mean square (RMS) error is a measure of the degree to which the subject's eye tracking matches the target waveform (Iacono & Lykken, 1979; as opposed to oculomotor gain, which is a measure of the degree to which the subject's eye movements reproduce the fundamental target frequency). To the extent that eye position lags behind target position, a tracking phase lag is introduced that can inflate the RMS error determination. In order to remove this effect, the target and eye-tracking channels were aligned so as to produce the maximum cross-correlation between the two signals. Shape differences between the time-adjusted performance and target channels were then calculated as the RMS deviation between the two signals for the 12 consecutively tracked cycles. Lower scores indicated more accurate pursuit tracking.

The S/N ratio, an estimate of the amount of target signal relative to the amount of nontarget signal (or noise) in a subject's smooth-pursuit waveform, has been used frequently in studies of pursuit tracking in schizophrenic patients (Holzman et al., 1984; Lindsey, Holzman, Haberman, & Yasillo, 1978). The means by which investigators calculate S/N, however, vary in both the technique used to obtain the signal and noise components of the ratio and the bandwidths used to define signal and noise. For the present study, both the signal and noise components were obtained from the same oculomotor FFT magnitude data used for calculating pursuit gain. The magnitude at the fundamental target frequency (0.4 Hz) was used to define the signal. Noise, following Holzman et al. (1984), was considered to lie in the area under the magnitude curve between 1.2 and 12 Hz. Higher scores indicated more accurate smooth pursuit.

**Results**

**Age Effects**

It has been demonstrated that oculomotor performance significantly worsens with increasing age in normal individuals.

1 Gunderson & Siever (1985) included Suspiciousness, but not Ideas of Reference, within their social-interpersonal symptom lists, although the latter could certainly be seen as part of the same interpersonal style. Clementz et al. (in press), however, found that correlations between SPEM and social-interpersonal and cognitive-perceptual characteristics were not significantly different when the data were analyzed in three different ways: (a) in the manner in which the characteristics are listed in the text, (b) excluding Ideas of Reference entirely, and (c) including Ideas of Reference with the social-interpersonal characteristics.

Researchers who have used this measure have typically calculated In(S/N). We used both S/N and In(S/N) in our data analyses: the results were the same. To present an untransformed distribution for visual inspection, therefore, we present the results for the untransformed S/N score only.
Therefore correlations between the oculomotor variables used in this study and age within the nonpsychiatric comparison group were calculated. None of the correlations were significantly different from zero: For oculomotor gain, \( r(41) = .11 \); for AS frequency, \( r(41) = -.04 \); for RMS error, \( r(41) = .03 \); and for S/N, \( r(41) = .21 \) (all ps > .10). Given that these correlations suggested that, at most, age accounted for only 4% (for S/N) of SPEM dysfunction variance, we used raw scores in subsequent analyses. Results using age-corrected data yielded the same pattern of findings.

Sample Comparisons

The New York and Minnesota samples were compared on demographic variables, oculomotor variables, and ratings of schizophrenia-related characteristics (see Table 2). These analyses were conducted separately for the nonpsychiatric comparison, proband, and relative groups. The nonpsychiatric comparison group did not differ across samples on demographic (age and gender distribution) or oculomotor variable scores. Likewise, although the Minneapolis probands were significantly older than the New York probands, \( t(36) = 2.33, p < .05 \), the proband groups did not differ in terms of gender distribution, oculomotor variable scores, or SSP ratings. The relative groups did not differ on the demographic variables. The Minneapolis relatives, however, demonstrated better oculomotor functioning than the New York relatives on all measures: For oculomotor gain, \( t(97) = 2.22 \); for AS frequency, \( t(97) = 3.37 \); for RMS error, \( t(97) = 2.03 \); and for S/N, \( t(97) = 2.41 \) (all ps < .05). The Minneapolis relatives also had fewer SSP symptoms than the New York relatives, \( t(97) = 2.91, p < .05 \).

Because the nonpsychiatric comparison and proband groups from the two samples did not differ in terms of either SPEM scores or SSP ratings, the differences between the groups of relatives did not seem to be attributable to methodological or measurement differences across studies. Nevertheless, the observed differences might lead one to question pooling of these samples for admixture analysis. The basic results of the admixture analyses were the same when the samples were analyzed either separately or together (except for the proportion of individuals in whom SPEM dysfunction was present, which was, of course, lower among the Minneapolis relatives). This relative-group difference, therefore, was not a confounding factor. Given the smaller standard errors of the parameter estimates obtained when the data were pooled, only the results based on the total relative group are presented.

Phenotypic Correlations

Table 3 provides the within-subject correlations between the different SPEM measures and schizophrenia-related characteristics for the first-degree relatives. Oculomotor gain and RMS error were significantly correlated with social–interpersonal schizophrenia-related features, but were essentially uncorrelated with the cognitive–perceptual features. AS frequency and S/N, however, were not significantly correlated with either set of schizophrenia-related characteristics. These results extend those of Clementz et al. (in press) using a much larger sample size and suggest that oculomotor gain and RMS error are associated with the types of schizophrenia-related characteristics that are hypothesized to be most closely related to a genetic predisposition for schizophrenia (Gunderson & Siever, 1983).

Admixture in the Oculomotor Variable Distributions

Iacono et al. (1992) have demonstrated that RMS error is bimodally distributed in patients with schizophrenia and their first-degree relatives. This finding is consistent with the hypothesis that SPEM dysfunction is the result of a discontinuous (perhaps single gene) cause (see Falconer, 1989; Murphy, 1964) and is potentially of considerable importance. A series of chi-square likelihood-ratio tests of the null hypothesis that SPEM scores are normally distributed in the present sample (including nonpsychiatric subjects, probands, and family members) was calculated using the program SKUMIX (MacLean, Morton, Elston, & Yee, 1976; McGue, Gerrard, Lebowitz, & Rao, 1989). This program enabled us to test for commingling while

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Table 2: Comparison of the Oculomotor Variables and Schizotypy Ratings Across Samples

<table>
<thead>
<tr>
<th>Sample</th>
<th>Gain</th>
<th>AS</th>
<th>RMS</th>
<th>S/N</th>
<th>SSP</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( M )</td>
<td>( SD )</td>
<td>( M )</td>
<td>( SD )</td>
<td>( M )</td>
</tr>
<tr>
<td>Nonpsychiatric controls</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>New York</td>
<td>0.97</td>
<td>0.07</td>
<td>0.63</td>
<td>1.2</td>
<td>152</td>
</tr>
<tr>
<td>Minneapolis</td>
<td>0.96</td>
<td>0.03</td>
<td>0.17</td>
<td>0.4</td>
<td>132</td>
</tr>
<tr>
<td>Proband</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>New York</td>
<td>0.83</td>
<td>0.14</td>
<td>1.50</td>
<td>3.3</td>
<td>224</td>
</tr>
<tr>
<td>Minneapolis</td>
<td>0.87</td>
<td>0.11</td>
<td>2.08</td>
<td>3.7</td>
<td>219</td>
</tr>
<tr>
<td>Relative*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>New York</td>
<td>0.88</td>
<td>0.12</td>
<td>3.74</td>
<td>5.0</td>
<td>206</td>
</tr>
<tr>
<td>Minneapolis</td>
<td>0.92</td>
<td>0.05</td>
<td>0.98</td>
<td>2.6</td>
<td>153</td>
</tr>
</tbody>
</table>

Note. Gain = oculomotor gain, AS = number of anticipatory saccades; RMS = root-mean-square error, S/N = signal-to-noise ratio; SSP = total score on the Schedule for Schizotypal Personalties (Baron, Annis, & Gruen, 1981).

* All \( t \)-test comparisons between the New York and Minneapolis samples were significant (ps < .05).
LIABILITY FOR SCHIZOPHRENIA

Table 3
Phenotypic Correlations Between the Oculomotor Variables and Schizophrenia-Related Characteristics for Family Members (n = 99)

<table>
<thead>
<tr>
<th>Schizotypy measure</th>
<th>Oculomotor variables</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Gain</td>
<td>AS</td>
<td>RMS</td>
<td>S/N</td>
</tr>
<tr>
<td>Social only</td>
<td>-0.42*</td>
<td>0.20</td>
<td>0.34*</td>
<td>-0.24</td>
</tr>
<tr>
<td>Cognitive only</td>
<td>-0.05</td>
<td>0.06</td>
<td>0.00</td>
<td>-0.07</td>
</tr>
</tbody>
</table>

Note: Gain = oculomotor gain, AS = anticipatory saccade frequency, RMS = root-mean-square error, S/N = signal-to-noise ratio. * p < .001 (one-tailed); these are the only significant p values after stagewise Bonferroni correction (Larzelere & Mulaik, 1977).

The model specified (similar to the model of Matthysse et al., 1986) that a completely dominant gene in a two-allele system determined SPEM dysfunction. The dominance parameter was fixed at 0.0 for oculomotor gain and S/N, because they were negatively skewed, and at 1.0 for RMS error, because it was positively skewed, for the one- and two-component models. The AS frequency was too positively skewed, manifesting a markedly J-shaped distribution, to yield a converged solution for any of the groups. The model further specified that there was no assortative mating (h^2 = 0.0 for the one- and two-component models) for this characteristic.

For oculomotor gain, the nonpsychiatric comparison, χ^2(I, N = 41) = 7.3, p < .01, proband, χ^2(I, N = 38) = 13.8, p < .01, and relative, χ^2(I, N = 99) = 68.6, p < .01, distributions were all significantly skewed (see Figure 1). The chi-square tests for one versus two components using power-transformed oculomotor gain scores were significant for both the probands, χ^2(2, N = 38) = 9.3, p < .01, and relatives, χ^2(2, N = 99) = 20.3, p < .01, but not for the nonpsychiatric comparison subjects, χ^2(2, N = 41) = 2.8. The tests for two versus three components for probands and relatives, however, were nonsignificant (both chi-squares were less than 3.4). These results suggest that two distributions best characterized the transformed RMS error scores for both the probands and the relatives. There was a 3.7σ separation between the two-component means for the probands, and a 4.0σ separation between the two-component means for the relatives (by maximum likelihood estimate). Using the point 2 standard deviations below the mean for the nonpsychiatric subjects (0.87; a value that roughly corresponded to the point of rarity on the untransformed oculomotor gain scale for the nonpsychiatric, proband, and relative groups) identified 4.9% of the normals, 36.8% of the probands, and 22.2% of the relatives as having SPEM dysfunction.

For RMS error, the nonpsychiatric comparison, χ^2(I, N = 41) = 21.2, p < .01, proband, χ^2(I, N = 38) = 28.7, p < .01, and relative, χ^2(I, N = 99) = 61.1, p < .01, distributions were all significantly skewed (see Figure 2). The chi-square tests for one versus two components using power-transformed RMS error scores were significant for both the probands, χ^2(2, N = 99) = 10.5, p < .01, and relatives, χ^2(2, N = 99) = 22.3, p < .01, but not for the nonpsychiatric comparison subjects, χ^2(2, N = 41) = 4.1. The tests for two versus three components for the probands and relatives, however, were not significant (both chi-squares were less than 3.4). These results suggested that two distributions best characterized the transformed RMS error scores for both the probands and the relatives. There was a 3.7σ separation between the two-component means for the probands, and a 3.4σ separation between the two-component means for the relatives (by maximum likelihood estimate). Using the point 2 standard deviations above the mean for the nonpsychiatric subjects (0.87; a value that roughly corresponded to the point of rarity on the untransformed RMS error scale for the nonpsychiatric, proband, and relative groups) identified 7.2% of the normals, 21.1% of the probands, and 19.2% of the relatives as having SPEM dysfunction.

For S/N, only the relatives' distribution was significantly skewed, χ^2(1, N = 99) = 11.7, p < .01; chi-squares for the probands and normals were less than 1.8. Only the nonpsychiatric comparison subjects demonstrated evidence for admixture, χ^2(2, N = 41) = 8.8, p < .05; chi-squares for the schizophrenic subjects and for their relatives were less than 5.6 (see Figure 3). Both the schizophrenic proband and relative distributions were best described by one component. Even after an extensive search of the likelihood surface, we were unable to get any of the three-component models to converge for S/N. This probably indicates that the three-component model is incorrect.

Oculomotor gain and RMS error yielded analogous results in the admixture analyses, as well as in the analyses to be presented. Additional relationships between these two measures, however, may be of interest. Table 4 provides the intercorrelation of all the oculomotor variables for the schizophrenic patients and their relatives. In both groups, RMS error and oculomotor gain were highly correlated. Furthermore, both RMS error and oculomotor gain identified significantly more subjects in the schizophrenic families as having SPEM dysfunction than were present in the nonpsychiatric comparison population: For RMS error, χ^2(1, N = 178) = 5.45, p < .05; for oculomotor gain, χ^2(1, N = 178) = 8.60, p < .05.

It was also of interest to determine whether the two methods were identifying largely the same subjects as having and not having SPEM dysfunction. Both methods tended to identify the same subjects (90%) as affected (25 of the total sample) and unaffected (135 of the total sample). Oculomotor gain identified 13 subjects as having oculomotor dysfunction who were not so identified by RMS error, and RMS error identified 5 subjects as having oculomotor dysfunction who were not so identified by oculomotor gain (Cohen's κ = 0.68). Oculomotor gain detected 21 families in which SPEM dysfunction was present; RMS error detected 22 such families. Twenty families were so identified by both methods.

Potential Heterogeneity of Families for Oculomotor Functioning

The cutoff score used to derive the prevalence of SPEM dysfunction in the normals, probands, and family members also provided a means for calculating sensitivity (38 for oculomotor gain and .42 for RMS error) and specificity (0.82 for oculomotor gain and 0.87 for RMS error) for SPEM dysfunction given presence or absence of spectrum diagnoses (schizophrenia or
schizophrenia-related personality disorder). These sensitivity and specificity calculations, however, suggest two troublesome conclusions regarding the use of SPEM dysfunction to define risk in all families of probands with schizophrenia: (a) SPEM dysfunction identified at most only 42% of the spectrum cases, and (b) the high specificity value suggested that SPEM dysfunction did little more than the clinical diagnosis for identifying potential gene carriers. These two results thus appear to create difficulty for inferring that this variable is a reasonable biological indicator for schizophrenia risk.

Classifying individuals as affected or unaffected with SPEM dysfunction on the basis of the empirically derived cutoff score, however, also allowed a means of investigating similarities and differences in oculomotor functioning across families. Iacono et al. (1992) demonstrated that probands with SPEM dysfunction were significantly more likely to have relatives with SPEM dysfunction than were probands without SPEM dysfunction. This finding suggests that SPEM dysfunction may be specific to particular families, rather than being ubiquitously related to schizophrenia risk. Interestingly, in the present sample, six rela-
Figure 2. Distributions of the untransformed root-mean-square (RMS) error scores for the probands and their relatives plotted against the normal sample.

Tively large families in whom both parents and all (or nearly all) siblings were tested did not demonstrate SPEM dysfunction, on the basis of either oculomotor gain or RMS error. In a family of 11, 10 members were tested and 2 were affected with schizophrenia; in a family of 8, 7 were tested and 1 was affected; all members of a family of 6 were tested, and 1 was affected; in one family of 5, all members were tested and 2 were affected; and, finally, in two other families of 5, all members were tested and 1 member in each family was affected.

Using Matthyse et al.'s (1986) gene frequency and penetrance estimates for a hypothetical predisposing gene related to SPEM dysfunction, we computed the likelihood of observing our families under the assumption that all families were segregating for SPEM dysfunction (correcting appropriately for the presence of schizophrenia in the proband). Probands and relatives were classified as affected or unaffected with SPEM dysfunction (on the basis of the oculomotor gain cutoff score; these results would be highly similar using RMS error) and as affected or unaffected with spectrum disorder, as in Matthyse et al.'s model. To decide how unusual our sample likelihood was, we
bootstrapped (Efron, 1982) the distribution to obtain a permutation test. This was done by randomly simulating families of the same sizes, the pattern of untested relatives, and the overall SPEM abnormality rate as in our sample, but otherwise following Matthyse et al.'s Mendelian segregation model. Under this permutation test (with 1,000 bootstrap pseudoreplications), we estimated the probability of observing our families, if the Matthyse et al. familial homogeneity model is correct, to be less than $2.4 \times 10^{-18}$ (by normal approximation).

This result supports the hypothesis that, although SPEM dysfunction is related to risk for schizophrenia, schizophrenia risk is not universally captured by SPEM dysfunction. Families were classified as having SPEM dysfunction present if at least one family member was affected (for oculomotor gain there were 21 such families; for RMS error there were 22 such families); otherwise, families were classified as SPEM dysfunction absent. For the families in which SPEM dysfunction was present, SPEM dysfunction now had higher sensitivity (0.74 for oculomotor gain and 0.76 for RMS error) and lower specificity (0.67 for oculomotor gain and 0.78 for RMS error) for the pres-
Table 4

Inter correlation of the Oculomotor Variables for the
Schizophrenic Probands (n = 38) and Their Relatives (n = 99)

<table>
<thead>
<tr>
<th>Oculomotor variable</th>
<th>Gain</th>
<th>RMS</th>
<th>S/N</th>
<th>AS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gain</td>
<td>-88**</td>
<td>-70**</td>
<td>-51**</td>
<td></td>
</tr>
<tr>
<td>RMS</td>
<td>-78**</td>
<td>-75**</td>
<td>76**</td>
<td></td>
</tr>
<tr>
<td>S/N</td>
<td>55**</td>
<td>-76**</td>
<td>-64**</td>
<td></td>
</tr>
<tr>
<td>AS</td>
<td>-30*</td>
<td>60**</td>
<td>-58**</td>
<td></td>
</tr>
</tbody>
</table>

Note: Correlations for the probands are above the diagonal; correlations for the relatives are below the diagonal. Gain = oculomotor gain, RMS = root mean square error, S/N = signal-to-noise ratio, AS = anticipatory saccade frequency.
*p < .01.  **p < .001.

ence or absence of spectrum cases. Furthermore, the tetra-
choric correlation between SPEM dysfunction and a spectrum
diagnosis was high (0.64 for oculomotor gain and 0.75 for RMS
error) in these families.

The phenotypic correlations with schizophrenia-related
characteristics were also calculated separately for relatives in
whom SPEM dysfunction was present and families in whom it
was absent. Dividing the subjects on the basis of oculomotor
performance, however, restricted the scoring range for those in
whom SPEM dysfunction was absent. Because this could have
affected the comparability of the correlations between families
without SPEM dysfunction and those with SPEM dysfunction,
the oculomotor gain scores were rank-ordered within each
group to eliminate the resulting correlations’ dependence on
ocular gain distributional variances. Oculomotor gain
and RMS error were related to schizophrenia risk when de-
defined by social–interpersonal characteristics, in the families in
which SPEM dysfunction was present: On the basis of social–
interpersonal features, r = -.49 (p < .001) for oculomotor gain
and .42 (p < .001) for RMS error; on the basis of cognitive–per-
ceptual features, r = -.21 (p > .05) for oculomotor gain and .02
(p > .05) for RMS error. Neither measure was related to schizo-
phrenia risk in families in which SPEM was absent: On the
basis of social–interpersonal features, r = -.06 for oculomotor
gain and .05 for RMS error; on the basis of cognitive–perceptual
features, r = .03 for oculomotor gain and -.12 for RMS
error (all ps > .05).

Patterns of Familial Correlations in SPEM-Dysfunction-
Present and -Absent Families

Evaluating patterns of familial resemblance is an important
means of determining the potential genetic contribution of a
trait to risk for a particular illness. In order to estimate patterns
of familial resemblance for oculomotor dysfunction and schizo-
phrenia-related characteristics, the regression of mean off-
spring values on single-parent points and sibling–sibling intra-
class correlations (ICC) were calculated separately for the
families in whom SPEM dysfunction was absent and those in whom
it was present (see Falconer, 1989, pp. 148–161) using oculomo-
tor gain, RMS error, social–interpersonal characteristics, and
cognitive–perceptual characteristics.

For the families who had no SPEM dysfunction, none of the
offspring–parent regressions (βs = 0.06 to 0.43, ps > .05) signifi-
cantly differed from zero. The sibling–sibling intraclass corre-
lations for these families yielded a significant association be-
tween social–interpersonal and cognitive–perceptual features for
the siblings, ICC(17) = 0.50, p < .05. The rest of the corre-
lations did not significantly differ from zero, ICCs = 0.00 to 0.20,
ps > .05.

For the families in whom SPEM dysfunction was present,
none of the offspring–parent regressions significantly differed
from zero. For comparison purposes, these results are pre-
seated for both the families in whom SPEM dysfunction was
defined by oculomotor gain (30 pairs of scores from 19 families)
and those in whom it was defined by RMS error (32 pairs of
scores from 21 families) (see Table 5). These offspring–parent
regressions were highly similar regardless of which measure
was used to define the presence of SPEM dysfunction. This
conclusion is supported by the correlation between the off-
spring–parent regressions calculated using the families in
whom SPEM dysfunction was defined by oculomotor gain and
those calculated using the families in whom SPEM dysfunction
was defined by RMS error. This coefficient, which was .95,
represents the correlation between the pairs of regression co-
eficients found within each cell in Table 5.

The sibling–sibling ICCs for the families in whom SPEM
dysfunction was present demonstrated that siblings with more
deviant oculomotor functioning had siblings with both more
deviant oculomotor functioning and more schizophrenia-
related characteristics. Again, for comparison purposes, these
results are presented using both the families in whom SPEM
dysfunction was defined by oculomotor gain (43 siblings from
21 families) and those in whom it was defined by RMS error (46
siblings from 22 families) (see Table 6). As with the offspring–
parent regressions, the sibling–sibling ICCs were highly similar
regardless of which measure was used to define SPEM
dysfunction. The correlation between the sibling–sibling correlations
calculated using the oculomotor-gain-defined families and
those calculated using the RMS-error-defined families was .98.

Siblings in families in whom SPEM dysfunction was present
were not similar on ratings of either social or cognitive schizot-
opal characteristics. However, as was the case with the families
in whom SPEM dysfunction was absent, there was a significant
cross-trait correlation between social–interpersonal and cogni-
tive–perceptual features. Furthermore, the sibling–sibling ICCs

---

3 These regressions were computed with the parental oculomotor and SSP variables to predict the sibling variables (see Table 5). In the top half of Table 5, the regressions were calculated with the families that had at least one member with oculomotor dysfunction when RMS error was used to identify deviant tracking. In the bottom half of Table 5, the same regressions were calculated with families identified as having SPEM dysfunction because at least one member had a deviant oculomotor gain score. For example, the regression coefficient was .23 when parental cognitive characteristics were used to predict offspring social characteristics using RMS-error-identified families (it was .21 using oculomotor-gain-identified families). Similarly, the regression coefficient was .25 when parental social characteristics were used to predict sibling cognitive characteristics for the RMS-error-identified families (it was .20 using the oculomotor-gain-identified families).