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Letter to the editors

Calcification of the choroid plexus as a marker of depression in schizophrenia

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Dear Editors,

Although depressive symptoms are a common and serious problem in schizophrenia, little is known about their biological substrate (Hirsch et al., 1989; Green et al., 1990). Depression has been linked to decreased cerebral serotonin (5-HT) functions in both nonpsychotic and chronic schizophrenic patients (Van Praag, 1982, 1983), particularly those with suicidal behavior (Van Praag, 1983) and enlarged cerebral ventricles (Potkin et al., 1983). The metabolic activity of the choroid plexus (CP), which is the major site for cerebrospinal fluid (CSF) production in the brain (Cserr, 1971), is regulated by the 5-HT system (Moskowitz et al., 1979; Napoleone et al., 1982; Faraci et al., 1989). We suggest, therefore, that alterations in the metabolic activity of the CP may underlie depressive symptoms in schizophrenia.

To test this hypothesis, we recruited 22 consecutive patients (20 men, two women) from predominantly male wards of an urban pyschiatric hospital. They were selected for a schizophrenic diagnosis by RDC and DSM-III criteria (Spitzer et al., 1978; American Psychiatric Association, 1980) and absence of focal abnormalities on a screening neurological examination. The sample characteristics appear in Table 1.

To standardize the psychotropic medication, all patients were stabilized on chlorpromazine over 4–5 weeks (group mean = 928.8 mg/day). Patients were then clinically assessed and subjected to non-enhanced CT scans using standard cuts on a GE 8800 CT scanner. CP calcification (CPC) in the lateral ventricles was independently evaluated by a research neurologist, who was blind to patients' identity, as 0 (no calcification), 1 (unilateral calcification), and 2 (bilateral calcification).

Assessment of depression was made according to the 7-point severity ratings of the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987), following the prescribed 30–40 min patient interview. This procedure was selected because of its validation for schizophrenia, its high reliability, and its provision of control measures for other facets of schizophrenic psychopathology.

Bilateral CPC was seen in 14 of our patients (63.6%). As hypothesized, CPC was significantly associated with the PANSS depression factor score ($r = 0.54$, $P < 0.01$) as well as two of the three constituent symptoms: depression ($r = 0.58$, $P < 0.005$) and guilt feelings ($r = 0.43$, $P < 0.05$). Conversely, CPC was not associated with any of the demographic or control variables such as age, years of illness, IQ and neuroleptic dose. It was also unrelated to control symptoms on the PANSS, including positive and negative syndromes and overall severity of illness as based on the sum of all 30 PANSS symptoms.

Our findings of a specific association of depressive symptoms with CPC suggest that it may be a neuroradiological marker of depression in schizophrenia. Elsewhere, factor analytic study of 240 schizophrenic patients (Kay and Sevy, 1990) revealed that depression represents one of the four principal components of schizophrenic psycho-

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TABLE I

Sample characteristics (n = 22)

Variable	*Mean*	*SD*
Age	31.6	6.04
Age at onset of illness	20.1	5.48
Years of illness since onset	11.5	4.29
Years of schooling	10.4	2.32
Verbal IQ (WAIS-R)	80.3	11.43
Verbal IQ (Quick Test)	82.6	12.27

pathology (along with negative syndrome, positive syndrome, and excitement/impulsivity) and is most closely aligned with prognosis.

Several lines of evidence suggest that 5-HT plays an important role in mechanisms that regulate CP functions: (a) 5-HT containing neurons project to the CP (Moskowitz et al., 1979; Napoleone et al., 1982); (b) 5-HT and 5-HT precursors decreased CSF production in rabbits and dogs (Maeda, 1983; Lindvall-Axelsson et al., 1988); (c) the CP contains a very high density of a unique receptor for 5-HT (5-HT_{1c}), which has marked effects on phosphatidylinositol turnover (Pazos et al., 1984; Conn et al., 1987); and (d) in monkeys and dogs, 5-HT increases blood flow selectively to the CP (Faraci et al., 1989). The findings that 5-HT increases CSF production suggest that it may have direct effects on the permeability and secretory activity of the epithelium of the CP.

The mechanisms underlying CPC in humans are poorly understood (Alcolado et al., 1986). In addition to its role in CSF production (Cserr, 1971), the CP has a 'sink-like' action, and several heavy metals such as lead may accumulate in the plexus throughout life (Friedheim et al., 1983; Manton et al., 1984). Excessive accumulation could lead to destruction of the plexus and accelerate the process of calcification (cf. Alcolado et al., 1986). Alternatively, reduced 5-HT innervation may decrease blood flow to the plexus, diminish its metabolic activity, disrupt the functions of its surrounding barrier, and subsequently enhance the accumulation of heavy metals in the plexus. This latter mechanism may conceivably underlie the association of CPC and depression in schizophrenia.

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