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ABSTRACT

Fifty schizophrenic patients fulfilling DSM-III-R criteria, and group matched normal healthy controls were selected for the study. The case and control groups have been compared in terms of VBR, WSF and WTF. In the study, schizophrenics have been divided into positive, negative and mixed subgroups on basis of SAPS and SANS, and these subgroups are compared with each other for VBR, WSF & WTF. Tomographic abnormalities were noted in schizophrenics, particularly with negative and mixed subtypes, when compared to controls,

Key Words: Schizophrenia, ventricle brain ratio (VBR), width of sylvian fissure (WSF), width of third ventricle (WTF), positive and negative subtypes, SAPS, SANS

The introduction of neuroimaging techniques has given schizophrenia research a new direction, the real breakthrough occurring in 1971 with the introduction of computed tomography (CT). This led to change in direction of research, and now CT abnormalities are being linked to phenomenology, treatment, course and outcome of schizophrenia.

Out of many studies available, only a few have employed normal controls (Weinberger et al., 1979 a; Jernigan et al., 1982; Turner et al., 1986), and sophisticated techniques of measurements (Owens et al., 1985; Turner et al., 1986; Delisi et al., 1986).

The positive and negative symptomatology in schizophrenia has been linked with favourable and not so favourable prognosis respectively, and it has been suggested that patients with prognostically poor symptomatology (negative and mixed type of schizophrenia) have more tomographic abnormalities (Weinberger et al., 1980; Andreasen et al., 1982b; Delisi et al., 1983; Schulz et al., 1983; Luchins et al., 1984;

Pearlson et al., 1984; 1985; Williams et al., 1985).

There appears to be a paucity of tomographic studies on schizophrenia in Indian literature. We could come across only one study (Jaiswal et al., 1981), who compared chronic schizophrenics with patients of headache. The study found enlargement of lateral ventricles, WSF and WTF in schizophrenics as compared to controls; these CT parameters were not affected by duration of illness or electroconvulsive therapy. Some of the studies have dealt with chronic institutionalized patients (Nasrallah et al., 1982), thus limiting the scope of such studies. This study was undertaken with the aims: to study the CT findings of schizophrenia; to evaluate the tomographic findings of schizophrenia of those patients having predominantly positive or negative symptomatology.

MATERIAL & METHOD

The sample comprised of consecutive hospitalized patients of either sex, diagnosed

as schizophrenia according to the DSM-III-R criteria, and between age range of 16-45 years. The patients who were already on neuroleptics were given a washout period of 7 days and 14 days for oral and depot preparations respectively. This was incorporated so as to minimize the masking effect of neuroleptic drugs and facilitate proper evaluation of affective component of SAPS & SANS. The prerequisites for selection were that the patients should be right handed and willing to give informed consent for the study, Exclusion criteria were history of organic brain syndrome. epilepsy, head injury, alcohol or drug abuse, pregnancy and having received ECT (s) in past 8 months.

Control group consisted of age-and sexmatched healthy, right handed volunteers with no past or family history of psychiatric illness, and with scores of less than 10 on M-R sections of Cornell Medical Index (CMI) (Broadman et al., 1949).

The schizophrenia group was evaluated on Scale for Positive Symptoms (SAPS) (Andreasen, 1983) and Scale for Negative Symptoms (SANS) (Andreasen, 1981).

The right handedness was determined clinically as has been usual practice by taking into consideration as to which hand the patient uses for fine and skilled motor functions (e.g. writing, sewing, using a knife, cutting with scissors). These have been specified by Devinsky (1994).

CT scan in both the groups, were performed on Hitachi-HSF CT scanner. The plane of reference was cantho-meatal line, and a minimum of 12 sections of non-enhanced scans were taken for every subject; slice thickness and pitch were 10 mm each. All measurements were made on the monitor. The area of cerebral hemispheres and ventricles were taken by "Joystick Method" using ROI manual option (Revely, 1985; Lasonczy et al., 1986). Ventricle to brain ratio was calculated as:

Measurement of width of third ventricle and sulcal widening were measured by distance option available on the console.

Statistical analysis was performed by paired 't' test considering both the groups and individual variables in pairs.

RESULTS

Out of a total of 137 consecutive schizophrenics who formed the index cases based on the diagnostic criteria of DSM-III-R, only 72 fulfilled the selection criteria, and a further 22 dropped out from the study for various reasons (withdrawal of consent =1; CT machine not functioning/left against medical advice before CT could be done= 9; disruption of hospital services = 12). Thus, only 50 patients were finally included in this study; the control group had 25 subjects taken from the hospital staff. The control subjects were group matched for age and sex to schizoprenic group.

The schizophrenia group was divided into 2 subgroups on the basis of duration of illness, as defined in DSM-III-R; 48% (n=24) patients had subchronic illness (<2 years duration) and the rest 52% (n=26) had chronic illness (>2 years duration). About one-third of schizophrenic patients (n=18) did not receive any treatment in past, 48% (n=24) had been treated with only drugs (mean duration of treatment=4 months), and another 16% (n=8)had received ECTs (mean number of ECTs=5) besides drugs, before they formed the subject of this study.

On SANS & SAPS, 22 (44%) patients could be rated as positive, 19 (38%) as negative and 9 (18%) as mixed schizophrenia.

The three parameters under study viz., ventricle brain ratio (VBR), width of sylvian fissure (WSF) and width of third ventricle (WTF), did not significantly differ in various age-groups in both the groups, i.e. schizophrenic and control groups (table 1). In the schizophrenia group no statistically significant effect of duration of illness (table 2) or past treatment (table 3) was observed on the three parameters. However, when schizophrenics as a groups were compared with controls, VBR, WSF & WTF were all significantly greater in the schizophrenic group (table 4).

TABLE 1
AGE AND TOMOGRAPHIC
FINDINGS

Age Group	VBR	WSF (in m	m) WTF (in mm)
(In yrs)	mean SD) megn S	D mean SD
I. SCHIZOPHRI	NIC GRO	UP	
A. 16-25 (n=14) B. 26-35 (n=21) C. 36-45 (n=15)	10.57	2.51 3.69 0.	
A:B d.f.=33 B:C d.f.=27 A:C d.f.=34	t= .29 f= .13 t= .11	t≠. 61 t≠. 32 t≠. 21	t=. 55 t=. 29 t=. 24
II. CONTROL G A. 16-25 (n≠7) B. 26-35 (n≠10) C. 36-45 (n=8)	8,29 1 8,15 2		2.68 0.57
A:B d. f.=15 B:C d. f.=13 A:C d. f.=16	t=. 16 t=. 02 t=. 19	t=, 32 t=, 13 t=, 42	i=, 11 t=, 22 t=, 07

TABLE 2 TOMOGRAPHIC FINDINGS AND DURATION OF ILLNESS

	VBR mean	SD	WSF (in r mean	nm) SD	WTF :	(in mm) n SD
ASubchronic(n=24 B. Chronic (n=26) C. Control (n=25)	10.50	1.90	3,80 3,30 2,51	0,08 0.68 0.48	3.50 3.90 2.70	00.71 90.91 0.49
A:C d. f.=47 B:C d. f.=49 A:B d. f.=48	t= 4.5 t= 4.6 t= 0.2	**	t= 6.6 t= 5.0 t= 0.9)		3.9** 5.2** 1.8

^{* *} p<0.001

TABLE 3
TOMOGRAPHIC FINDINGS AND PAST TREATMENT

	VBR	WSF (in mm)	WTF (in mm)
	mean SD	mean SD	mean SD
·	10.60 1.76	3.62 0.61	3.96 0.76
	10.50 2.00	3.50 0.67	3.84 0.91
	10.12 2.29	2.95 0.75	4.27 0.85
A:B d.f.=40	t= .16	t= .59	t= .44
B:C d.f.=30	t= .43	t= .18	t= 1.1
A:C d.f.=24	t= .56	t= .23	t= .88

TABLE 4
TOMOGRAPHIC FINDINGS OF SCHIZOPHRENICS
AND CONTROLS

-	VBR mean S	WSF (In mir D mean S	n) WTF (in mm) D mean SO
Schizophrenic (n=50)	10.44 1.9	8 3.50 0.67	3.95 0.96
Controls (n=25)	8.12 1.5	55 2.50 0.68	2.75 0.50
	1=5.1 **	t=6.6**	t=5.5**

for all comparison- d.f.=73, " *-p< 0.01

The comparison of subtypes of schizophrenia is interesting (table 5). The positive group had significantly smaller VBR and WTF than the negative or mixed group, but larger WSF and WTF than the control group. The negative and mixed subgroups differed significantly from the control group for all three parameters.

TABLE 5
CT FINDINGS OF POSITIVE, NEGATIVE AND MIXED SCHIZOPHRENIC SUBTYPES AND CONTROLS

	VBR	WSF (in mm)	WTF (in mm)
	mean SD	mean SD	mean SD
A. Positive (n=22)	9.12 1.96	3.32 0.71	3.60 0.74
B. Negative (n=19)	11.50 1.31	3.40 0.59	4.10 0.90
C. Mixed (n=9)	11.30 0.94	3.80 0.76	4.10 0.97
D. Controls (n=25)	8.10 1.50	2.50 0.48	2.70 0.49
A:B d.f.=39 8:C d.f.=26 A:C d.f.=29 A:D d.f.=45 B:D d.f.=42 C:D d.f.=32	t=4.5** i=0.4 l=3.1** t=1.9 t=7.5** t=5.6**	t=0.6 t=1.6 t=0.3 t=4.4*** t=5.9***	t= 2.1* 1= 1.2 1= 1.5 1= 3.8** 1= 6.8** 1= 4.2**

^{*-}p <0.05, **-p<.001

DISCUSSION

A total of 50 right handed schizophrenics formed the sample of this open design study and were categorized in three subgroups of positive, negative and mixed schizophrenia based on ratings on SAPS and SANS (Andreasen et al., 1981). The control group was

constituted by 25 normal healthy volunteers who were age and sex matched to the schizophrenic group, and did not have any past or family history of psychiatric illness themselves.

The observations indicate that the 3 tomographic parameters viz. ventricle to brain ratio (VBR), width of third ventricle (WTF) and width of sylvian fissure (WSF), were significantly greater in schizophrenic subjects than in the controls(p<.001). Till date, a number of studies have been carried out with regard to these parameters and majority of them, though employing varying methodologies, have reported similar abnormalities. Noteworthy in this regard are studies of Johnstone et al. (1976; 1978), Weinberger et al. (1979b; 1981), Takahashi et al. (1981), and Turner et al. (1986) who employed normal healthy controls, as in the present work, and reported parallel observations. Only two studies (Nyback et al., 1982; Jernigan et al., 1982) have reported negative findings with regard to lateral ventricles while employing normal healthy controls. Also these investigators employed linear measurement techniques which are less sensitive and hence, different from the present work.

Gluck et al. (1980) and Largen et al. (1984) reported findings about lateral ventricle which are contradictory to our findings. The subjects in these studies included schizophrenic and schizoaffective patients, hence experimental group was heterogeneous in nature, and medical and neurological patients, instead of healthy volunteers served as controls. Similarly, using medical and neurological patients as controls Okasha et al. (1981) did not find any increase in the width of sylvian fissure.

In our study, when tomographic findings were seen in various age groups, no significant difference could be elicited in either group with the advancement of age. Similarly, no significant difference was seen between the subgroups—subchronic and chronic schizophrenics, but both were significantly different from controls. And, since schizophrenics as a whole have tomographic abnormali-

ties, it appears that it is the illness *per se* causing these tomographic abnormalities. Similar have been the observation of several other workers (Weinberger et al., 1979b; Nyback et al., 1982; Williams et al., 1985).

In our study, at phenomenological level, all the schizophrenics were subjected to SAPS & SANS. Twenty two patients were found to have positive symptomatology, 19 had negative and 9 had mixed symptomatology. Comparison of these subtypes with controls on the three tomographic parameters revealed that patients with positive symptomatology had significantly increased WTF and WSF (p<.001), and though VBR was marginally increased, the change was not statistically significant. Interestingly, patients with negative and mixed symptomatology showed significant increase on all the three CT parameters (p<.001). Intragroup comparisons of the three subtypes reveals that the patients with negative symptomatology, who are generally known to have poor prognosis, had statistically greater neuropathology as compared to positive ones, and those with mixed psychopathology were closer to negative syndrome in terms of abnormalities of the three CT parameters. This observation finds support from a number of studies (Weinberger et al., 1980; Andreasen et al., 1982b; Delisi et al., 1983, Williams et al., 1985). Our findings seem to support the concept of negative symptoms as proposed by Hughlings Jackson (1931) (cited in Andreasen et al., 1994), which he attributed to neuronal loss. In more recent times Crow (1980) gave the two syndrome hypothesis along similar lines, and stated that type II schizophrenia has prominent negative symptoms associated with structural brain abnormalities (ventricular enlargement on CT) owing to neuronal loss.

The ventricular system has no structure of its own. The size of it is decided by the various adjoining structures of the forebrain such as thalamus, hypothalamus, limbic system and basal ganglia in case of lateral ventricles, and thalamus, hypothalamus, fornix

and habenula in case of third ventricle. Abnormal developments, atrophic degenerative states and other pathologies of these structures determine the eventual shape and size of these ventricles. Thus, it is pertinent to attribute ventricular enlargement to the damage of periventricular structures, most of which has been linked with schizophrenic etiopathology (Neito & Escobar, 1972; Stevens, 1982). It will therefore, seem logical to infer that if ventricular enlargement is specific to schizophrenia, an organic damage to surrounding structures is probably the underlying cause or result of a disease. Unfortunately till date organic damage of such magnitude to these structures that could account for the ventricular enlargement, has not been demonstrated. At most, either a subtle damage (Andreasen, 1989) or a functional hyperactivity at microlevels only has been reported, that by no means can account for ventricular enlargement of such an extent. The natural corollary of arguments therefore, would seem to end at this juncture and conclude that with the available knowledge, ventricular enlargement is a nonspecific finding in schizophrenics (Nasrallah et al., 1982). The ventricular enlargement has been considered to be nonspecific because it is reported to occur in a variety of situation such as in control population of schizophrenic subjects (Morriquchi, 1981; Andreasen et al., 1982a), in affective disorders (Rieder et al., 1983; Pandurangi et al., 1984), senile dementia (Gado et al., 1983), in alcoholism (Ron et al., 1982) and in autism (Campbell et al., 1982).

With this work it cannot be safely concluded that tomographic abnormalities are because of schizophrenic pathology per se. This conclusion would require a more comprehensive and extensive work, particularly a longitudinal study involving at risk subjects who are followed up before the onset of illness. It will also require comparison with other major psychiatric disorders like mood disorder, using all illness variables including genetic, personality, environmental, clinical, therapeutic and outcome profile of subjects. Till

such studies are available it will be more justifiable to link these abnormalities to the phenomenology of schizophrenia rather than to its etiology.

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