

Cortical and Central Atrophy in Chronic Schizophrenia a Controlled Study

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ABSTRACT

CT of the brain was carried out in 43 chronic schizophrenics of more than 5 years duration and less than 60 years of age, and 39 normal controls matched for age, sex and education. There was no statistical difference between controls and schizophrenics as regards cortical atrophy (as measured by the inter-hemispheric and Sylvian fissures and mean sulcal width). Highly significant differences were found regarding central atrophy. Third ventricle measurements were normal in 9.3%, slight enlargement in 37.2% moderate in 48.8% and extreme in 4.7%. The cella media index denoting lateral ventricular dilatation showed moderate changes in 46.5%, slight in 9.3% and the remaining 44.2% were normal.

This study shows that a large number of chronic schizophrenics have an associated central atrophy.

INTRODUCTION

Many studies have been made on the aetiology of schizophrenia with disputable results. Recently the application of computer tomography as a means of examining brain morphology in many diseases was introduced (1, 5, 7, 12, 14, 15). Subtle manifestations of brain atrophy, specifically enlargement and dilatation of cortical sulci have been observed of CT findings (4, 11, 8, 15). It is unclear from these studies whether such abnormalities are related to the pathogenesis of the illness or to non-specific factors to which schizophrenic patients are particularly exposed e.g. duration of illness, institutionalization, ECT, neuroleptic drugs.

The aim of this study is to investigate the presence or absence of ventricular enlargement and cortical atrophy in chronic schizophrenia in

a different culture as most of the previous studies were in USA, Europe or Japan.

The subjects were 43 chronic schizophrenics of more than 5 years duration (35 men & 8 women) aged 15 to 59 years (mean age 33 years). As controls (patients with peculiar symptoms in the head and needed reassurance by CT) were 39 cases (24 men & 15 women) who showed no positive neurological signs. The age of the controls ranged from 15 to 59 (mean age 33 years) (Table I).

TABLE I

Age Distribution of Schizophrenic Patients and Controls.

AGE (Years)	SCHIZOPHRENIC n=43 (35 males; 9 females)	CONTROLS n=39 (24 males; 15 females)
Less than 19	7	7
20-29	13	8
30-39	10	12
40-49	9	7
50-59	4	5
Mean age	32.84 $\pm$ 12.41 SD	33.41 $\pm$ 12.17 SD

31 patients were in hospital for a period ranging from 3 weeks to 2 years, the remaining 12 were outpatients living with their families. All our patients had their illness for at least 5 years duration.

METHODS

All CT scans were performed with a 128 $\times$ 128 head scanner of the type Densitone (CGR) using 9 mm thick slices. Two slices were obtained for each 180 degree scan and 4 to 6 scans were carried out for each subject. The following dimensions were measured :

1. The width of the third ventricle.
2. The largest external distance of the lateral ventricles in the region of the cella media and the biparietal diameter of the skull. The cella media index of Schiersmann (1952) (13) is the largest distance of the biparietal diameter.
3. The maximum width of the Sylvian and the interhemispheric fissures and the width of the 3 broadest sulci, taking the mean value of the latter. If one of these structures was not measurable, it was assigned a value of less than 1 mm.

Measurements were expressed in millimeters as measured on the Polaroid photographs. Multiplying these values by a factor of 4 would give the actual dimension being measured.

RESULTS

Control subjects: The different measurements carried on the control subjects are shown in Table II. In normal individuals the Sylvian and interhemispheric fissures measured less than 3 mm and the mean sulcal width less than 2 mm (15). In the 13 subjects where the interhemispheric fissure could be measured the highest value obtained was 2.5 mm. As for the Sylvian fissure, it measured less than 1.5 mm in 2 cases. The mean sulcal width was 1.3 mm in one case.

Meese et al. (1976) (10) have reported a normal third ventricle width of less than 8 mm while a slight dilatation ranges from 8-10 mm, moderate dilatation from 11-14 mm and marked dilatation more than 14 mm. The mean of our control Egyptian subjects was completely different as 1.65 mm, probably because of technical and exposure differences and so our measurements were taken accordingly. The normal cella media index is more than 4, it ranges from 3.6-4 in slight, 3-3.5 in moderate and less than 3 in marked dilatation.

Schizophrenic patients: The measurements carried out in the schizophrenic patients are shown in Table II.

TABLE II

Measurable Values in Schizophrenics and Controls

VARIABLES	SCHIZOPHRENICS				CONTROLS			
	Measurable cases	%	Mean	S.D.	Measurable cases	%	Mean	S.D.
CORTICAL :								
Interhemispheric	16	37.2	2.795	0.906	13	33.50	1.580	0.368
Sylvian	6	13.9	3.173	0.759	2	5.12	1.305	0.205
Sulcal	3	6.9	3.466	0.604	1	2.50	1.000	
CENTRAL :								
III Ventricle	43	100	5.228	1.903	39	100	1.65	0.425
Cella media index	43	100	3.81	0.477	39	100	4.604	0.298

Cortical structural abnormalities were seen in 8 patients (18.6%). Five patients showed only one abnormality, in the interhemispheric fissure in 3 and the Sylvian fissure in 2. The remaining three patients showed abnormalities of all the parameters. Widening of the third ventricle of more than 8 mm was present in 2 patients only (4.7%) (Table III). Yet only 4 patients had a third ventricle of less than 2.5 mm which corresponds to the mean control third ventricular size + 2 S.D. Of the remaining 37 patients (86%) 16 had a third ventricular size of less than 5 mm and in 21 patients the third ventricular size of less than 5 mm and in 21 patients the third ventricular size ranged between 5-8 mm.

The cella media index was less than 4 in 24 patients (55.8%). It was more than 3.6 in 4 patients (9.3%) and ranged from 3-3.6 in 20 (46.5%) (Table III). Of the 8 patients who had shown cortical abnormalities 7 had moderately dilated lateral ventricles. Only one patient who showed a slightly dilated interhemispheric fissure had a normal

cella media index. The 3 patients with combined widening of the inter-hemispheric Sylvian fissures and cortical sulci had third ventricles wider than 6 mm.

TABLE III
Graded Classification of Values and Parameters of the Ventricular System in Relation to Egyptian Controls.

	III VENTRICLE			CELLA MEDIA INDEX		
	Stand. values for controls	No. Egyp. Schiz.	%	Stand. values for controls	No. Egyp. Schiz.	%
Normal	3	4	9.3	4	19	44.2
Slight	3 - 5	16	37.2	3.6 - 4	4	9.3
Moderate	5 - 8	21	48.8	3 - 3.5	20	46.5
Extreme	8	2	4.7	3	—	—

DISCUSSION

In a previous investigation using CT, Weinberger (1979) (15a) found that cerebral ventricular size in a group of 58 chronic schizophrenic under 50 years of age was significantly greater than in a similarly aged group of 56 healthy subjects. In a further study the same authors (1979) (15b) examined whether atrophy also involves the cerebral cortex. There was no significant relationship found between ventricular enlargement and cortical abnormalities in the chronic schizophrenic group. This lack of correlation may raise the possibility that more than one pathological event or aetiology may be involved in producing these abnormalities.

Tanaka *et al.* (1981) (14) found no marked difference in ventricular size or cortical atrophy between schizophrenics and controls; however in the groups aged 41-60 years enlargement of the ventricular size and atrophy were highly significant in the schizophrenic group. Positive

correlation was observed between enlargement of the third ventricle and duration of illness.

Our results showed no significant differences between chronic schizophrenics and controls regarding the measurements of the fissures and sulci i.e. cortical atrophy. However, a highly significant difference was obtained on third ventricle and cella media index.

Only 46.5% of our schizophrenics showed moderate changes in the cella media index, slight changes in 9.3% and the remaining 44.2% were normal.

Regarding the third ventricle, our mean for the control was very low compared with previous studies in different centres, because only 2 patients (4.6%) had more than 8 mm, while 4 had less than 2.5 mm, 16 less than 5 mm and 21 between 5-8 mm comprising 86% of our schizophrenics.

Since both the cortical abnormalities and ventricular enlargement are presumed to represent mild cerebral atrophy, it is reasonable to expect a notable correlation between these findings. This is usually the case with typical degenerative brain disease. The lack of such correlation with chronic schizophrenia is surprising. It raises the possibility of more than one pathological process. This investigation demonstrates that lateral and third cerebral ventricular enlargement is associated with chronic schizophrenia. This finding challenges the widely held belief that structural brain abnormalities do not occur in schizophrenia and demand careful interpretation and further research.

Chronic institutionalization could theoretically lead to ventricular enlargement if it predisposed the patient to malnutrition, intercurrent infections, metabolic deficiency states, or other stigmata or neglect. None of our patients has been confined to the so-called backwards or neglected or had evidence of malnourishment.

Neuroleptic medication might be postulated as a cause of ventricular enlargement. Several observations suggest that ventricular enlargement occurs independent of drug treatment. Johnstone *et al.* (1976, 1978) (8,9) showed enlarged ventricles in patients who never received phenothiazines, also abnormal ventricles were found by pneumoencephalography in patients who had never received neuroleptics (2,6). Weinberger *et al.* (1979) (15) found no significant correlation between the length of the illness and the ventricular size. The opposite was found by Tanaka *et al.* (1981) (14), a factor which needs further evaluation. In our study we could not find any positive correlation between the cella media index and the duration of illness.

Johnstone *et al.* (1976, 1978) (8,9), Weinberger *et al.* (1979) (15) found no ECT effect on ventricular enlargement, although the latter found that ECT was associated with larger ventricles, significant ventricular enlargement was found in patients who had never received ECT. This variable could not be measured in our study as all our schizophrenic patients had received ECT.

Weinberger *et al.* (1980) (16) showed that schizophrenic patients with CT evidence suggestive of brain atrophy had significantly worse premorbid scores, particularly during childhood than did the patients with normal scores. Their findings provide further support for the clinical relevance of CT findings in chronic schizophrenics and implicates a neuropathological process that occurs early in development.

Crow (1980) (3) suggested two types of schizophrenia, type I equivalent to acute schizophrenia associated with a change in dopaminergic transmission and type II equivalent to chronic schizophrenia or the "defect state" associated with cell loss and structural changes in the brain. It seems that the second type is the one that CT studies may lead to further clarification of its pathogenesis and aetiology.

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الضمور المركزى والمحائى فى مرض الفصام المزمن دراسة مقارنة لفحص المخ بالكومبيوتر

تم فحص المخ بالكومبيوتر فى ثلاث وأربعون حالة فصام مزمن يمتد مرضهم لأكثر من خمسة أعوام ويقل عمرهم عن ستين سنة ، وكانت المجموعة الضابطة تتكون من تسع وثلاثون حالة متشابهة فى السن ، والجنس والتعلم ولم يلاحظ أى اختلاف احصائى بين مرضى الفصام والمجموعة الضابطة من ناحية ضمور لحاء المخ ، ولكن كانت الدلالة الاحصائية واضحة فى الضمور المركزى ، فكان البطين الثالث طبيعى فى ٩٣٪ ، تمدد بسيط فى ٣٧٢٪ ، تمدد متوسط فى ٤٨٨٪ ، تمدد كبير فى ٤٧٪ أما البطين الجانبى فكان التمدد المتوسط ٤٦٥٪ ، والبسيط ٩٣٪ ، وكان طبيعيا فى ٤٤٢٪ . وتوضح الدراسة أن جزءا كبيرا من مرضى الفصام المزمن يصاحبهم بعض الضمور المركزى فى المخ .

ABSTRACT

Étude comparée pour l'examen du cerveau à l'aide de l'ordinateur

Le cerveau a été examinée par l'ordinateur à travers 43 cas de la schizophrénie chronique et cela chez des personnes âgées de moins de 60 ans, et chez qui cette maladie dure plus de 5 ans et un groupe de contrôle normal composé de 39 personnes qui se ressemblent quant à l'âge, le sexe et l'éducation.

Aucune différence statistique n'a été constaté entre ceux qui souffrent de la schizophrénie et le groupe sous-mentionné ayant trait à l'atrophie corticale. Mais les indices statistiques étaient claires au niveau de l'atrophie centrale commune suit; le troisième ventricule était normal dans 9,3%, extension simple dans 37%, extension moyenne dans 48,8%, extension énorme dans 4,7%.

Quant au ventricule de côté; l'extension moyenne était de 46,5%, la simple de 9,3%, la normale de 44,2%. L'étude indique qu'une grande partie des patients chroniques donnent signe de quelque atrophie centrale dans le cerveau.