Relationship between Nailfold Plexus Visibility and Clinical, Neuropsychological, and Brain Structural Measures in Schizophrenia

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Background: *Although all published studies investigating the association between nailfold plexus visibility and schizophrenia have found the subpapillary plexus (the vascular network into which capillaries drain) to be unusually visible in many schizophrenia patients, little else is known about this putative marker for schizophrenia liability.*

Methods: *Plexus visibility was rated in 63 chronic schizophrenia, 67 first–episode schizophrenia, 9 schizophreniform, and 66 unipolar and bipolar depressed patients, all with psychosis, and 119 nonpsychiatric controls. Smooth–pursuit eye tracking, clinical features, neuropsychological performance, and lateral ventricle size were assessed.*

Results: *Approximately 21% of chronic schizophrenia, 22% of first–episode schizophrenia, and 22% of schizophreniform patients had highly visible plexus compared to only 8% of unipolar, bipolar, and nonpsychiatric controls. Schizophrenia patients with visible plexus had worse oculomotor performance. Additionally, chronic schizophrenia patients with visible plexus had more negative symptoms, worse course, more severe illness, worse occupational functioning, and worse neuropsychological performance on tasks thought to be sensitive to frontal dysfunction. An inverse relationship between plexus visibility and lateral ventricle size was found.*

Conclusions: *This study provides evidence that schizophrenia patients with plexus visibility are characterized by oculomotor dysfunction, negative symptoms, severe symptomatology, chronic course, neuropsychological dysfunction, and an absence of enlarged ventricles.* Biol Psychiatry Biol Psychiatry 1999;46:102–109 © *1999 Society of Biological Psychiatry*

Key Words: Nailfold plexus visibility, schizophrenia, neuropsychology, lateral ventricles, frontal lobes

Introduction

The subpapillary plexus is the vascular network at the base of the finger nailfold into which capillaries drain. It is normally visible at birth, but by adolescence visibility becomes increasingly rare, and after puberty only a few individuals have visible plexus (Maricq 1964; Whitson and Jones 1971). The mechanism underlying plexus visibility is unknown but is likely to be related to the thinness or transparency of the skin. Although some studies have reported morphological abnormalities of the capillary endrow loops in the nailbeds of patients with schizophrenia (Hauptmann and Myerson 1948; Norris and Chowning 1964), plexus visibility refers specifically to the visibility, not morphology, of the vasculature.

Adult plexus visibility has been repeatedly demonstrated to be associated with schizophrenia (Clementz et al 1992b; Maricq 1963a, 1969; Norris and Chowning 1964; but for reviews see Iacono 1985; Poole et al 1991). It has been reported that between 17% and 72% of persons with schizophrenia have highly visible plexus (Clementz et al 1992b; Hauptmann and Myerson 1948; Maricq 1963a), while only about 6% of the general population have the trait (Clementz et al 1992b; Maricq 1977). A high plexus visualization score (PVS; Maricq 1970), a quantitative index reflecting the amount of visible plexus, does not appear to be associated with other psychiatric disorders such as bipolar disorder and major depression, even when such patients are psychotic (Clementz et al 1992b).

A few studies have investigated the genetic transmission of plexus visibility and its association with schizophrenia and schizotypy in relatives. Maricq and Jones (1976) found that 78% of high PVS non–psychiatric teenagers had at least one parent with high PVS. Only 7% of the low PVS teens had parents with high PVS, which is close to the expected base rate of high PVS in a normal population. A family study conducted by Buchanan and Jones (1969) reported a .56 rank-order correlation between plexus scores and schizotypy ratings among first-degree relatives (40 siblings and 66 parents) of high plexus schizophrenia probands. A study by Clementz et al (1992)

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showed that high plexus visibility was not found in greater proportions in the relatives of probands experiencing their first-episode of schizophrenia. However, the relatives of high PVS schizophrenia probands had higher PVS than relatives of low PVS schizophrenia probands.

Increased visibility of the nailfold plexus has also been shown to be more strongly associated with familial than with sporadic schizophrenia. Maricq (1963b) reported that 70% of patients with familial schizophrenia and 19% of patients with sporadic schizophrenia had high PVS. Maricq et al (1968) demonstrated that first-degree relatives of schizophrenia patients with high PVS have almost a three-fold risk for schizophrenia compared to the risk for relatives of patients with low PVS. She and her colleagues found that 10% of the low PVS probands had an affected first-degree relative, whereas 28% of the high PVS probands had an affected relative. Almost identical figures were derived from a large state–hospital sample in which 30% of high PVS schizophrenia probands, compared to 13% of low PVS probands, had a first-degree relative with schizophrenia (Poole 1993).

It is known that the skin and brain both develop from the same ectodermal tissue and thus abnormalities of the skin may provide clues from which inferences about brain development and integrity can be made. Unfortunately, very little is known about the relationship between plexus visibility and neuropsychological or brain structural integrity in schizophrenia. Indeed, it is a large theoretical leap from the nailfold to the brain when one tries to link plexus visibility to neurological and cognitive deficits because of the dearth of research into these matters. There is some evidence that plexus visibility may be associated with a liability for neurological dysfunction. One study by Alson (1965) found that schizophrenia patients with high PVS ratings performed more poorly than those with low PVS ratings on the following cognitive and motor tasks: visual reaction time, writing serial Xs for 90 seconds, Memory for Digits (backward; there were no differences when digits were recalled forward), the Quick Test, Porteus Maze Test, Absurd Sentences, and tests of pattern learning.

Other evidence that plexus visibility might be related to neurological dysfunction comes from 2 recent studies that found that plexus visibility was associated with negative symptoms but not positive or affective symptoms. The first study (Poole et al 1991), using a sample of severely affected chronic schizophrenia patients, found a moderately strong correlation ($r = .49$) between PVS ratings and negative symptoms including motor, expressive, cognitive, and motivational deficits. However, the effects of neuroleptic medications and long-term hospitalization could not be ruled out as playing a role in the specific relationship of plexus visibility and negative symptoms. These confounds were the focus of the second study (Poole et al 1993), in which a medication-controlled design was employed with a less severely affected schizophrenia sample. PVS ratings were again correlated with motor and expressive deficits ($r = .45$), specifically flat affect, poverty of speech, and catatonic behavior.

Aside from the finding that plexus visibility is associated with schizophrenia, which has been replicated many times without failure, the significance of this association remains something of a mystery. Most of what we do know is limited in that it is based on research conducted prior to 1970 using outdated and relatively unsophisticated methodology. The current study attempts to shed some light on the nature of nailfold plexus visibility by investigating its relation to neuropsychological functioning, brain morphology, and clinical features in a large epidemiological sample of first episode psychotic patients and chronic schizophrenia patients. Also of great interest is the relationship between plexus visibility and smooth-pursuit eye tracking, a well-researched marker for schizophrenia liability (Iacono and Clementz 1993; Levy et al 1993).

Methods and Materials

Sample

One-hundred and forty-one persons (97 men and 44 women) experiencing their first lifetime episode of psychosis (i.e., all had hallucinations and/or delusions) participated in the study. First episode patients were drawn from a large epidemiological study of the course of psychosis, the Markers and Predictors of Psychosis project (MAP) (see Iacono and Beiser [1989] for details of the study and a description of the recruitment of these participants). To avoid potential biases involved with obtaining participants from a single source, a wide referral network was established to identify all persons having their first psychotic episode whom were living in the Vancouver, British Columbia area. Diagnostic information was obtained from a semistructured interview, the Present State Exam, 9th edition (PSE, Wing et al 1974), which was administered by a trained psychiatrist or clinical psychologist. Collateral diagnostic information was obtained from clinical chart reviews, family members, and interviews with friends of the patients. This information, along with the PSE, was presented at a case conference to establish a DSM–III diagnosis (APA 1980) based on a "best estimate" approach (Leckman et al 1982). An additional clinical assessment based on the Diagnostic Interview Schedule (DIS; Robins et al 1981) 9 months after intake, plus a second PSE interview 18 months after intake was used to confirm the intake diagnosis and to formulate a DSM-III diagnosis based on this longitudinal information collected over 18 months.

A group of 119 nonpsychiatric controls of similar age and gender, screened for any personal or family history of treatment for a psychiatric disorder, were recruited from family practices in low-income neighborhoods and unemployment centers. A total of 67 schizophrenia, 9 schizophreniform, 26 depressed, 39

Table 1. Demographic Characteristics of the Sample

Diagnosis	*n*	Age (mean [SD])	% male
Chronic schizophrenia	63	28.5 (4.5)	88.9
First episode schizophrenia	67	22.8 (5.2)	77.6
Schizophreniform	9	20.4 (4.8)	55.6
Unipolar	26	26.0 (7.4)	65.3
Bipolar	39	25.8 (7.1)	59.0
Nonpsychiatric control	119	31.0 (14.0)	52.9

bipolar, and 119 nonpsychiatric control subjects underwent capillaroscopy (see Table 1). In 2 earlier reports involving these participants, the familial nature of plexus visibility and its prognostic significance in first episode schizophrenia were investigated (Beiser et al 1994; Clementz et al 1992b); however, for these earlier reports, diagnostic classification was based on interview information available at the onset of the participant's psychosis. For the current report, best estimate diagnoses based on interviews covering the course of disorder over 18 months were used to assign patients to diagnostic groups. Beiser et al (1989) reported how the diagnoses of these participants changed during the 18 months following study intake.

Additionally, a group of 63 chronic DSM-III diagnosed schizophrenia patients, including 39 inpatients and 24 outpatients, participated in the study. Patients recruited for study carried a hospital diagnosis of schizophrenia. Patients were excluded if after interview with the PSE by a doctoral level clinical psychologist, they did not meet DSM-III criteria for schizophrenia. Finally, another psychologist reviewed chart and interview data and confirmed the diagnosis. All of the chronic schizophrenia patients and all but 19 of the first-episode psychotic patients were receiving medications at the time of capillaroscopy. Furthermore, all of the participants were free of finger injuries or inflammation that could obscure the plexus, and none had darkly pigmented skin.

Procedure

CAPILLAROSCOPY. Hildegard Maricq's Scale of Plexus Visualization (Maricq 1970) was used to formulate plexus visibility scores (PVS). For all 10 digits, the skin proximal to the nail (i.e., the nailfold) was coated with type B immersion oil and examined under a wide-field stereo zoom dissecting microscope. Scores for each digit, ranging from 0 (no visible plexus) to 4 (plexus covers full width of nailfold, extends proximally over 1/2 of the nailfold width or greater) were determined by matching to 5 prototypic photographs illustrating the 9-point range of plexus visibility (Figure 1). Half points were used when the plexus visibility fell between the plexus rating depicted in 2 adjacent photographs. The scores for each finger for both hands were summed to yield the PVS (possible range 0–40). All ratings were made without knowledge of the participant's diagnosis.

The PVS is reliably determined and stable over time. Interrater reliabilities for PVS reportedly range from .83 to .99 (Buchanan and Jones 1969; Maricq 1966). With this study's sample, 9 months after the first ratings were made, PVS was again estimated for 136 of the participants. Analysis of the test-retest data from this study's sample indicated that PVS was highly stable over time yielding an intraclass correlation coefficient of .992, $p < .001$ (Clementz et al 1992b).

ELECTROOCULOGRAPHY. A more detailed description of the method and analysis of electrooculography (EOG) used in this study has been reported elsewhere (Iacono and Lykken 1979; Iacono et al 1992). Briefly, smooth-pursuit eye movements were recorded while participants watched a 5-mm luminous spot move in a 20 degree sinusoidal pattern across an oscilloscope cathode–ray tube at a frequency of .4 Hz for 20 cycles. Electrooculograms were recorded by applying silver-silver chloride electrodes to the outer canthus of each eye and a ground electrode to the earlobe. Vertical EOG was also recorded to monitor blink activity. Electrode impedance was usually below 5 kΩ and always below

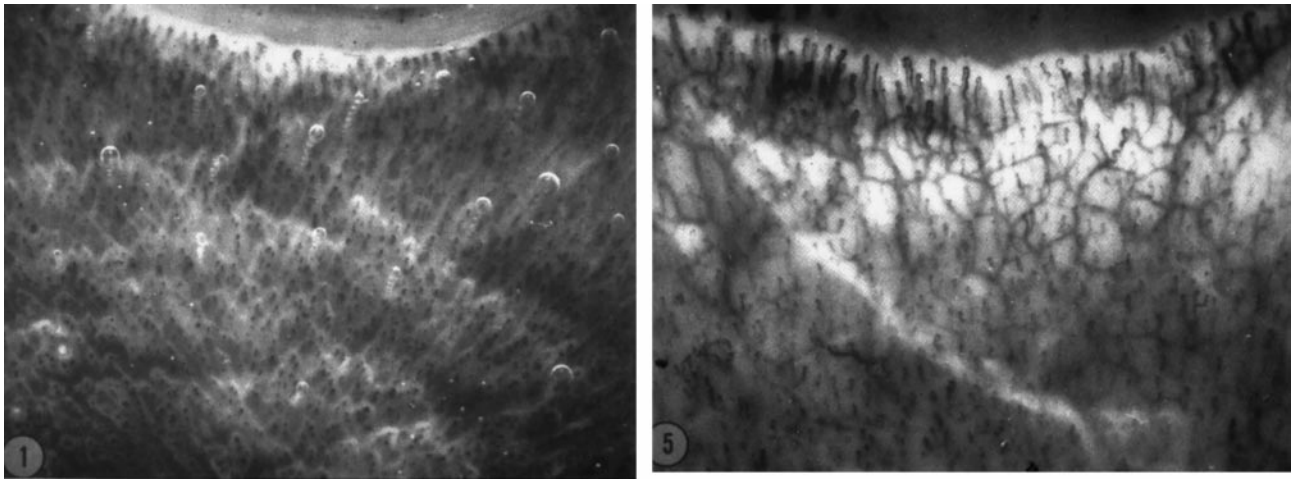

Figure 1. Microphotographs of 2 nailfolds coated with immersion oil. The top of the picture is the distal end of the nailfold, just proximal to the nail. The nailfold on the left has no visible plexus and is an example of a plexus visibility rating of 0. The nailfold on the right is an example of a plexus visibility score of 4 because plexus covers the entire width of the nailfold and extends proximally at least one-half of the nailfold's width. Reproduced from Maricq (1970), with permission from publisher, Academic Press.

10 kΩ. Eye movements and target position were fed into a Beckman Type R–612 Dynograph (Beckman Instruments, Schiller Park, IL) and recorded on FM tape. AC coupling with a 3–s time constant was used. Each subject's head was stabilized by a chin and forehead rest. Eye tracking data was not available on 3 subjects (1 schizophrenia patient, 1 unipolar affective disorder patient, and 1 nonpsychiatric control).

Smooth-pursuit eye tracking was analyzed by a computer program that calculated the root mean square (RMS) error deviation between the eye position and the target position. RMS was calculated after the eye tracking channel had been adjusted for phase and amplitude differences. Higher RMS indicated worse tracking. RMS scores have been found to be an excellent global index of smooth-pursuit eye tracking proficiency (Clementz et al 1992a; Clementz et al 1996; Iacono and Lykken 1979; Iacono et al 1992). RMS scores have been found to be reliably assessed and stable over time. RMS correlates highly with other commonly used measures of tracking proficiency, including qualitative ratings ($r = .91$) (Iacono and Lykken 1979), oculomotor gain ($r = -.88$) (Clementz et al 1992a; Gooding et al 1994), and time domain ($r = -.74$) and frequency domain gain ($r = -.74$) (Katsanis et al 1998). As reported previously, 9 month test–retest reliability for RMS error, estimated from this sample, ranged from .44 to .68 and was unrelated to psychological, clinical, and medication status (Gooding et al 1993).

CLINICAL PHENOMENOLOGY. Only for the chronic patients with schizophrenia was clinical state assessed with the Scale for the Assessment of Negative Symptoms (SANS; Andreasen 1981) and the Global Assessment Scale (GAS; Endicott et al 1976) by two clinical psychologists experienced in the use of the measures. At the outset, the two clinicians interviewed and rated 10 patients together to calibrate their ratings. The clinician made the ratings after conducting the PSE and an additional brief interview covering the SANS subscales. Negative symptoms were indexed by the SANS which has five subscales: a) affective flattening, b) alogia, c) avolition–apathy, d) anhedonia–asociality, and e) attentional impairment. Positive symptoms were indexed by summing the number of symptoms keyed positive from the following PSE symptoms clusters: a) hallucinations, b) delusions, and c) thought disorder. Overall level of functioning was measured by the GAS, which ranges from low level of functioning (1) to high level of functioning (100). In addition, the occupational functioning of patients was assessed using a scale ranging from unemployed all of adult years (0) to full–time employment throughout adult years (4). An example of an intermediate level of occupational functioning would be a score of 2 indicating partial employment (20–50% of the time). (For a more detailed description of the occupational functioning scale and how the scores were derived, see Katsanis and Iacono 1991). The age at onset, number of hospitalizations, and total length of hospitalization were also recorded. The interviews and symptom ratings were made without knowledge of plexus, eye tracking, CT, or neuropsychological status.

NEUROPSYCHOLOGY. The chronic patients with schizophrenia were administered a battery of neuropsychological tests intended to be sensitive to frontal lobe, temporal lobe, and the temporal–parietal–occipital convexity (e.g., overall general intelligence) functioning. All tests were administered in the standard format described in Lezak (1995). Overall intellectual functioning was measured by the Wechsler Adult Intelligence Scale–Revised (WAIS–R).

Putative frontal lobe functioning was assessed by a variety of measures. Verbal fluency was measured with the Controlled Word Association Test (COWAT; number of words generated). Conceptual flexibility was assessed by the Wisconsin Card Sorting Test (WCST; number of categories, number of perseverative and non–perseverative errors). Patients with frontal lobe impairments have been shown to perform poorly on the above tests (Lezak 1995).

Putative temporal lobe functioning was assessed by two memory tests. Verbal memory was measured by the Rey Auditory Verbal Learning Test (RAVLT; total number of words recalled during the five initial trials). Figural memory was assessed with the Benton Visual Retention Test (BVRT; number of correctly reproduced designs).

COMPUTERIZED TOMOGRAPHY. Ventricle size for chronic and first-episode patients was determined from noncontrast CT scans. A detailed description of the CT procedures used can be found elsewhere (Iacono et al 1988). Briefly, the CT scan slice that contained the lateral ventricles at their largest was enlarged to 60% of life size. A manual planimeter was used to trace the circumference of the lateral ventricles and the brain. The ventricle area was traced 6 times and the brain area was traced 3 times. The average of each of these measures was used to compute the ventricle–brain ratio (VBR), which was computed by dividing the area of the lateral ventricles by the total brain area and multiplied by 100.

Results

Preliminary one-way ANOVAs indicated that there were no age, gender, or medication effects on plexus visibility scores. This is consistent with previous studies of plexus and schizophrenia (Clementz et al 1992b; Poole et al 1993).

Group Differences in Plexus Visibility

Plexus scores were highly skewed and were significantly heteroscedastic between diagnostic groups (Bartlett-Box $F = 8.61$, $p < .001$). Logarithmically transformed PVS [log 10 (PVS + 1)] resulted in normally distributed scores and homogeneous variances (Bartlett-Box $F = .47$, $p > .05$) and thus was used for all analyses. Analysis of variance (ANOVA) was used to investigate group differences in PVS. The independent variable, diagnostic group, included schizophrenia (first-episode and chronic), schizophreniform, bipolar disorder with psychosis, unipolar disorder with psychosis, and nonpsychiatric controls. The main effect of group membership on PVS was significant, $F(4321) = 7.20$, $p < .0001$. Orthogonal contrasts indi-

Table 2. Percentage of Persons in Low and High Plexus Visibility Groups by Diagnosis

Diagnosis *(n)*	Plexus visibility group	
	Low (0–1)	High (10+)
Chronic schizophrenia (63)	29.5%	21.3%
First episode schizophrenia (67)	28.4%	22.4%
Schizophreniform (9)	44.4%	22.2%
Unipolar (26)	44.4%	7.4%
Bipolar (39)	61.5%	7.7%
Nonpsychiatric control (119)	54.6%	7.6%

cated that the schizophrenia spectrum group (chronic + first-episode schizophrenia + schizophreniform patients) had higher PVS than the combined comparison group (nonpsychiatric + affective disorder patients), t (316) = 2.91, $p < .004$. Other contrasts indicated that chronic and first-episode schizophrenia patients did not differ in PVS, t (316) = .108, $p > .05$. Similarly, the combined chronic and first-episode schizophrenia group did not have significantly higher PVS than the schizophreniform group, t (316) = 1.11, $p > .05$. The PVS of the bipolar and unipolar groups were not different from one another, t (316) = .53, $p > .05$, and the combined affective disorder group (bipolar + unipolar) was not different from the nonpsychiatric comparison group, t (316) = .61, $p > .05$.

For all remaining analyses, participants were divided into two groups based on PVS so as to maximize the likelihood that one group definitely had the plexus trait while the other definitely did not. The significance of having a moderate PVS is unknown and was not the goal of this preliminary study. The high plexus group was composed of participants whose PVS was 10 or greater. This cutoff, although arbitrary (Clementz et al 1992b), has been used repeatedly and consistently in the plexus literature to identify those who possess the trait (Maricq 1963a, 1963b, 1970). Moreover, in their family study, Maricq and Jones (1976) found that a cutoff score of 10 identified families in which the plexus trait showed a pattern of transmission consistent with autosomal dominant inheritance. A low plexus comparison group was composed of participants with PVS less than 1 indicating that these participants definitely did not carry the plexus trait. Table 2 shows the distribution of plexus by diagnosis using the conventional cutoff of a PVS of 10 as demarcating those with high PVS. Overall, about 22% of the schizophrenia spectrum group subjects compared with about 7.5% of the nonpsychiatric, unipolar, and bipolar control group participants had highly visible plexus (χ^2 (2) = 13.3, $p < .001$).

PLEXUS AND EYE–TRACKING PERFORMANCE. RMS error scores were positively skewed and were thus logarithmically transformed. Ignoring diagnostic group, individuals with high plexus visibility had worse eye–tracking than those with low plexus, t (177) = 2.57, $p < .02$. Follow–up comparisons indicated that this relationship only held within the schizophrenia group mainly because almost all of the subjects in the high plexus group were in the schizophrenia group as well. Within the combined chronic and first–episode schizophrenia group, high plexus individuals had worse eye–tracking than those with low plexus visibility, t (64) = 2.38, $p < .03$ (Table 3).

PLEXUS AND COMPUTED TOMOGRAPHY. Lateral ventricle-to-brain ratios were positively skewed and were thus logarithmically transformed. Within the schizophrenia group, individuals with high plexus had significantly smaller lateral ventricles than those with low plexus visibility, t (54) = 2.67, $p < .02$ (Table 3). (Note that only 55 of the 66 schizophrenia patients had VBR data). There was no association between plexus and VBR in the unipolar and bipolar groups.

PLEXUS AND CLINICAL PHENOMENOLOGY. The high and low plexus groups of schizophrenia patients were then compared on the clinical data that were available for the chronic schizophrenia patients. A plexus group (high vs. low) MANOVA, with the course/severity indicators (age of onset, length of hospitalization, number of hospitalizations, GAS, and occupational functioning) as dependent variables was significant, F (5,22) = 3.90, $p < .02$. Univariate comparisons indicated that those schizophrenia patients with high plexus had been hospitalized longer, had worse ratings of occupational functioning, and had lower (more severe) GAS ratings (all ps $< .05$). The high and low plexus groups of schizophrenia patients were then compared on measures of positive and negative symptomatology. Plexus was unrelated to positive symptoms, t (32) = .41, $p > .05$; however, patients with high PVS had more negative symptoms, t (32) = 2.11, $p < .05$ (Table 3).

PLEXUS AND NEUROPSYCHOLOGICAL PERFORMANCE. Potential associations between plexus visibility and neuropsychological performance was available for the chronic schizophrenia patients only. Because IQ can often mediate neuropsych–ological performance, the high and low plexus groups were first compared on WAIS–R derived full scale IQ. There was no difference between the plexus groups in IQ, t (32) = 1.46, $p > .05$.

Next, two MANOVAs, with plexus group (high versus low) as the independent variable, were run to test potential associations between plexus visibility and tests thought to be sensitive to frontal versus non–frontal dysfunction. The

Table 3. Dependent Variable Means and Standard Deviations for the Schizophrenia Patients with Low and High Nailfold Plexus Visibility

		Low plexus		High plexus	
Dependent variable	*N*	Mean	SD	Mean	SD
RMSE	66	168.9	98.8	241.5[a]	144.1
(Log RMSE)		(2.15)	(.22)	(2.44)[a]	(.25)
VBR	55	8.4	2.6	5.6[a]	2.4
(Log VBR)		(.83)	(.15)	(.75)[a]	(.14)
Clinical measures	33				
Global Assessment Scale		40.6	13.3	30.4[a]	11.1
Age of onset (years)		19.7	3.1	18.1	2.7
Length of hospitalization (years)		4.0	7.6	10.9[a]	9.4
Occupational functioning		2.0	.8	1.3[a]	.9
Positive Symptom Index		13.3	6.2	12.0	10.6
Negative Symptom Index		5.4	5.8	9.8[a]	6.0
Neuropsychological measures	33				
WAIS-R FSIQ		86.6	12.0	80.9	10.3
Nonfrontal tests					
RAVLT (total words recalled)		40.5	14.4	35.2	16.3
BVRT (number of correct designs)		4.8	2.4	4.6	2.6
WCST nonperseverative errors		17.4	9.9	26.7	14.9
Frontal tests[a]					
WCST categories		3.9	1.9	2.6[a,b]	1.7
WCST perseverative errors		21.8	7.4	27.1[b]	9.2
COWAT (number of words)		35.6	12.6	25.4[a,b]	13.0

RMSE, Root Mean Square Error; VBR, lateral ventricle-to-brain ratio; WCST, Wisconsin Card Sorting Test; COWAT, Controlled Oral Word Association Test; RAVLT, Rey Auditory Verbal Learning Test; BVRT, Benton Visual Retention Test; WAIS-R FSIQ, Wechsler Adult Intelligence Scale-Revised Full Scale Intelligence Quotient. RMSE and VBR means and standard deviations are based on combined chronic and first-episode patients (*N*'s = 66 & 55, respectively). The remaining data was available only for the chronic patients (*N* = 33).

[a]Low and High Plexus group means are significantly different at $p < .05$, using two-tailed test.

[b]Low and High Plexus group means are significantly different at $p < .05$, using FSIQ as a covariate.

"non-frontal" MANOVA, which included the total number of words recalled on the RAVLT, the number of correct designs reproduced on the BVRT, and number of nonperseverative errors from the WCST, was not significant, F (3,24) = 1.16, n.s. The "frontal" MANOVA, which included number of words generated on the COWAT, number of categories achieved, and number of perseverative errors on the WCST, was, however, found to be statistically significant, F (3,24) = 3.02, $p < .05$. Univariate tests indicated that high plexus schizophrenia patients generated fewer words on the COWAT, achieved fewer categories on the WCST ($p < .05$), and there was a trend that the high plexus schizophrenia patients made more perseverative errors ($p > .08$). The MANOVAs were again run, this time controlling for IQ. This had no impact on the "non-frontal" MANOVA; however, the "frontal" MANOVA results became stronger, F (3,24) = 3.74, $p < .03$. In addition, the number of perseverative errors made on the WCST became significant ($p < .04$) after controlling for IQ differences, indicating that the high plexus schizophrenia patients made more perseverative errors (Table 3).

Overall, the results from the neuropsychology analyses indicated that high plexus schizophrenia patients performed significantly more poorly on tests thought to be sensitive to frontal dysfunction. Since IQ was unassociated with having high or low plexus and IQ was used as a covariate in the MANOVAs, this effect cannot be attributed to IQ differences.

Discussion

The present study replicated the finding that visibility of the vascular plexus at the nailfold is specifically related to the diagnosis of schizophrenia, this time using an 18-month longitudinal diagnosis. Almost one–fourth of the chronic and first–episode schizophrenia and schizophreniform patients had highly visible plexus. Approximately 7% of the nonpsychiatric controls and psychiatric controls that had a mood disorder with psychotic features had highly visible plexus. Less than 8% with visible plexus in a nonschizophrenia population is consistent with base rate estimates from previous studies (Maricq 1977). Overall, the current study provides strong evidence suggesting that the plexus trait is relatively specific to schizophrenia.

Smooth pursuit eye tracking performance has been shown to be a robust biological marker for a genetic liability for schizophrenia (Iacono and Clementz 1993;

Levy et al 1993). In the current study, the high plexus group had worse eye-tracking than the low plexus group of schizophrenia patients. This association with ocular motor dysfunction suggests that plexus may also be an indicator of genetic predisposition for schizophrenia, which is consistent with studies that have shown that plexus is found more often in schizophrenia patients who have a positive family history for schizophrenia (Maricq 1963a, 1963b).

Within the schizophrenia group, those with high plexus ratings had more negative symptoms, while there was no relationship to positive symptoms. These findings are consistent with those from past studies (Poole et al 1991, 1993). In addition, those schizophrenia patients with higher plexus ratings had more severe symptoms, had been hospitalized for a longer period of time, and had worse ratings of occupational functioning. Using the same sample used for the present study, Beiser et al (1994) showed that after premorbid occupational functioning, plexus ratings were the best predictor of occupational functioning 18 months after the onset of subject's first episode of schizophrenia. In general, among persons with schizophrenia, increased visibility of the nailfold plexus is associated with a more pathological condition characterized by more negative symptoms, greater severity of symptoms, and worse course and prognosis.

The schizophrenia patients with visible plexus performed more poorly on neuropsychological tests thought to be sensitive to frontal lobe dysfunction. Patients with more visible plexus tended to obtain fewer categories, generate more perseverative errors on the WCST, and generated fewer words on a verbal fluency task, even when IQ was controlled. Plexus was not associated with measures of verbal and figural recall, typically attributed to temporal lobe integrity. The pattern of findings relating plexus visibility and neuropsychological performance may suggest frontal lobe dysfunction in the schizophrenia patients with visible plexus. The impaired performance of the high plexus schizophrenia patients could be due to inattention, distractibility, reduced ability to spontaneously generate words, and poor concept formation, all of which are functions attributed, in part, to the prefrontal cortex. Nonetheless, further studies relating neuropsychological performance and plexus visibility are necessary in order to clarify the nature of the cognitive dysfunction detected in this preliminary study.

Among the schizophrenia patients, plexus visibility was inversely associated with lateral ventricle size. The schizophrenia patients with visible plexus did not have larger ventricles; the patients with low plexus visibility tended to have larger ventricles both among the chronic and first episode schizophrenia patients. Given that plexus visibility is associated with measures of poor outcome and negative symptoms, both of which have been associated with ventricular enlargement (Cannon and Marco 1994), it may seem anomalous that plexus was not associated with increased lateral ventricle size in the schizophrenia patients in this study. Indeed, this finding was not predicted and requires replication before its significance can be understood. Nonetheless, the inverse association between plexus visibility and lateral ventricle size may help explain why half of the imaging studies relating lateral ventricle size to negative symptomatology fail to find an association (Cannon and Marco 1994); there may be multiple independent pathways, of which plexus visibility and enlarged ventricles are but two, that give rise to negative and/or deficit symptomatology.

In summary, this study provides evidence that schizophrenia patients with the plexus visibility trait are characterized by oculomotor dysfunction, negative symptoms, more severe symptomatology, chronic course, neuropsychological dysfunction on tests thought to be sensitive to frontal dysfunction, and an absence of enlarged ventricles. Although the significance and cause of the plexus trait continues to remain a mystery, there exist few variables with a more robust association with schizophrenia. This fact alone justifies additional inquiry.

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