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Language processing and memory in ill and well siblings from multiplex families affected with schizophrenia

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Abstract

The present study was designed to extend the investigation of genetic factors for schizophrenia to cognitive and linguistic signs of central nervous system dysfunction. Of 51 siblings studied from 19 schizophrenia multiplex families, 37 had a DSM-III-R diagnosis of schizophrenia or related schizophrenia spectrum disorder and 14 were well. Controls were 17 unrelated healthy individuals within the same social class and age range. Subjects were tested on measures of memory, attention, reading and expressive language ability. Schizophrenic and spectrum disorder siblings were significantly more impaired in tests of auditory discrimination and memory than their well siblings or controls and displayed significantly reduced syntactic complexity to their speech. While well siblings did not differ from controls on most measures, some aspects of language complexity were reduced. A familial effect was observed for tests of reading ability, attention, some syntactic measures, and short-term memory, although these were not the measures that distinguished patients from controls in this cohort; the scores were not correlated among the ill sibling pairs, and poorer scores did not segregate with schizophrenia within these families. Thus, while some measures of language, memory and attention are deviant in patients with schizophrenia, they may not be heritable and directly related to the genetics of the disorder. Instead, they may be a manifestation of, rather than a vulnerability to, the illness. © 1997 Elsevier Science B.V.

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1. Introduction

Functional cerebral deficits, such as poor memory and attention (Taylor and Abrams, 1984; Gruzelier et al., 1988) and anomalies of language processing (Morice and Ingram, 1983; Morice and McNichol, 1986; Sims, 1995) have each been reported in schizophrenia and could be indicators of the underlying pathophysiological process. Although family, twin, and adoption studies have clearly demonstrated the heritability of schizo-

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phrenia (e.g., Kety, 1983; Kendler, 1988), it is unclear whether the genetic factors are responsible for these abnormalities. Previous investigators have examined the nonschizophrenic relatives of schizophrenic probands for clues, or vulnerability factors, to the inheritance of schizophrenia, assuming that non-schizophrenic first-degree relatives as a group are more likely to carry the defect than the general population. Physiological abnormalities, such as impaired saccadic eye movements (Holzman et al., 1984) and lengthened P300 latency (Roxborough et al., 1993), brain structural abnormalities (Weinberger et al., 1981; Reveley et al., 1982; DeLisi et al., 1986), anomalies of language expression (Condray et al., 1992), thought disorder (Shenton et al., 1989) and cognitive performance on a wide range of neuropsychological measures (Goldberg et al., 1990; Pogue-Geile et al., 1991; Erlenmeyer-Kimling and Cornblatt, 1992; Yurgelun-Todd and Kinney, 1993; Cannon et al., 1994; Kremen et al., 1994; Park et al., 1995) all have been examined in relatives of patients with schizophrenia.

Goldberg et al. (1990) reported no cognitive abnormalities among a group of 16 nonschizophrenic, discordant monozygotic co-twins of schizophrenics, but later (Goldberg et al., 1993) reported abnormal logical memory and mental control abilities among an overlapping group of 24 non-psychotic co-twins of schizophrenic subjects when tested with a more sensitive test battery. Yurgelun-Todd and Kinney (1993) reported impaired frontal lobe function compared with normal controls on either the Wisconsin Card Sort test or the Trails test among a group of 15 nonschizophrenic siblings of 28 schizophrenic probands. Cannon et al. (1994) reported that for a group of 16 nonschizophrenic siblings of 15 schizophrenic probands, the nonschizophrenic siblings' performance in an extensive neuropsychological test battery was statistically inferior to a group of matched controls for all composite measures. Pogue-Geile et al. (1991) reported abnormal performance on tests of fluency, executive reasoning, and associative abilities among a group of 40 nonschizophrenic siblings of schizophrenic probands. In his study, the nonschizophrenic siblings' performance was inferior to that of 40 controls and 40 of the controls' siblings on these measures. Faraone et al. (1995) reported that abstraction, verbal memory and auditory attention were impaired in 35 nonpsychotic siblings or adult children of 25 schizophrenic probands when compared to specifically selected controls; and Park et al. (1995) reported both impaired spatial working memory as well as poor performance on a visual delayed-response task among 27 first-degree relatives of 18 schizophrenic patients as compared to controls.

In an attempt to identify factors that might predict which well siblings of schizophrenic probands would demonstrate neuropsychological impairments, some have examined additional physiological and diagnostic characteristics of the well sibling group. Roxborough et al. (1993) reported deficits in card sorting, trail-making and fluency among 30 nonschizophrenic, first-degree relatives of 36 schizophrenic probands compared with controls. In her study, only the relatives with abnormal P300 latency were impaired neuropsychologically while those with normal P300 were not. In addition, Condray et al. (1992) reported language functions to be impaired in a group of 41 nonschizophrenic brothers of 36 schizophrenic probands only if the nonschizophrenic brothers carried the diagnosis of schizotypal personality disorder.

Nonschizophrenic siblings examined in each of the above-cited studies are a heterogeneous mix of individuals who share family membership with a schizophrenic sibling but not necessarily the genetic information responsible for the inheritance of schizophrenia. They also may be at risk for later development of schizophrenia or have an undiagnosed (but genetically related) schizophrenia spectrum personality disorder. Thus it is expected that, as a group, nonschizophrenic siblings will appear less impaired than those with schizophrenia, but possibly more impaired than unrelated controls, depending on how they were selected.

In most of these studies, neuropsychological measures were compared between single schizophrenic probands and their nonschizophrenic siblings or parents or between unaffected, but at-risk relatives, such as children or siblings of schizo-

phrenic probands and healthy controls. While such studies will suggest factors that may be associated with having schizophrenia, they do not clarify whether there is co-inheritance of associated factors with schizophrenia within these families (Rieder and Gershon, 1978). Studies of co-inheritance require more than one ill individual within families for comparison with the unaffected siblings. The putative defect, if related to the genetics of schizophrenia, will be correlated among ill sibling pairs, and in addition, the within family variance will be less than that among families. Thus, families with multiply affected individuals ('multiplex families') provide a further step toward examining the genetic core of the clinical syndrome, schizophrenia.

The present study design involves families in which there are two or more individuals with schizophrenia in the same generation, who are examined and compared with their non-psychotic siblings and controls. A familial effect on brain ventricular size has been previously reported by one of us in a similar but independent set of families (DeLisi et al., 1986). The present preliminary study extends the investigation of genetic factors that may serve as markers of inherited schizophrenia in multiplex families to the cognitive domain.

2. Methods

2.1. Subjects

A total of 51 subjects from 19 schizophrenia multiplex families and 17 unrelated controls completed the study. Participants from each family were as follows: one family with three ill and three well; one with three ill; eight with two ill; one with two ill and two well; one with one ill and two well; one with one ill and one well; six with two ill and one well. These families represent a subset of multiplex families participating in molecular genetic studies searching for genes for schizophrenia. Families were recruited for the present evaluations if the sibship included at least two available schizophrenic siblings and at least one available non-schizophrenic sibling. After complete description of the study to the subjects, written informed consent was obtained. Thirty-four individuals were diagnosed with schizophrenia or schizoaffective disorder, two were diagnosed with schizotypal personality disorder and one was diagnosed with psychosis not otherwise specified (also included in the schizophrenia-spectrum group). Fourteen well siblings were identified. All subjects (including well siblings and controls) were screened and diagnosed based on structured interviews, information from relatives and medical records. Interviews were performed by trained clinical interviewers using structured instruments for DSM-III-R (1987) diagnoses including: the Structured Interview for DSM-III-R Personality Disorders (SIDP-R) (Pfhol et al., 1990), the Relative Psychiatric History Questionnaire (Gershon, unpublished instrument, Clinical Neurogenetics Branch, Intramural Program NIMH, Bethesda, MD) and either the Diagnostic Interview for Genetic Studies (DIGS) (Nurnberger et al., 1994) or a modified Schedule for Affective Disorders and Schizophrenia (SADS-L) (Spitzer and Endicott, 1978). The schizophrenic subjects had been ill for a mean of 11.34 years (range, 0.5–28 years) and only three were hospitalized at the time of testing. Twenty-six of the schizophrenic siblings were receiving antipsychotic medications at the time of testing and 13 reported the additional use of anticholinergics. Seven of the non-schizophrenic siblings met criteria for past substance or alcohol abuse while an additional seven had no diagnoses.

The group of 17 control subjects were a subset of normal volunteers who were participating in longitudinal studies with our research group and who were percentage matched by age and socioeconomic status (SES) (Hollingshead and Redlich, 1958) to the subjects. Potential controls were originally recruited by verbal solicitations from the hospital visitors' lobby and other public facilities. The controls were evaluated in the same extensive manner as the members of the multiplex families. The SADS-L and SID-P interviews were used for screening, and subjects were excluded if there was a history of substance abuse or central nervous system pathology including meningitis, seizures, migraine headaches, loss of consciousness, or head

injury, as well as major psychiatric disorders (AXIS-I) and/or schizophrenia spectrum personality disorders. The control subjects had no psychiatric diagnoses. Characteristics of the subject groups are listed in Table 1. There were no differences between the groups for age, socioeconomic status or handedness.

2.2. Neuropsychological testing

All subjects were given a neuropsychological battery that included tests of premorbid intellectual skills and common tests of memory and attention. Reading ability, a skill that is not generally affected in schizophrenia and can be used to predict premorbid IQ, was assessed by the Wide Range Achievement Test-Reading (WRAT) (Jastaks and Wilkenson, 1984) and the Word Attack (WAT) subtest from the Woodcock Reading Mastery Test (Woodcock, 1987). The following tests from the Weschsler Memory Scale-Revised (Weschler, 1945) were used to assess memory and attention: Logical Memory, immediate recall (Log 1) and delayed recall (Log 2), Visual Reproduction, immediate (Vis 1) and delayed recall (Vis 2), and Digit Span forward (Dig F) and backwards (Dig B). Attention was also assessed by means of the Goldman-Fristoe-Woodcock Test of Auditory Discrimination, quiet condition (Aud Q) and noise condition (Aud N) (Goldman et al., 1970; Goldman and Fristoe, 1986).

2.3. Analysis of expressive language

Expressive language was measured by a spontaneous 6-min, taped, oral soliloquy and was assessed by two different measures of linguistic performance: linguistic complexity and verbal fluency. Thirty-seven of the 51 participants from 18 of the 19 families participated in the linguistic analysis (ill siblings = 25, well siblings = 12, controls = 12). During the collection of the verbal sample, subjects were instructed to speak on a topic of their choice. Prompts such as "tell me about something you like to do; tell me about a day in your life; tell me about something you're interested in..." were given to the subjects when they could not think of any topic spontaneously. Subjects' statements were transcribed without punctuation into written prose. All soliloquies were coded to disguise subject status. Transcripts were blindly assessed by a linguistics graduate student who was trained to perform these measures reliably by Dr. D. Finer, a professor in The Department of Linguistics, SUNY, Stony Brook.

Four different clause types were chosen by one of us (DLF) for complexity analysis in our verbal sample based on their commonality in the English language. Relative embeddedness of a clause may be regarded as a general index of verbal sophistication, in that greater depth implies more complex thought and language organization (Morice and Ingram, 1983; Morice and McNichol, 1986). For example, a level-1 embedded clause such as "Joe went to the store that was on the corner" is actually a complex sentence containing two simple clauses (i.e., "Joe went to the store"; "the store was on the corner"). By embedding, the speaker is able to organize language and make speech more parsimonious.

The different clause types used for analysis were

Table 1
Subject demographics: families ($n = 19$)

	Ill siblings[a] ($n = 37$)	Well siblings ($n = 14$)	Controls ($n = 17$)	Test of group differences	$p <$
Mean age (±SD)	33.8 (7.7)	33.1 (6.9)	31.9 (4.7)	$F = 0.44$	0.64
Range	19-51	21-48	25-42		
Sex	M = 29, F = 8	M = 5, F = 9	M = 9, F = 8	$\chi^2 = 8.9$	0.01
Handedness	L = 5, R = 32	L = 2, R = 12	L = 1, R = 16	$\chi^2 = 0.76$	0.68
SES**	2.8 (0.8)	2.9 (0.8)	2.8 (0.8)	$F = 0.16$	0.84
Illness duration	2.9 (3.4)				

[a]With schizophrenia/or schizoaffective disorder.

as follows: tensed clauses with overt complementizers (e.g., the dog that barked); tensed clauses without overt complementizers (e.g., the dog barked); infinitive clauses under subject control (the fireman persuaded Joe to jump); and infinitive clauses under object control (the fireman promised Joe to jump). The frequency of these different clause types were hand scored by a trained linguistics student and supervised by one of us (DLF).

Depth of clausal embedding was calculated by taking a weighted average of the frequency of each variable. For example, if a subject gave four level-1 clauses, three level-2 clauses and two level-5 clauses in their verbal sample, the average level of embedding in that variable for that subject was $((4\times1)+(3\times2)+(2\times5)/9=$ weighted average $=$ 2.2 levels embedding).

Another aspect of expressive language, verbal fluency, was assessed through the frequency of six other variables: syntactic and selectional violations, morphological (grammatical) errors, false starts, pause fillers, and minor sentences. A syntactic violation is part of a clause that violates the normal rules of language (e.g., "I went to the store" versus "I went to store"). A selectional violation involves a mistake in choosing the correct word from the verbal lexicon, though grammar and syntax is correct (e.g., "I am going to watch my height" instead of "I am going to watch my weight"). A false start occurs when a sentence is begun, stopped and restarted again ("I am going to talk about...Maybe I should tell you about"). A repetition occurs when a word is repeated in a sentence ("I am going — going — to wash my car"). A morphological error is a mistake in common grammar or verb conjugation ("I is going to the store" rather than "I am going to the store"). A pause filler is a nonsensical item put in a sentence to fill in gaps and pauses in speech ("I uh am going to um"). A minor sentence is a sentence that does not contain all the elements of a normal sentence (i.e., verb, object, subject) but can be understood (e.g., "Going to the store today" rather than "I am going to the store today").

All the above measures of language structure have been previously delineated and appear in standard linguistics textbooks (Radford, 1988; Haegeman, 1994). Their validity and application have been previously described, particularly with respect to studies of both first and second language acquisition (Finer, 1990, 1991).

2.4. Statistical analyses

All statistical analyses were conducted using the CSS-Statistical package. Analyses of neuropsychological performance across families were conducted with 2-way analysis of covariance (ANCOVA) using sex and diagnosis as independent variables, and socioeconomic status and age as covariates. The effect of family membership was assessed through similar 2-way ANCOVAs using sex and family as independent measures, and socio-economic status, age and diagnosis as covariates. For those variables with significant familial affects, further analyses were performed, using Spearmans correlations among ill sibling-pairs and tabulating whether performance on these measures was consistently poorer among ill members than well members within families.

3. Results

Neuropsychological performance for siblings with schizophrenia spectrum disorders ($n=37$) was compared to the test performance of well siblings without psychiatric diagnoses ($n=14$) and controls ($n=17$). Two-way ANCOVAs on the ten neuropsychological measures as dependent variables indicated significant effects for diagnosis across most of the tests of neuropsychological function: verbal memory, immediate (Log 1; $F=11.6$, $p<0.001$) and delayed (Log 2; $F=14.9$, $p<0.001$); nonverbal memory, immediate (Vis 1; $F=4.28$, $p<0.05$); auditory attention (Aud Q; $F=4.36$, $p<0.05$); and auditory discrimination (Aud N; $F=5.75$, $p<0.01$) (see Table 2). Using a Bonferoni correction for multiple comparisons ($n=21$), only verbal memory remains significant. There were no differences between any of the three groups in reading ability as measured on the WRAT and WAT. The well siblings' performance did not differ

Table 2
Neuropsychological test scores (±SD)

Test	Ill sibs.	Well sibs.	Controls	F	$p<$
Memory					
Verbal memory (immediate)	14.6 (7.9)	21.2 (6.2)	23.1 (6.5)	11.6	0.001[a]
Verbal memory (delayed)	10.5 (6.9)	18.9 (8.0)	19.8 (6.3)	14.9	0.001[b]
Nonverbal memory (immediate)	11.2 (2.3)	12.7 (1.3)	12.4 (2.2)	4.3	0.02[c]
Nonverbal memory (delayed)	10.1 (3.3)	11.8 (2.0)	11.2 (4.0)	2.8	0.07
Reading/premorbid IQ	98.0 (16.0)	97.4 (11.6)	105 (7.2)	1.3	0.29
Reading/Word Attack	42.1 (9.8)	44.6 (5.5)	47.8 (2.1)	1.8	0.17
Attention					
Auditory attention	1.7 (1.9)	0.9 (0.9)	0.3 (0.5)	4.4	0.02[d]
Auditory discrimination	8.9 (2.6)	6.9 (3.2)	6.0 (2.4)	5.8	0.005[e]
Attention (DIG F)	6.3 (1.5)	6.6 (1.1)	7.1 (1.1)	2.1	0.13
Attention/STM (DIG B)	4.9 (1.4)	5.6 (1.2)	5.7 (1.5)	2.3	0.11
Clausal embedding					
Tensed complement					
with overt complementizer	1.7 (3)	1.8 (0.3)	1.9 (0.5)	1.06	0.35
without overt complementizer	1.4 (0.5)	1.4 (0.4)	2.0 (0.6)	6.8	0.001[f]
Infinitive					
subject control	1.4 (0.7)	1.7 (0.4)	1.7 (0.5)	0.21	0.81
object control	2.0 (1.0)	2.0 (0.7)	1.6 (0.9)	0.31	0.74
Syntax					
Syntactic violations	2.0 (2.1)	1.8 (1.7)	2.6 (3.9)	0.57	0.56
Selectional violations	1.2 (1.9)	1.2 (1.1)	1.0 (1.6)	0.08	0.92
False starts	15.4 (4.0)	11.8 (9.0)	16.1 (19.5)	0.08	0.92
Morphological errors	0.7 (0.6)	1.4 (1.2)	1.8 (2.2)	2.1	0.13
Filler sentences	24 (38.7)	28 (13.8)	3.8 (35.4)	0.76	0.47
Minor sentences	3.3 (2.7)	8.1 (6.0)	5.7 (5.2)	3.7	0.03[g]

Planned comparisons:
[a]Well vs. ill sib, $p<0.001$; control vs. ill sib., $p<0.001$; control vs. well sib., $p<0.53$; main effect of sex, $F=11.78$, $p<0.05$.
[b]Well vs. ill sib, $p<0.001$; control vs. ill sib., $p<0.001$; control vs. well sib., $p<0.73$.
[c]Well vs. ill sib, $p<0.001$; control vs. ill sib., $p<0.015$; control vs. well sib., $p<0.73$.
[d]Well vs. ill sib, $p<0.13$; control vs. ill sib., $p<0.01$; control vs. well sib., $p<0.33$.
[e]Well vs. ill sib, $p<0.03$; control vs. ill sib., $p<0.001$; control vs. well sib., $p<0.29$.
[f]Well vs. ill sib, $p<0.67$; control vs. ill sib., $p<0.001$; control vs. well sib., $p<0.01$.
[g]Well vs. ill sib, $p<0.003$; control vs. ill sib., $p<0.07$; control vs. well sib., $p<0.30$.

statistically from the controls on any of the neuropsychological measures.

In the analyses of expressive language, a significant diagnosis effect emerged for one of the four indices of linguistic complexity/clausal embedding (tensed clauses without overt complementizers; $F=6.8$; $p<0.001$), which remains significant when controlled for the number of comparisons made. Planned comparisons for this variable revealed that controls exhibited speech significantly more complex than either ill ($p<0.001$) or well siblings ($p<0.01$). Well and Ill siblings were not distinguished by this variable. A main effect of diagnosis emerged for one of the six other soliloquy variables (frequency of minor sentences; $F=3.7$; $p<0.03$). Planned comparisons revealed that ill and well siblings differed significantly in the frequency of minor sentence production ($p<0.003$) while there was no difference between well sibs and controls.

Two-way ANCOVAs for the effect of family membership on each test revealed significant between family differences in reading tests, WRAT ($F=4.0$; $p<0.001$) and WAT ($F=7.0$; $p<0.001$), and attention tests, Aud Q ($F=3.6$; $p<0.001$), Dig F ($F=2.28$; $p<0.02$) and Dig B ($F=2.06$; $p<0.04$) (Table 3). Analysis of the oral soliloquies revealed

Table 3
Effect of family membership on neuropsychological test scores. (N = 19 families) sum of squares

	Between families	Within families	F	$p<$
Memory				
Verbal memory immediate	1263	1345.6	1.51	0.16
Verbal memory delayed	1213	1258.8	1.55	0.14
Nonverbal memory immediate	80.64	125	1.04	0.45
Nonverbal memory delayed	161.8	264	0.98	0.50
Reading/premorbid IQ	7650	309	4.0	0.001
Reading/Word attack	3159	737	7.0	0.001
Attention				
Auditory attention	86.04	38.86	3.6	0.001
Auditory discrimination	182	182	1.6	0.12
Attention (DIG F)	38	26	2.28	0.02
Attention/STM (DIG B)	53	41	206	0.04
Clausal embedding				
Tensed complement with overt complementizer	0.868	0.712	1.2	0.37
Tensed complement without overt complementizer	2.3	2.6	1.1	0.46
Infinitive, subject control	4.5	3.6	1.4	0.30
Infinitive, object control	3.4	19.1	1.3	0.29
Syntax				
Syntactic violations	19.2	29	0.79	0.64
Selectional violations	35.6	27.5	1.6	0.23
False starts	19998	1292	18.5	0.001
Morphological errors	7.49	16.7	0.81	0.63
Filler sentences	18663	4587	4.88	0.006
Minor sentences	91.9	269.4	0.41	0.92

familial influence on false start production ($F=18.5$; $p<0.001$) and filler statements ($F=4.88$; $p<0.006$). No significant familial effects were found for any of the four measures of clausal embedding. No significant correlations for any of the above significant factors were observed for schizophrenia–schizophrenia sibling pairs, when adjusted for the number of correlations run, with the exception of the WAT (Spearman $r=0.61$, $p<0.006$). When the pattern of scores was examined in detail within families where both ill and well individuals were tested ($n=11$), ill siblings did not score consistently worse than well siblings for any of the variables.

Thus, for those factors that distinguished patients and controls, no familial effects were present and for those factors with a familial effect, no distinction could be made between the performance of ill and well siblings within families.

In order to investigate the influence of medication on test performance, an analysis of variance (ANOVA) was performed on test scores for the group of schizophrenic siblings who were treated with antipsychotics alone (including clozapine) and the group who were treated with a combination of antipsychotics with anticholinergics at the time of testing. Antipsychotic use alone was not associated with any changes in performance while anticholinergics plus antipsychotics (df = 34,1, $F=10.23$, $p=0.003$) was associated with significant decrements in performance on only the immediate recall condition of the visual reproduction test, but no other tests. Illness duration among the schizophrenic siblings was also examined by performing Spearman's rank order correlations. In these analyses, duration of illness in years as measured from the age at first psychotic symptoms was not correlated with any scores on the neuropsychological tests.

4. Discussion

The present study confirms numerous past publications reporting impairment in cognitive perfor-

mance, specifically with respect to verbal memory, language, and attention among patients with schizophrenia. Except for performance on the visual reproduction subtest, the cognitive impairment observed in this study cannot be attributed to the effects of medication. The association of anticholinergic medication and impairment in copy of a complex figure is likely related to a direct effect of cholinergic blockade on visual acuity rather than an effect on memory or attention as the medication effect was not observed in the delayed recall condition of the same test nor any other test. The duration of psychotic symptoms was also unrelated to degree of cognitive impairment. Parental socioeconomic status appears to be unrelated to memory and attention test performance and did not correlate with any tests other than those of reading skill, an ability likely to be more robust in subjects with higher levels of education (Golstein et al., 1991, which is likely to explain the significant familial correlation with this skill). Thus, observed impairments in immediate and delayed memory and attention among schizophrenics in this study appear to be associated with the underlying illness process rather than a spurious finding associated with family socioeconomic status or psychopharmacology.

The results of the analysis of expressive language are in partial support of our previous findings of reduced verbal fluency and increased frequency of morphological errors in the language of schizophrenic subjects (DeLisi et al., in press). Interestingly our findings suggest that, for at least one language measure, sentence complexity, non-ill siblings are similar to their schizophrenic siblings and significantly reduced from that of controls. Similarly, the language variables measured were independent of illness duration and medication effects, thus likely to be part of the illness process. The question remains whether any of these are a direct result of the genetic defect(s) producing susceptibility to schizophrenia.

The neuropsychological and linguistic measures employed in the present study were chosen as potential markers for genetic vulnerability because they reflect different aspects of memory and language processing. Attention is integrally related to both. All have been shown in extensive past literature to be deviant in schizophrenia. Furthermore, it has been suggested that genes for psychosis are related to genes responsible for the development of language; more specifically, that these genes determine the growth and formation of brain regions providing centers for language processing (Crow, 1993, 1995a,b). The present study, however, failed to show a direct connection of a defect in any of the cognitive processes related to language processing and the genetics of schizophrenia. With no familial effect (and correlation among ill sibling pairs) for many of these variables which are significantly worse in the schizophrenics as a group than controls, we would assume then that these are not defects directly associated with the core genetic defect, but rather are, to a varying degree, manifest as a consequence of the severity of the illness process. However, it is possible that in the present study either the number of subjects was too small or the battery of tests chosen was not sensitive or specific enough to definitively test this hypothesis. Further work is in progress to determine a more specific and sensitive marker of language dysfunction in schizophrenia and then to apply this to a larger study of multiply affected families.

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