Familial Prevalence and Coaggregation of Schizotypy Indicators: A Multitrait Family Study

William M. Grove and Boyd S. Lebow
Department of Psychiatry
University of Minnesota

Brett A. Clementz, Anna Cerri, Carlota Medus, and William G. Iacono
University of Minnesota

Schizophrenic probands \( n = 17 \), their first-degree relatives \( n = 61 \), and medically and psychologically screened normal control subjects \( n = 18 \) were studied with structured interviews for DSM-III Axis I disorders and schizotypal personality disorder, questionnaire measures of schizotypy, measures of smooth-pursuit eye movement dysfunction, and attention dysfunction. Schizophrenic subjects scored abnormally on essentially all measures. Relatives differed significantly from control subjects on most measures. Correlational analyses indicate that many characteristics tested in these measures run together in families. The data are consistent with the hypothesis that a single vulnerability dimension or typology, presumably in part genetically transmitted, may account for phenotypically distinct abnormalities. These traits, taken together, may have joint usefulness for identifying persons with a predisposition to schizophrenia.

It is now beyond dispute that at least many cases of schizophrenia are in part genetically caused. However, how genes influence the development of this disorder remains obscure. A simple theory that, if correct, would allow eventual physical isolation of a cause is the major gene model. A major gene alone does not account for the family and twin risks for schizophrenia ( McGue, Gottesman, & Rao, 1985 ), but this does not rule out the possibility that a single gene plays a major contributory role in all cases of schizophrenia, nor does it imply that such a gene is not the sole genetic cause in some cases. Identifying such a gene would obviously be a great advance in our knowledge of schizophrenia.

Unfortunately, many obstacles stand in the way of corroborating or refuting the single-gene theory. A major problem is that schizophrenia is not very familial; risks to first-degree relatives range around 10% ± 5%. Offspring of grossly psychotic relatives in the general population are about as likely to be schizophrenic as are the offspring of the schizophrenic twin ( Gottesman & Bertelsen, 1989 ). Therefore, absence of diagnosable psychiatric illness is perfectly consistent with being a carrier of a predisposing gene or genes. If carriers could be identified, the transmissible phenotype could be better defined, and it would be easier to test competing genetic theories.

We think that using several schizophrenia-related traits simultaneously to define a multivariate phenotype may prove quite enlightening. These traits should meet as many as possible of the following criteria: (a) The abnormality is present in schizophrenia; (b) the abnormality is (relatively) specific to schizophrenia (abnormalities seen in other disorders, if any, are quantitatively or qualitatively different); and (c) the abnormality is genetically influenced or, at any rate, familial.

Among the most promising measures for identifying relatives at elevated risk are diagnosed schizophrenia itself ( Gottesman, Shields, & Hanson, 1982 ), smooth-pursuit eye movement ( SPEM ) dysfunction ( see Clementz & Sweeney, 1990 ; Holzman, 1987 ; and Iacono, 1988, for reviews ), questionnaire-assessed schizotypal traits ( Grove, 1982 ), and attention dysfunction as measured by the Continuous Performance Test ( CPT ; Friedman, Cornblatt, Vaughan, & Erlenmeyer-Kimling, 1986 ).

The literature contains few published studies of multiple schizophrenia-related traits in the relatives of schizophrenics. Baron, Gruen, Asnis, and Kane (1983) studied only a single trait, schizotypal personality features, as have other investigators ( reviewed by Kendler, 1988 ). Holzman and colleagues ( Holzman et al., 1977 ; Holzman et al., 1988 ; Holzman et al., 1974 ) have reported on eye-tracking abnormalities in several classes of relatives ( parents, twins and siblings, children, and grandchildren ), whereas other researchers have concentrated on parents or younger children alone ( Kuechenmeister, Linton, Mueller, & White, 1977 ; Mather, 1985 ). Siegel, Waldo, Mizner, Adler, and Freedman (1984) studied both eye tracking and sensory gating ( an auditory evoked-potential measure ) in parents and siblings. Erlenmeyer-Kimling, Golden, and Cornblatt (1989) administered a large cognitive and information processing battery to preadolescent children.

This study was supported by a grant from the Graduate College of the University of Minnesota and by a McKnight-Land Grant Professorship, both given to William M. Grove.

We thank Paul E. Meehl for innumerable enlightening discussions and David T. Lykken for generously allowing us to use his laboratory. Ruth Thomson-Brown, Christine Gedde, Elizabeth Ghiszinski, Molly Ryan, Mary Sutherland, Christopher Yee, and Ronda Way assisted in data collection.

Correspondence concerning this article should be addressed to William M. Grove, who is now at the Department of Psychology, University of Minnesota, N218 Elliott Hall, Minneapolis, Minnesota 55455.
Our study improves on or complements the work of these investigators by the study of (a) multiple classes of relatives (i.e., not just offspring), (b) persons within the schizophrenia risk period (as opposed to young children, so that genes related to risk are more likely to actively influence behavior), and (c) more varied types of abnormalities (rather than psychophysiology, personality, or information processing alone). Of importance is that we do not simply treat these abnormalities as isolated phenomena, but we use quantitative behavior-genetic methods to study their familial interrelations.

Method

Proband

Proband were recruited from inpatient admissions and the outpatient clinic at the Department of Psychiatry, University of Minnesota. Inclusion criteria were: Diagnostic and Statistical Manual of Mental Disorders (3rd ed.; DSM-III; American Psychiatric Association, 1980) diagnosis of schizophrenia, knowledge of the identity of living biological first-degree relatives (i.e., not an adoptee), and being age 18 or older (Minnesota legal consent age). Exclusion criteria were: English not being the primary language of the proband and relatives (e.g., Southeast Asian refugee); a measured IQ of less than 70 or chart diagnosis of mental retardation; current or past psychoactive substance use, the extent or timing of which would make the diagnosis of schizophrenia doubtful (as implied in DSM-III criteria); current or past central nervous system disease (e.g., acquired immunodeficiency syndrome, epilepsy) or head injury with skull fracture or loss of consciousness; and presence of a physical problem that would render study measures difficult or impossible to administer or interpret (e.g., blindness). The study was described verbally and in writing to each subject. Written informed consent was obtained.

Relatives

For each consenting proband, a list of all live-born first-degree relatives (parents, siblings and half-siblings, and offspring) was compiled. With the proband’s permission, a reliable relative was contacted to ensure complete and correct information on relatives’ identities and addresses. Relatives aged 17 years and older were contacted by mail and a telephone follow-up. The study was described, and the relative was invited to participate. For relatives living within approximately a 250-mile radius of the Twin Cities, they were invited to the laboratory so that SPREM and CPT data could be gathered; otherwise, they were invited to the laboratory only if they planned to be in the Twin Cities area within approximately 6 months of the proband’s admission date. Relatives who could not or would not come to the laboratory were asked to complete questionnaires and telephone interviews.

Control Subjects

Data from these subjects enabled us to gauge whether the probands and their relatives indeed scored abnormally on study measures. Therefore, we required a sample from a psychiatrically normal population. We studied patients from the Family Practice Clinic of our hospital because it serves much the same community as our Department of Psychiatry. We wished to examine sex and age effects on our measures, and so we stratified the control sample on these factors. The control group comprised 2 men and 2 women in each of the age ranges 18–29, 30–39, 40–49, 50–59, and 60 or over, selected by chart review, who met no exclusion criterion applicable to probands (e.g., epilepsy, diabetes). Control subjects were seen in the clinic typically for acute illnesses (e.g., respiratory infections) or minor injuries. Potential control subjects were also screened for the absence of charted personal or family history of psychiatric disorder. (Psychiatric and family questions were asked on an intake form that patients filled out, and doctors’ notes were also checked.) Subjects who fulfilled inclusion criteria were contacted by telephone and invited to participate; written informed consent was obtained. They received the same assessments as did the probands’ relatives. After testing, they were screened again for a history of psychiatric problems in the same way that the probands’ relatives were screened before the structured interview, as a double check. Subjects with Shipley Institute of Living Scale Conceptual Quotients below 70 were not included in the study (see Results section).

Assessment of Psychopathology

DSM-III (American Psychiatric Association, 1980) Axis I diagnoses were assessed (by William M. Grove or his assistant) in a structured interview (to be described). All probands were assessed with the Axis I structured interview, as were some but not all relatives. Relatives were first screened with structured questions from the Schedule for Affective Disorders and Schizophrenia—Lifetime Version (Endicott & Spitzer, 1978), which concerned major depressive and manic or hypomanic syndromes, potentially psychotic symptoms (hallucinations, delusions, ideas of reference or persecution), alcohol or drug abuse, and panic attacks. Any subjects who gave a history of any of these symptoms (except for less than 1 week’s duration or for two or fewer depressive symptoms) then received one of two structured interviews. Early in the study, subjects were evaluated with the Diagnostic Interview Schedule (Robins, Helzer, Croughan, & Ratcliff, 1981), chosen because when the study began, it was the only instrument through which DSM-III diagnoses could be obtained. However, it did not systematically allow for clinical combination of probe questions and medical record information on ostensibly psychotic features in interviewees. When a usable version became available, we began using the Structured Clinical Interview for DSM-III-R (Spitzer, Williams, Gibbon, & First, 1987), which does incorporate all available clinical data into ratings. We changed the revised DSM-III-R (American Psychiatric Association, 1987) diagnoses to make them conform to the DSM-III DSM-III Schizotypal Personality Disorder was assessed with the Schedule for Schizotypal Personalities (SSP; Baron, Asnis, & Gruen, 1981).

Questionnaires

Two scales were used developed by the Chapmans and colleagues to assess traits putatively related to Meehl’s concept of schizotypy, namely Physical Anhedonia (Chapman, Chapman, & Raullin, 1976) and Perceptual Aberration (Chapman, Chapman, & Raullin, 1978). The former scale contains items such as “The beauty of sunsets is greatly overrated”; the latter contains items such as “My hands and feet have never seemed far away” (keyed false).

The third scale comprised seven Minnesota Multiphasic Personality Inventory (MMPI) items (none obviously schizophrenia-related) reported by Golden and Meehl (1979) to fit a mathematical model for the latent taxonomic entity, schizotypy; these items were included because when this study was conceived, results of two investigations had supported their use (Asarnow, Nuechterlein, & Marder, 1983; Golden & Meehl, 1979) and results of one study had not (Miler, Streiner, & Kallace, 1982). Subsequently, two investigations have questioned its utility in identifying schizotypics and subjects who may be at risk for schizophrenia. Nichols and Jones (1985) reported that these items did not discriminate between patients with schizophrenia, affective disorders, and nonpsychotic illnesses. Van den Bosch, Rozendaal, and Mol (1987)
found no significant difference in the number of items endorsed by psychiatric patients who were good and poor eye trackers.

**Smooth-Pursuit Eye Movements**

The subject was seated in an electrically and acoustically isolated room in a chair, and his or her head was restrained in an occipital head rest. Sinusoidal stimuli at 0.4 Hz were produced by a waveform generator, which drove a galvanometer connected to an oscillating mirror. A spot of white light with a centered dark cross emitted from a Kodak slide projector was reflected onto a white screen 127 cm from the subject's eyes and subtended ±10° of visual angle. The screen was curved so that spot size remained constant over its traverse. Thirteen-millimeter Ag/AgCl electrodes filled with redox paste were attached with adhesive collars to the outer canthi of both eyes and above and below the right eye. These served to record horizontal eye movements and blinks, respectively. The patient was electrically grounded by a Grass gold clip on the right ear lobe. Tape-recorded directions instructed participants to relax their facial muscles, refrain from blinking, keep their head still and follow the target only with their eyes. The electro-oculographic (EOG) method does include some non-eye-movement biopotential but produces results very highly correlated with the infrared method (Iacono & Lykken, 1981).

Eye movements and target motion were recorded on a Beckman Type R Dynograph. The horizontal EOG and target waveform were conditioned by Type 9806A AC couplers modified to provide a 3-s time constant, and blinks were recorded through an AC coupler with a time constant of 0.1 s. All data were recorded on an FM recorder. Recordings were digitized offline (sampling rate of 128 Hz) by a custom program (Datascope, Paradigm Systems, Inc.) by means of a Data Translation DT2821 analog-to-digital converter card in an IBM AT-compatible computer.

SPEM performance was quantified from the digitized records in three ways: root mean square (RMS) error, oculomotor gain, and anticipatory saccades. RMS error is a global measure of eye-tracking proficiency and is essentially a measure of errors of eye position. Oculomotor gain is an approximate measure of pursuit gain, which is the matching of eye movement velocity to target velocity. Schizophrenics (Clementz & Sweeney, 1990) and their relatives (Clementz, Sweeney, Hirt, & Haas, 1990) have low pursuit gain. Anticipatory saccades are thought to be attempts by the pursuit system to compensate for low gain and have been reported to be more frequent specifically in schizophrenics' relatives (Clementz et al., 1990). RMS error was calculated by a custom program (SPEM, Paradigm Systems, Inc.) that takes into account phase lag and computes overall differences of eye movements (as described by Iacono & Lykken, 1981) after adjusting recorded eye movement amplitude to best match recorded target amplitude. This measure provides an estimate of how accurately overall a subject's eye tracking matches the target waveform.

Oculomotor gain, which is an estimate of the degree to which the subject's eye tracking reproduces the target waveform velocity, was calculated in the frequency domain through Fourier analysis (Yee et al., 1987). The data were inspected (without knowledge of subject status), and the 12 most artifact-free consecutive cycles were selected. The data were then filtered with a 30-Hz low-pass Blackman filter. The calibrated oculomotor and target waveforms were scaled to 2^12 data points through a linear interpolation program. Both waveforms were then fast Fourier transformed by means of ASYST interactive waveform analysis software (ASYST Software Technologies, Inc., Version 3.0), 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 target frequency was calculated as a ratio of eye to target waveform magnitudes at 0.4 Hz. Scores close to 1.0 indicated more accurate gain. This procedure also allowed ready calculation of pursuit gain from sinusoidal tracking data, so that RMS error and gain were computed from the same eye-movement task.

Anticipatory saccades were defined as large-amplitude (greater than 5°) saccadic movements in the direction of target motion (Abe1 & Ziegler, 1988; Whicker, Abe1, & Dell'Osso, 1985). During the intersaccadic interval there is a significant reduction in pursuit velocity that is contemporaneous with the initial saccade. Either the eyes await the target before resuming pursuit or another saccade that accurately refoveates the target is generated. The intersaccadic interval is of at least 250 ms (Clementz et al., 1990). Anticipatory saccades were counted after being blindly identified in 30-Hz Blackman-filtered records. In order to assess reliability of anticipatory saccades, two scorers (Boyd S. Lebow and Brett A. Clementz) independently counted these events for 20 records (intraclass R = .82).

**Continuous Performance Test**

Our CPT required subjects to detect the numeral 8 flashed on a computer screen, mixed in series with other numerals 0 to 9. Stimuli were degraded in visual clarity to make the task more difficult because this increases the test's discriminating power (Nuechterlein & Dawson, 1984). Experimental procedure was as follows: In a quiet, darkened room, the subject was seated in a comfortable chair 18 in. from a Taxan Multivision 770 Plus cathode ray tube (CRT) computer monitor (which has rapidly decaying phosphors to avoid image persistence) held at eye level, connected to an IBM XT microcomputer with a Hercules Corp. monochrome graphics card. Instructions and stimuli were generated and displayed by a computer program written by William M. Grove (available on request). Stimuli were presented in the center of the CRT in a matrix 3.5 x 2.25 cm (64 x 64 pixels) for 40 ms, with a 960-ms interstimulus interval. The probability that an "8" would be presented on a trial was .25. There were two practice blocks of 40 trials each, followed by four scored blocks of 360 trials each. In order to degrade stimuli, pixels were pseudorandomly moved within the matrix (to maintain constant screen luminosity within the matrix for a given stimulus). Pixel movement occurred with a different constant probability on each block: 0 or .60 (in that order; the latter was reported by normal subjects as being subjectively nearly undegraded) for the two practice blocks, followed by .70, .80, .75, and .85 (in that order) for the four scored blocks. The subject pressed a key on the keyboard to indicate the presence of an 8. The program computed d', a signal-detection theory measure of demonstrated abnormality in schizophrenics and their offspring (Friedman et al., 1986; Nuechterlein & Dawson, 1984). It is a measure of the degree to which subjects discriminate between criterial and noncriterial trials, independently of readiness to press the response key. High d' scores signify good performance. Pilot data from a number of schizophrenics and a normal control sample (not the control subjects in this study) were used to refine the task; this led us to analyze only data from the 75% degradation condition in this study.

**Data Reduction**

From study data we derived the following measures: diagnosis of DSM-III schizotypal personality disorder (yes/no); total schizotypal personality disorder rating score on the SSP (sum of all individual item ratings); SSP rating totals broken down into social-interpersonal and cognitive-perceptual content domains (in accordance with Siever & Gunderson's, 1983, procedures); total scores on each of the three questionnaires; SPEM RMS error; oculomotor gain; anticipatory saccade frequency; and CPT d'. We emphasize quantitative measures such as the SSP score over diagnostic rubrics because dichotomization entails the loss of information about genetic transmission (MacLean, Morton,
Results

Consent and Completion

Probands. Twenty-two patients were asked to participate; 18 agreed, but 1 withdrew, and thus the net consent rate was 77%. Of the 17 probands, 4 (24%) were female. Age range was 22–53 years; the median was 29 (M = 31.24), and interquartile range Q = 24–35 (SD = 9.18). Age of onset ranged from 12 to 40 years (Mdn = 23 and Q = 18.5–27). No proband had ever been fully in remission since onset, and so durations of the current episode were the same as total durations of illness: Mdn = 7 years and Q = 3–10 years. DSM-III subtypes were distributed as follows: 6 paranoid, 5 disorganized, and 6 undifferentiated. SPEM data were obtained for 14 probands. Because the CPT task was not available when the study began, CPT data were obtained for only 12 probands.

Relatives. In all, 102 live-born first-degree relatives were identified. Of these, 9 were deceased, 1 was under age 18, 1 could not be located, 3 lived outside the 250-mile radius, 25 were contacted but refused to participate, 2 agreed to participate but repeatedly failed to keep appointments, and 61 actually participated, of whom 50 came to the laboratory; 46 had SPEM data. Fifty-four percent of the relatives were female, and their median age was 35 (Q = 29–39, range, 18–69). All parents tested were past the period of risk for schizophrenia (which we take to be ages 15–45). Siblings were on average 53% through the risk period (range, 10%–100%, Q = 43%–70%). No children were tested (there was only one nonadult relative, a preschool child). Data on the CPT were obtained for 30 relatives.

Control subjects. Of 22 control subjects recruited, 4 were excluded from the study. One subject was excluded because of a history of skull fracture. Two elderly subjects were excluded because they had Shipley Conceptual Quotients below 70. One subject admitted on the posttest screen to a history of substance abuse. This left 9 men and 9 women, two of each in each age range except one of each in the over-59 group. Data on the CPT were obtained for all control subjects.

Familial Psychopathology

Among relatives personally seen, 1 was schizophrenic and 2 others had psychoses (one each with mood-congruent and mood-incongruent psychotic depressive episodes). An ostensibly schizophrenic sibling could not be induced to participate, and an ostensibly chronically psychotic parent could not be located. For a definite diagnosis of schizotypal personality disorder, we required that each symptom count have at least one rating in that SSPI symptom group of 3 or more (Perry, O'Connell, & Drake, 1984). Our rate of 10% is fairly similar to that of Baron et al. (1983), who reported definite schizotypal personality in 16% of the relatives of schizophrenics.

Study Measures

Probands and their relatives are compared with control subjects in Tables 1 and 2. One-tailed t tests were computed be-

<table>
<thead>
<tr>
<th>Measure</th>
<th>Probands (n = 17)</th>
<th>Control subjects (n = 18)</th>
<th>Estimated effect size</th>
<th>t</th>
<th>df</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSP</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>75.87</td>
<td>13.84</td>
<td>43.94</td>
<td>3.86</td>
<td>8.27</td>
<td>8.66</td>
</tr>
<tr>
<td>Social-interpersonal</td>
<td>18.47</td>
<td>3.91</td>
<td>9.50</td>
<td>1.04</td>
<td>8.60</td>
<td>8.64</td>
</tr>
<tr>
<td>Cognitive-perceptual</td>
<td>57.40</td>
<td>11.85</td>
<td>34.44</td>
<td>3.28</td>
<td>7.00</td>
<td>7.28</td>
</tr>
<tr>
<td>Physical Anhedonia</td>
<td>14.38</td>
<td>5.74</td>
<td>9.61</td>
<td>3.60</td>
<td>1.32</td>
<td>2.86</td>
</tr>
<tr>
<td>Perceptual Aberration</td>
<td>7.44</td>
<td>7.51</td>
<td>1.89</td>
<td>1.81</td>
<td>3.07</td>
<td>2.88</td>
</tr>
<tr>
<td>MMPI schizotypy items</td>
<td>2.88</td>
<td>1.09</td>
<td>2.44</td>
<td>0.86</td>
<td>0.51</td>
<td>1.29</td>
</tr>
<tr>
<td>SPEM</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RMS Error × 100</td>
<td>218.86</td>
<td>165.47</td>
<td>132.28</td>
<td>58.78</td>
<td>1.47</td>
<td>1.87</td>
</tr>
<tr>
<td>Gain</td>
<td>0.87</td>
<td>0.11</td>
<td>0.95</td>
<td>0.03</td>
<td>-2.71</td>
<td>-2.71</td>
</tr>
<tr>
<td>Anticipatory saccades</td>
<td>1.50</td>
<td>3.28</td>
<td>0.44</td>
<td>1.20</td>
<td>0.88</td>
<td>1.15</td>
</tr>
<tr>
<td>CPT d</td>
<td>1.22</td>
<td>0.59</td>
<td>2.43</td>
<td>0.88</td>
<td>-1.37</td>
<td>-4.17</td>
</tr>
</tbody>
</table>

Note. SSP = Schedule for Schizotypal Personalities; MMPI = Minnesota Multiphasic Personality Inventory; SPEM = smooth-pursuit eye movement; RMS = root mean square; and CPT = Continuous Performance Test.
Table 2
Comparison of Probands' Relatives and Control Subjects

<table>
<thead>
<tr>
<th>Measure</th>
<th>Probands</th>
<th>Control subjects</th>
<th>Estimated effect size</th>
<th>t</th>
<th>df</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( n = 61 )</td>
<td>( n = 18 )</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SSP</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>47.32</td>
<td>43.94</td>
<td>0.88</td>
<td>2.71</td>
<td>49</td>
<td>.0047</td>
</tr>
<tr>
<td>Social-interpersonal</td>
<td>11.22</td>
<td>9.50</td>
<td>1.65</td>
<td>4.38</td>
<td>65</td>
<td>.0001</td>
</tr>
<tr>
<td>Cognitive-perceptual</td>
<td>36.10</td>
<td>34.44</td>
<td>0.51</td>
<td>1.63</td>
<td>44</td>
<td>.0556</td>
</tr>
<tr>
<td>Physical Anhedonia</td>
<td>13.00</td>
<td>9.61</td>
<td>0.94</td>
<td>2.79</td>
<td>72</td>
<td>.0034</td>
</tr>
<tr>
<td>Perceptual Aberration</td>
<td>2.25</td>
<td>1.89</td>
<td>0.20</td>
<td>0.59</td>
<td>53</td>
<td>.2792</td>
</tr>
<tr>
<td>MMPI schizotypy items</td>
<td>2.41</td>
<td>2.44</td>
<td>-0.03</td>
<td>-0.14</td>
<td>72</td>
<td>1.0000</td>
</tr>
<tr>
<td>SPEM</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RMS error \times 100</td>
<td>153.00</td>
<td>132.28</td>
<td>0.35</td>
<td>1.09</td>
<td>46</td>
<td>.1412</td>
</tr>
<tr>
<td>Gain</td>
<td>0.93</td>
<td>0.95</td>
<td>-0.87</td>
<td>-2.63</td>
<td>62</td>
<td>.0054</td>
</tr>
<tr>
<td>Anticipatory saccades</td>
<td>0.98</td>
<td>0.44</td>
<td>0.45</td>
<td>1.12</td>
<td>60</td>
<td>.1331</td>
</tr>
<tr>
<td>CPT ( d )</td>
<td>1.81</td>
<td>2.43</td>
<td>-0.70</td>
<td>-2.14</td>
<td>44</td>
<td>.0991</td>
</tr>
</tbody>
</table>

Note: SSP = Schedule for Schizotypal Personalities; MMPI = Minnesota Multiphasic Personality Inventory; SPEM = smooth-pursuit eye movement; RMS = root mean square; and CPT = Continuous Performance Test.

cause the literature offers clear and relatively strong predictions of the direction of differences from controls. All measures except the MMPI items and anticipatory saccades discriminated probands from control subjects. The column headed “Estimated ES” is Glass’s (Smith, Glass, & Miller, 1980) effect size measure,

\[
(M_{\text{patient}} - M_{\text{control}}) / SD_{\text{control}}
\]

to give an idea of discriminating power independent of sample size.

In the relatives, many measures discriminated as predicted. The Perceptual Aberration scale, the MMPI items, the cognitive–perceptual domain of the SSP, and two of the SPEM measures did not, although differences were (except for the MMPI items) all in the predicted direction. Although the cognitive–perceptual section of the SSP did not discriminate as predicted (\( p = .0556 \)), it did have an appreciable effect size, and a Type II error may have resulted from small sample size.

Before computing sibling correlations, we eliminated some measures. Anticipatory saccades occurred so infrequently that we dropped them from correlational analyses. Because the MMPI items discriminated neither probands nor relatives from control subjects, they also were dropped. Perceptual Aberration showed a floor effect: 39% of relatives scored 0 on it. However, because it discriminated probands from control subjects and because enough relatives had appreciable scores, we retained this measure. In Table 3 we show the phenotypic correlations between measures among all relatives. Almost all correlations were positive, even though with our small sample not all were significant.

Shown in Table 4 are estimated heritabilities (twice the sibling intraclass correlation) with standard errors. Estimated genetic correlations (±SE) are also given in the table. Again, almost all familial correlations are positive, and the social–interpersonal aspect of schizotypy again appears most central. We touch on the figures for gain, which are anomalous, in the next section.

Table 3
Phenotypic Correlations of Schizotypy Indicators Among Relatives

<table>
<thead>
<tr>
<th>Measure</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSP</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Cognitive–perceptual</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Social–interpersonal</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Physical Anhedonia</td>
<td>-.14</td>
<td>-.14</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Perceptual Aberration</td>
<td>.30*</td>
<td>.33*</td>
<td>.21</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SPEM</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. RMS error \times 100</td>
<td>.03</td>
<td>.45*</td>
<td>.22</td>
<td>.46*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. Gain</td>
<td>.18</td>
<td>.23</td>
<td>.31</td>
<td>.30*</td>
<td>.44*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. CPT ( d )</td>
<td>-.05</td>
<td>.25</td>
<td>.39*</td>
<td>.49*</td>
<td>.29</td>
<td>.31</td>
<td></td>
</tr>
</tbody>
</table>

Note: The sample size for each correlation is given in parentheses; the significance for correlations of a given size varies because of the different sample sizes. Signs of SPEM gain and CPT \( d \) are reversed so that high scores are abnormal. SSP = Schedule for Schizotypal Personalities; SPEM = smooth-pursuit eye movement; RMS = root mean square; and CPT = Continuous Performance Test.

\( * p < .05 \).
Table 4
Estimated Heritabilities and Genetic Correlations of Schizotypy Indicators in Siblings of Schizophrenics

<table>
<thead>
<tr>
<th>Measure</th>
<th>Heritability</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$h^2$</td>
<td>SE</td>
<td>$r$</td>
<td>SE</td>
<td>$r$</td>
<td>SE</td>
<td>$r$</td>
</tr>
<tr>
<td>SSP</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Cognitive-perceptual</td>
<td>.32</td>
<td>.12</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Social-interpersonal</td>
<td>.46</td>
<td>.11</td>
<td>.68</td>
<td>.32</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Physical Anhedonia</td>
<td>.79</td>
<td>.03</td>
<td>.03</td>
<td>.18</td>
<td>.53</td>
<td>.14</td>
<td></td>
</tr>
<tr>
<td>4. Perceptual Aberration</td>
<td>.60</td>
<td>.08</td>
<td>.80</td>
<td>.26</td>
<td>.84</td>
<td>.21</td>
<td>.35</td>
</tr>
<tr>
<td>SPEM</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. RMS error × 100</td>
<td>.39</td>
<td>.12</td>
<td>.11</td>
<td>.35</td>
<td>.44</td>
<td>.28</td>
<td>.61</td>
</tr>
<tr>
<td>6. Gain</td>
<td>.01</td>
<td>.09</td>
<td>.31</td>
<td>1.00</td>
<td>.81</td>
<td>1.00</td>
<td>.75</td>
</tr>
<tr>
<td>7. CPT $d^c$</td>
<td>.79</td>
<td>.03</td>
<td>.33</td>
<td>.18</td>
<td>.66</td>
<td>.14</td>
<td>.49</td>
</tr>
</tbody>
</table>

Note: SSP = Schedule for Schizotypal Personalities; SPEM = smooth-pursuit eye movement; RMS = root mean square; and CPT = Continuous Performance Test.

Discussion

We have extended reports by others that personality features, SPEM performance, and vigilance performance distinguish the relatives of schizophrenics from control subjects. Our results go beyond previous reports by showing essentially that all of these abnormalities run together in families. The implication, if these preliminary results are replicable, is that a single core dimension or typology contributes to variation in these measures. The results of group comparisons establish that this trait variation is related to schizophrenia. Finally, our finding that each measure (except perhaps oculomotor gain) is familial, in the context of the twin and adoption literature on schizophrenia (Gottesman et al., 1982), is evidence of a genetic basis for the dimension or type underlying these traits.

A larger study of this kind, now underway, will involve samples large enough for more sophisticated genetic analyses to be conducted. In order to fully explore the familial structure of schizotypy measures, computer programs for multivariate segregation and path analysis are required. They will enable researchers to look for major gene influence, to allow for assortative mating, and to estimate the effects of shared environments.

Three anomalous findings require discussion: Perceptual Aberration did not significantly discriminate relatives of schizophrenics from control subjects; SPEM RMS error likewise did not; and SPEM oculomotor gain did not appear to be familial.

It is noteworthy that 39% of relatives had a Perceptual Aberration score of 0, in comparison with 28% of control subjects; this difference is actually opposite to that predicted. The Perceptual Aberration Scale's poor performance in this setting is paralleled by other data. In a study of first-episode psychotics, schizophrenics' relatives scored nonsignificantly lower on the Perceptual Aberration Scale than did control subjects (Katsanis, Iacono, & Beiser, 1990). We agree with Katsanis et al.'s hypothesis that the Perceptual Aberration Scale's failure to discriminate these groups in the expected direction stems from its fairly obvious pathological content. When relatives know that they are being studied because they are related to a psychotic patient, they may not reveal certain kinds of pathology. Alternatively, this kind of cognitive-perceptual abnormality may not be as strong a discriminator as, for example, social-interpersonal deviations.

Our SPEM RMS error data for relatives differ somewhat from results with other SPEM measures in the literature (Holzman et al., 1977; Holzman et al., 1978; Holzman et al., 1974; Kuenenmeister et al., 1977; Mather, 1985). We adduce two possible explanations for our partial negative finding with RMS error. First, our sample size was small, and so a Type II error may have occurred. This is plausible because the difference between groups was fairly clearly in the expected direction. Second, gain may simply be a better discriminator of eye-tracking abnormality than is RMS error, although replication of a gain-RMS discrepancy would be needed to support such a conclusion.

Finally, oculomotor gain does not appear to be familial. Because gain correlated .60 with RMS error in our total sample, and because RMS error is heritable (Iacono & Lykken, 1979), such a finding is not plausible (although it is mathematically possible). The estimated heritability may reflect a sampling error. Much larger samples are required for precise estimation of heritability and genetic correlation. For this reason, our correlational results are not offered as parameter estimates. Instead we simply suggest that the overall pattern of positive intercorrelations is consistent with positing common genetic causes for diverse schizophrenia-related abnormalities in the personality, psychophysiological, and information-processing domains.

References


Baron, M., Gruen, R., Asnis, L., & Kane, J. (1983). Familial relatedness


Received May 7, 1990
Revision received July 27, 1990
Accepted October 9, 1990