Indian J. Psychiat., 1998, 40 (2), 180-185

NEUROLOGICAL SOFT SIGNS, COGNITIVE DYSFUNCTION AND VENTRICULAR BRAIN RATIO IN SCHIZOPHRENICS

NAROTTAM LAL, S.C. TIWARI, SHRIKANT SRIVASTAVA, ABDUL KHALID, SIDDHARTHA & NEERA KOHLI

ABSTRACT

An association between cognitive dysfunction, neurological soft signs, enlarged brain ventricles and widened cortical sulci has been reported in schizophrenia. The present work aimed to study the relevance of positive and negative dichotomy with relation to neuropsychological performance of the schizophrenic patients, and the presence of neurological soft signs. In 23 schizophrenics patients diagnosed according to DSM-III-R of which 14 were of positive subtype and 9 were of negative subtype. At least one neurological soft sign was present in all the patients. The positive group had higher WMS and IQ scores and lower BGT scores than the negative group. Negative correlation was seen for WMS and BGT scores with Ventricular Brain Ratio (VBR), and the soft signs showed positive correlation in the positive subtype only.

Key words : Schizophrenia, positive subtype, negative subtype, neurological soft signs, neuropsychological tests, ventricular brain ratio

The advent of new neuroimaging techniques has nebulised the dividing line between organic and functional disorders. In schizophrenia, about three decades ago, employment of pneumoencephalography revealed enlarged VBR (Haug, 1962). This finding has now been replicated with Computed Tomography (CT) (Ras & Raz, 1990; Van Horn & McManus, 1992) as well as on Magnetic Resonance Imaging (MRI) scanning (Andreasen et al., 1986; Beeson et al., 1987; Andreasen et al., 1990).

Kraepelin (1919) was the first to observe abnormalities in attention, association and volition in schizophrenics. Reider and colleagues (1989) much later observed an association between intellectual deficit and neurological soft signs, enlarged brain ventricle and widened cortical sulci. Increased ventricular size has been seen to correlate with deficits that placed greatest demand on memory (Johnstone et al., 1976; Weinberger et al., 1979). Owens and colleagues (1985) in 112 chronically hospitalised schizophrenic found no relationship of the size of lateral ventricle on one hand and positive and negative symptoms or intellectual impairment on other hand. Some workers (Johnstone et al., 1978; Golden et al., 1980; Williams et al., 1985; Kolakowska et al., 1985) have negated the presence of association between Ventricle Brain Ratio (VBR) and cognitive deficit. Lewis (1990) in a review of 41 CT scan studies found that majority of studies have reported a positive correlation between lateral ventricular enlargement and neuropsychological impairment in schizophrenics.

The problems in thinking, attention and information processing persist even after clinical improvement following treatment (Spohn & Straus, 1989; Goldberg et al., 1993), and the cognitive deficit was found to be stable over long term follow-ups (Hyde et al., 1994). Moreover, in one study when young and old schizophrenic patients were compared, those without neurological comorbidity, had the same degree of cognitive decline with advancing age as controls (Goldstein & Zubin, 1990).

Neurological soft signs are minor neurological signs of doubtful localizing significance (Kolakowska et al., 1985), and have been reported to be more commonly present in schizophrenia than in other psychiatric disorders or in controls (Cox & Ludwig, 1979). They are regarded as an indicator of nonspecific brain damage (Wells & Duncan, 1980) and their significance is yet unclear.

We aimed to study the relevance of positive-negative dichotomy of schizophrenia with relation to neuropsychological performance of the patients and the presence of neurological soft signs. Further, both these parameters were correlated against VBR to see if enlarged ventricular size affects them, and if yes, then is there any difference between the positive and negative subtype in this regard.

MATERIAL & METHOD

The sample comprised of consecutive hospitalised, right handed patients of either sex, between age range of 16-45 years, diagnosed as schizophrenia according to DSM-III-R criteria. 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 effect of neuroleptic on affect. During this period, if required Lorazepam upto a maximum dose of 6 mg/day for excitement and Trihexyphenydyl upto 6 mg/day for extrapyramidal symptoms was used. The prerequisites for selection were that the patient 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 Electro Convulsive Therapy (ECT) in past 6 months.

The schizophrenia group was evaluated on Scale for Positive Symptoms (SAPS) (Andreasen, 1993) and Scale for Negative Symptoms (SANS) (Andreasen, 1981), and were thus divided into positive subtype and negative subtype. The patients were examined for neurological soft signs for all the 4 lobes (frontal, parietal, temporal and occipital), and the ratings were given as 0=absent and 1 =present. The list of soft signs examined is shown in table 1.

All the patients were administered Weschler Memory Scale, Bender-Gestalt Test and Weschler Adult Intelligence Scale Revised (WAIS-R) by a trained clinical psychologist who was blind to the subtype of schizophrenia.

The further details of the methodology, including CT scanning and determination of handedness are given elsewhere (Sidhartha et al., 1997).

The statistical analysis for the neurological soft signs was carried out by Fisher's Exact Probability Test, while the total scores for WMS, BGT and IQ were compared by student 't' test. Further, Pearson's Product Moment correlation coefficient was obtained for total number of soft signs present, scores of WMS, BGT and IQ and VBR for each group.

RESULTS

A total of 50 schizophrenic subjects were included in the study, out of which only 23 were cooperative for psychological testing. Fourteen of these 23 schizophrenics were classified as positive subtype, and 9 as negative subtype, as per the criteria of Andreasen et al. (1981). The mean age of the positive group was 29.0±4.7 years and that of the negative group was 31.4±7.1 years. The male/female ratio was 9/5 in positive subgroup and 4/5 in negative subgroup.

TABLE 1
NUMBER OF PATIENTS HAVING NEUROLOGICAL SOFT SIGNS

Neurological soft signs	Positive subtype (n=14)	Negative subtype (n=9)
Frontal lobe		
1. Grasp reflex	3 (21.4)	1 (11.1)
2. Palmomental reflex	4 (28.5)	3 (33.3)
3. Visual perseveration and spoken commands	6 (42.9)	2 (22.2)
4. Conceptualization and follow through of difficult task	2 (14.3)	5 (55.5)
5. Amnestic disturbance due to poor effort or perseveration	7 (50.0)	2 (22.2)
Parietal lobe		
1. Imaginary acts	5 (35.7)	1 (11.1)
2. Oral apraxia	9 (64.6)	3 (33.3)
3. Blunt vs sharp discrimination	6 (42.9)	4 (44.4)
4. Simultaneous bilateral tactile extinction	5 (35.7)	2 (2.20)
5. Stereognosis	6 (42.9)	3 (3.30)
6. Graphisthesia	2 (14.3)	0 (0.0)
7. Optokinetic nystagmus	7 (50.0)	3 (3.31)
Temporal lobe		
1. Memory test	4 (28.5)	0 (0.0)
2. Draw-a-face test	5 (35.7)	3 (33.3)
3. Failure to recognize anomalies	3 (2.14)	2 (22.2)
4. Tapping rhythm test	8 (57.1)	3 (3.30)
Occipital lobe		
1. Visual fields	3 (21.4)	3 (33.3)
2. Optic gnosis	6 (42.9)	3 (3.30)
3. Optic agnosia	5 (35.7)	4 (44.4)

TABLE 2
NEUROLOGICAL SOFT SIGNS & SUBTYPE OF SCHIZOPHRENIA

	Positive subtype (n=14) n	Negative subtype (n=9) n
Frontal lobe sings		
1	6	4
>1	8	5
Fisher's exact test : p = 1.00, N.S.		
Temporal lobe sings		
1	2	4
>1	12	5
Fisher's exact test : p = 0.21, N.S.		
Parietal lobe signs		
1	8	7
>1	6	2
Fisher's exact test : p = 0.39, N.S.		
Occipital lobe signs		
1	14	8
>1	0	1
Fisher's exact test : p = 0.39, N.S.		
Total soft signs		
upto 5	2	4
>5	12	5
Fisher's exact test : p = 0.10, N.S.		

At least one neurological soft sign was present in all the patients of both the groups. The commonest soft sign seen in the positive group were oral apraxia (64.6%), Tapping rhythm test (57.1%) and Amnestic disturbance (due to poor efforts or to perseveration 50%). The common soft signs in the negative group were conceptualisation and follow-through of difficult task (55.5%), blunt vs sharp discrimination (44.4%), and optic agnosia (44.4%) (table 1). The total number of patients presenting with lobe sign are shown in table 2. number statistically significant differences existed between the groups with regard to number of patients with soft signs present (table 2).

As compared to negative group the positive group had significantly higher WMS scores ($t=7.69$, d.f.=21, $p<0.001$) and higher but significantly not different IQ scores ($t=1.47$, d.f.=21, N.S.) and significantly lower BGT scores ($t=3.97$, d.f.=21, $p<0.001$). When the total scores was correlated with VBR in each group, a weak negative correlation was seen for WMS and BGT scores, and the soft signs showed a significantly positive correlation in the positive group (table 3). The negative group showed a weak negative although statistically insignificant correlation of VBR with IQ scores

TABLE 3
CORRELATION BETWEEN VBR AND COGNITVE FUNCTION FOR SUBTYPES OF SCHIZOPHRENIA

	Positive subtype (n=14)			Negative subtype (n=14)		
	Mean	S.D.	Correlation with VBR	Mean	S.D.	Correlation with VBR
WMS	91.07	4.40	-0.39	83.33	11.68	0.25
BGT	7.14	2.75	-0.29	13.67	4.78	0.10
IQ	88.57	8.88	0.01	83.89	2.62	-0.03
SOFT SIGNS	6.57	1.23	0.61*	5.33	2.62	-0.33
VBR	10.93	1.44		10.00	2.78	2.78

* p<0.5, d.f. for positive subtype = 12; for negative subtype = 7

and total soft signs.

DISCUSSION

CT scan studies in schizophrenia have shown that there does exists a significant ventricular enlargement in such patients, which relates to neuropsychological impairment, negative symptoms, poor premorbid adjustment, and poor response to neuroleptic drug treatment. MRI and Single Photon Emission Computed Tomography (SPECT) studies have shown that the neuropsychological deficit has its origin in frontal-medial temporal dysfunction. Further, negative symptoms have been found to be prominent in patients with hypofrontality, thus localising the level of dysfunction to frontal lobe level.

Neurological soft signs are present not infrequently in schizophrenic patients (Kolakowska et al., 1985) though their etiological significance is still debatable. They are found in acute as well as in chronic schizophrenics although with more frequency in the latter group (Nizamie et al., 1989). In the present study, neurological soft signs were present in all the patients, but showed no significant relation with the negative subtype of schizophrenia. A statistically significant correlation was seen in the positive schizophrenics, when correlated with VBR. As the VBR was slightly higher in the positive group, it could mean that such signs are not specific to a particular subtype of schizophrenia, instead are the consequences of degree of cerebral damage. Similar results have been reported by Kolakowska et al. (1985) where no significant correlation of these signs was seen with negative symptomatology, although they were present more in those with enlarged VBR. Donnely et al. (1980) have observed that greater the size of ventricle, more is the cognitive dysfunction. The size of the body of lateral ventricles has been found to be related to the motor speed and the immediate verbal memory. Also weak association between negative symptomatology and cognitive deficit has been seen (Johnstone et al., 1976; 1978). This also argues against the two-model hypothesis of Crow (1980) which implied that structural damage was the main reason for the deficit state seen in type II schizophrenics.

As commented by Chua & Mckenna (1995), selection of controls in studies of lateral ventricular size play an important role in the outcome of results. Thus studies with better control selection are required before any definite comment can be made on the organic lesion (s) in schizophrenia and their significance regarding symptomatology, outcome and treatment.

ACKNOWLEDGEMENT

We acknowledge the help of Dr. Krishna

Dutt, Clinical Psychologist, Department of Psychiatry, K.G.'s Medical College, Lucknow for psychometric evaluations.

REFERENCES

Andreasen, N.C. (1981) Scale for the assessment of negative symptoms (SANS). Department of Psychiatry, University of Iowa : Iowa city.

Andreasen, N.C. (1983) Scale for the assessment of positive symptoms (SAPS). Department of Psychiatry University of Iowa : Iowa City.

Andreasen, N.C., Nasrallah, H.A., Dunn, V., Oson, S.C., Grove, W.M., Ehrhardt, J.C., Hoffman, J.A. & Crosset, J.H.W. (1986) Structural abnormalities in the frontal system in schizophrenia. *Archives of General Psychiatry,* 43, 136-144.

Andreasen, N.C., Ehrhardt, J.C., Swayze, V.W., Alliger, R.J., Yuh, W.T.C., Cohen, G. & Ziebell, S. (1990) Magnetic resonance imaging of the brain in schizophrenia. Pathophysiologic significance of structural abnormalities. *Archives of General Psychiatry,* 47, 35-44.

Beeson, J.A.O., Corrigan, F.M., Cherryman, G.R. & Smith, F.W. (1987) Nuclear magnetic response brain imaging in chronic schizophrenia. *Archives of General Psychiatry,* 43, 136-144.

Chua, S.E. & Mckenna, P.J. (1995) Schizophrenia a brain disease ? A critical review of structural and functional cerebral abnormality in the disorder. *British Journal of Psychiatry,* 166, 563-582.

Cox, S.M. & Ludwig, A.M. (1979) Neurological soft signs and psychopathology. I. Findings in schizophrenia. *Journal of Nervous and Mental Diseases,* 167, 161-165.

Crow, T.J. (1980) Molecular pathology of schizophrenia : more than one disease process. *British Medical Journal,* 280, 66-68.

Doonely, E.F., Weinberger, D.R., Waldman, I.N. & Wyatt, R.J. (1980) Cognitive impairment associated with morphological brain abnormalities on computed tomography in chronic schizophrenic patients. *Journal of Nervous and Mental Disease,* 168, 305-308.

Goldberg, T.E., Greenberg, R.D., Griffin, S.J., Gold, J.M., Kleinmin, J.E., Picker, D., Schulz, S.C. & Weinbeger, D.R. (1993) The effect of clozapine on cognition and psychiatric symptoms in patients with schizophrenia. *British Journal of Psychiatry,* 162, 43-48.

Golden, C.J., Moses, J.A., Zelazowski, R., Graber, B., Matz, L.M., Horvath, T.B. & Berger, P.A. (1980) Cerebral ventricular size and neuropsychological impairment in young chronic schizophrenics : measurement by the standardise Luria Nebraska Neuropsychological battery. *Archives of General Psychiatry,* 37, 619-623.

Goldstein, G. & Zubin, J. (1990) Neuropsychological differences between young and old schizophrenics with and without associated neurological dysfunction. *Schizophrenia Research,* 3, 117-126.

Haug, J.D. (1962) Pneumoencephalographic studies in mental disease. *Acta Psychiatrica Scandinavica,* 38, (Suppl 165) 66-86.

Hyde, T.M., Nawroz, S., Goldber, T.E., Bigelow, L.B., Strong, D., Ostram, J.L., Weinberger, D.R. & Kleinman, J.E. (1994) Is there cognitive decline in schizophrenia ? A cross-sectional study. *British Journal of Psychiatry,* 164, 494-500.

Johnstone, E.C., Crow, T.K., Frith, C.D., Stevens, F.M., Kreel, L. & Husband, J. (1976) Cerebral ventricular size and cognitive impairment in schizophrenics. *Lancet,* 2, 924-926.

Johnstone, E.C., Crow, T.K., Frith, C.E., Stevens, F.M., Kreel, L. & Husband, J. (1978) The dementia of dementia praecox. *Acta Psychiatrica Scandinavica,* 57, 305-324.

Kolakowska, T., Williams, A.O., Jambor, K. & Arden, M. (1985) Schizophrenia with good and poor outcome. III. Neurological soft signs and cognitive impairment and their clinical significance. *British Journal of Psychiatry,* 164, 348-357.

Kraepelin, E. (1919) Cited in : Dementia Praceox and paraphrenia. New York : R.F. Kreiger.

Lewis, S.W. (1990) Computerised tomography in schizophrenia of 15 years duration. *British Journal of Psychiatry,* 157 (supll 9), 16-24.

Nizamie, S.H., Nizamie, Alka, Sangama, M.W. & Sharma, P.L. (1989) Soft neurological signs

and minor physical anomalies in schizophrenia. *Indian Journal of Psychiatry*, 31, 230-237.

Owens, D.G.C., Johnstone, E.C., Crow, T.J., Frith, C.D., Jagoe, J.R. & Kreel, L. (1985) Lateral Ventricular size in schizophrenia : relationship to disease process and its clinical manifestation. *Psychological Medicine*, 14, 27-41.

Raz, S. & Raz, N. (1990) Structural brain abnormalities in the major psychosis : a quantitative review of the evidence from computerized imaging. *Psychological Bulletin*, 108, 93-108.

Reider, R.O., Donnely, E.F., Herdt, R.J. & Walderman, I.N. (1989) Sulcal prominence in young chronic schizophrenic patients CT findings associated with impairment on neuropsychological tests. *Psychiatry Research*, 1, 1-12.

Sidhartha, Lal, N., Tiwari, S.C., Dalal, P.K., Kohli, N. & Srivastava, S. (1997) A computed tomography study of schizophrenia. *Indian Journal of Psychiatry*, 39, 115-121.

Spohn, H.E. & Straus, M.E. (1989) Relation of antiepileptic and anticholinergic medications to cognitive functions in schizophrenia. *Journal of Abnormal Psychology*, 98, 367-380.

Wells, C.E. & Duncan, G.W. (1980) Neurology for Psychiatrists. FN Davis : Philadelphia.

Weinberger, D.R., Torrey, E.F., Neophytides, A.N. & Wyatt, R.J. (1979) Lateral cerebral ventricular enlargement in chronic schizophrenia. *Archives of General Psychiatry*, 36, 735-739.

Williams, A.A., Revely, M.A., Kolakowska, T., Andren, M. & Madelbrote, B.M. (1985) Schizophrenia with good and poor outcome : II. Cerebral ventricular size and its clinical significance. *British Journal of Psychiatry*, 146, 239-246.

Van Horn, J.D. & McManus, I.C. (1992) Ventricular enlargement in schizophrenia : a meta-analysis of studies of the Ventricular Brain Ratio (VBR). *British Journal of Psychiatry*, 160, 687-697.

NAROTTAM LAL[1], M.D., Professor, S.C. TIWARI[2], M.D., M.N.A.M.S., Associate Professor, SHRIKANT SRIVASTAVA[3], M.D., Senior Resident, ABDUL KHALID[4], M.D., Senior Resident, SIDDHARTHA[5], M.D., Ex-Resident, NEERA KOHLI[6], M.D., Associate Professor, [1-5]Department of Psychiatry, [6]Department of Radiodiagnosis, K.G. Medical College, Lucknow.*

** Corresponding*