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## Normal ventricles in chronic schizophrenics

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**ABSTRACT** - The computed tomography (CT) scans of 46 chronic schizophrenic patients and 46 controls were studied using ventricular-brain ratio, Ewans' index, and cella media index. None of the indices used revealed significant differences between the patient and the control groups.

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Since Jacobi (1) first examined structural abnormalities of schizophrenic brains by pneumoencephalography, several structural studies on brains of schizophrenics have been undertaken, and some investigators have reported enlargement of lateral and third ventricles and sulcal widening. Johnstone et al. (2), using CT scan, were the first to report increased ventricular size among schizophrenics. Studies by Weinberger and associates (3, 4) have provided further evidence: ventricular enlargement seems to correlate with poor premorbid adjustment and poor response to treatment. Andreasen et al. (5) revealed some impairment in the sensorium and a preponderance of "negative symptoms", which are thought equivalent to "Type II syndrome" (6). Other investigators have revealed similar findings (7-11), while others found no morphological abnormalities in schizophrenics (12-15). We have recently reported that the

bifrontal and occipital regions of chronic schizophrenics have significantly lower densities compared with controls (16, 17).

The aim of this study is to confirm ventricular enlargement by means of ventricular-brain ratio (VBR), Ewans' index, and cella media index (CMI) using the same subjects as reported on previously (16, 17).

### Methods

The patient sample comprised 46 chronic schizophrenic inpatients (22 female, 24 male; mean age  $\pm$  SD  $36.6 \pm 6.7$ ; range 23-48) according to DSM III criteria. The control group comprised 38 healthy, asymptomatic volunteers (19 females and 19 males) and eight patients with headache as their main complaint, in whom no neurological abnormalities were found

Table 1  
Comparison of measuring values between schizophrenic patients and controls

	N	VBR	Ewans' index	CMI
Patients	46	8.2 ± 2.3	0.25 ± 0.03	5.6 ± 1.1
Controls	46	7.6 ± 1.8	0.26 ± 0.03	5.7 ± 1.1

(4 female, 4 male). The age of the controls ranged from 25 to 47 years (mean age ± SD 36.9 ± 6.6). All patients and volunteers gave informed consent to participate.

CT scans were obtained using CTHF (Hitachi) which provides a 256 × 256 matrix. The width of slices was 10 mm. VBR was calculated using a curve digitizer (ROI) at the level where the ventricles were seen at their largest. Ewans' index (18) (the ratio of the transverse diameter of the anterior horns of the lateral ventricles to the greatest internal diameter of the skull) and cella media index (19) (the ratio of the maximum distance of cella media to the maximum transverse outer diameter of the skull) were calculated by the digitizer. These measurements were done blindly by the rater.

## Results

In schizophrenics the average age at onset was 23.0 ± 5.8 years and the average duration of illness was 13.3 ± 6.7 years. The average length of hospitalization was 6.7 ± 6.4 years and the average number of hospitalizations was 2.9 ± 1.9. The mean neuroleptic dosage at the time of examination was 848 ± 776 mg (chlorpromazine equivalents) (20). The patients had had an average of 11.9 ± 2.2 years of education. The subjects were all Japanese.

Table 1 shows the measurements for schizophrenic patients and controls. VBR, Ewans' index and CMI showed no significant differences between these groups (Student's *t* test).

Table 2 shows the correlation between age and several measurements in the controls. A significant correlation was observed between age and VBR ( $P < 0.01$ ). We also found significant correlations between VBR and Ewans' index ( $P < 0.05$ ) or CMI ( $P < 0.05$ ).

Table 2  
Correlation between age and various measurements in controls

	VBR	Ewans' index	CMI
Age	0.39**	0.27	-0.21
VBR		0.31*	-0.33*
Ewans' index			-0.17

\*  $P < 0.05$ .

\*\*  $P < 0.01$ .

Table 3  
Correlation between age and various measurements in schizophrenic patients

	VBR	Ewans' index	CMI
Age	0.44**	0.22	-0.13
VBR		0.36*	-0.14
Ewans' index			-0.39**

\*  $P < 0.05$ .

\*\*  $P < 0.01$ .

In schizophrenic patients there was a significantly positive correlation between age and VBR ( $P < 0.01$ ) (Table 3). The positive correlation between VBR and Ewans' index was also significant ( $P < 0.05$ ). A significantly negative correlation was observed between Ewans' index and CMI ( $P < 0.01$ ). A weak positive correlation was found between VBR and length of illness ( $r = 0.35$ ,  $P < 0.05$ ) or present medication ( $r = 0.31$ ,  $P < 0.05$ ).

## Discussion

Johnstone et al. (2) first found that increased cerebral ventricular size in schizophrenic patients was associated with substantial impairments on intellectual testing. Since their report many studies on computed tomographic investigations of schizophrenia have appeared. However, structured abnormalities in schizophrenics remain controversial, although negative results are in the minority. Thus Weinberger et al. (3, 4) and Andreasen et al. (5) have confirmed ventricular enlargements in chronic schizophrenics. Tanaka et al. (7) found significantly larger ventricles and marked cortical atrophy in schizophrenics aged 41 to 60 years as compared with controls, but not in schizophrenics aged 21 to 40 years. In a study of twins Reveley et al. (8) revealed that schizophrenics had significantly larger ventricles than the control twins and their own co-twins. Nasrallah et al. (9) disclosed significantly larger ventricles in schizophrenics than controls. Regarding subtypes, the paranoid and nonparanoid-hebephrenic groups had significantly larger ventricles than the nonparanoid-undifferentiated group. Nybäck et al. (10) studied acute psychoses and found sig-

nificantly larger ventricles both in the whole sample and in the schizophrenic group as compared with the controls. Okasha et al. (11) reported highly significant differences in central atrophy between chronic schizophrenics and controls.

On the other hand, some studies have found no differences between patients and controls. Trimble et al. (12) reported normal ventricular sizes in all their study patients. Glück et al. (13) also found no differences between chronic schizophrenics and controls. Benes et al. (14), examining young schizophrenics, disclosed normal ventricles. Jernigan et al. (15) also reported negative study using well-controlled design.

These inconsistent results might be due to sample differences. The studies had varying patient populations and diagnostic criteria and the control groups used were either healthy normal volunteers or patients. In addition, methods for measuring lateral ventricles also differed.

In the present study there was no evidence of increased ventricular size in chronic schizophrenic patients.

Weinberger et al. (21) reviewed neuropathological studies of schizophrenia and pointed out some of the methodological issues to be considered in CT studies: 1) "rigorously diagnosed patients and an adequate control group must be scanned on the same machine using a uniform procedure". Our subjects were all Japanese and under 50 years of age. Chronic schizophrenic inpatients were selected according to DSM III criteria. The controls were mostly volunteers, but as they included eight headache patients we re-analysed the data excluding the patient controls. Again no significant differences emerged between schizophrenics and non-patient controls. 2) "The scans must be

blindly evaluated", and 3) "at least for determining ventricular size, a quantitative measure must be used". Our study would seem to fulfil these conditions.

The mean VBR in our control subjects was much greater than those in other studies. Other investigators found that the mean VBR in normal groups was from 2.7 to 5.0 (21), whilst 7.6 in ours. This discrepancy might have derived primarily from measurement differences. This, however, is not a serious problem, as both patients and controls were examined in a uniform manner in this study. Sampling factors are also thought to have some influence on this result. However, our Ewans' index and CMI values were not very different from those in previous studies (18, 19), which suggests that our high mean VBR value was not mainly due to sampling bias.

The same subjects in our previous investigation were found to have significantly lower CT density in the bilateral frontal and occipital areas (16, 17). Of great interest is the finding that our schizophrenic patients with brains of low density had normal ventricles. At present no reasonable explanation can be given.

Further studies will solve these important issues.

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