VENTRICULAR ENLARGEMENT AND WATER INTOXICATION IN SCHIZOPHRENIA

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Received September 22, 1995

Abstract: To determine the extent to which atrophy was related to water intoxication in schizophrenic patients, ventricular enlargement in polydipsic schizophrenic patients with hyponatremia and schizophrenic controls without hyponatremia was measured in a linear way. Ventricular enlargement was found in both schizophrenic patient groups, and larger ventricles were associated with water intoxication. It is suggested that ventricular enlargement may reflect a developmental or degenerative pathological process involving the occurrence of water intoxication in schizophrenia.

Index Terms

schizophrenia, water intoxication, polydipsia, hyponatremia, ventricular enlargement

INTRODUCTION

Enlargement in the size of cerebral ventricles is one of the most frequently replicated neurobiological findings in schizophrenia[1]. This abnormality has been demonstrated by in vivo structural brain imaging techniques, including pneumoencephalography[2], computerized tomography (CT)[1], and magnetic resonance imaging[3]. CT studies also confirmed neuropathological[4] and pneumoencephalographic[5,6] findings of cortical and subcortical atrophy in alcohol users[7,8]. However, despite evidence that hyponatremia can injure or kill brain cells, little attention has been focused on the longer-time sequelae on brain structure in schizophrenia with water intoxication or polydipsia and hyponatremia.

The purpose of present study was to examine four indices of brain atrophy or ventricular enlargement in polydipsic schizophrenic patients with hyponatremia and schizophrenic controls without hyponatremia and to determine the extent to which atrophy was related to water intoxication in schizophrenic patients.

METHODS

All subjects, nine inpatients with polydipsia and hyponatremia (<134 mEq/L, normal values ;

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135-145 mEq/L) and ten age-matched control inpatients without hyponatremia, were admitted at Nara Medical University Hospital. Each individual gave informed consent to participation in the research protocol. Demographic data from interviews with the patients and family, and from medical records, included age, age at first symptoms, age at first hospitalization, duration of illness, neuroleptic administration, and cigarette smoking. All patients were evaluated by a staff psychiatrist; all met DSM III-R (American Psychiatric Association 1987) criteria for schizophrenia. All patients were free of medical and neurological disease (based on screening history and physical exam), history of corticosteroid treatment, recent substance abuse, and treatment with electroconvulsive therapy. Patients were nutritionally intact and well hydrated throughout the course of the study. Each person was assessed with the Brief Psychiatric Rating Scale (BPRS)[9] and the Scale for Assessment of Negative Symptoms (SANS)[10].

Head CT scans were performed on each patient, (GE 9800 scanner, GE Medical Systems) with a matrix size 512 by 512. Slices were taken parallel to the orbito-mental line; slice thickness was 10 mm. According to Iwasaki's method[11], four indices of ventricular size were calculated, i. e., maximum distance between tips of anterior horns (A), maximum distance of cellae mediae at the level of head of caudate nuclei (C), width of third ventricle at the thalamic segment (III-P), and the sum width of trigones of both sides (TRIG) were measured, divided

Table 1. Demographic and clinical data of the two paient groups

	Polydipsia & hyponatremia patients (N=9)	Control patients (N=10)
Age (yr)	48.3±10.7	47.2±11.1
Sex (M/F)	9/0	10/0
Smoker/non-smoker	9/0	10/0
Diagnosis on DSM-IIIR	Schizophrenia	Schizophrenia
Neuroleptic dosage (mg of Chlorpromazine equivalent per day)	887.5±373.7*	1531.1±329.7
Duration of illness (yr)	18.4±9.2	12.3±11.5
Duration of hospitalization (yr)	10.1±10.3	5.8±8.8
BPRS total score	33.4±7.8	37.8±11.1
SANS total score	47.9±23.8	39.9±19.6

* $p<0.05$ vs the control patient group
BPRS: Brief Psychiatric Rating Scale
SANS: Scale for Assessment of Negative Symptoms

Table 2. Four indices of ventricular size in the normal control group and the two pātient group

	Normal controls	Polydipsia & hyponatremia patients	Control patients
A	26.9±3.6	25.6±1.2	24.0±1.2
C	12.0±3.0	16.8±1.0*	17.0±1.5*
III-P	3.3±1.5	8.3±0.5*	7.2±0.5*
TRIG	16.7±5.0	24.7±1.9*+	19.5±1.4

A: maxdimum distance between tips of anterior horns
C: maximum distance of cellae mediae at the level of head of caudate nuclei
III-P: width of third ventricle at the thalamic segment
TRIG: width of trigone
* $p<0.05$ vs the normal control group
+ $p<0.05$ vs the control patient group

by maximum transverse inner diameter of the skull and multiplied by 100.

In the statistical analysis, student-t test was used.

RESULTS

Table 1 shows the demographic and clinical state data for the two groups of subjects. All patients were male smokers. Neuroleptic dosages of the polydipsia and hyponatremia group were significantly less than those the control patient group. In terms of BPRS and SANS, there was no difference between these two groups.

Table 2 shows the measured mean values of four indices of ventricular enlargement in both patient groups and the normal control data which had been obtained by Iwasaki[11]. Compared with normal controls, the values of C, III-P and TRIG were significantly greater in the polydipsia and hyponatremia grous, and the values of C and III-P were significantly greater in the control patient group. Between both patient groups, there was a significant difference in the value of TRIG, showing that larger ventricles were associated with polydipsia and hyponatremia.

DISCUSSION

Ventricular size in schizophrenia was first investigated in 1976 by Johnstone and her colleagues[12] using CT scanning, in a multi-cited study where they noted significant ventricular enlargement in a group of chronic schizophrenics. That study clarified those earlier studies which had lumbar encephalography[2] and had often found conflicting evidence for vetricular enlargement. The results of Johnstone et al were replicated by Weinberger et al[13] who confirmed in their sample that the lateral ventricles of schizophrenics were significantly larger than those of controls. Since those two papers were published there have been many studies attempting to identify the etiological factors responsible for ventricular enlargement in schizophrenia, and to correlate psychological deficits with what has been presumed to be an indicator of neuronal loss brain atrophy.

Ventricular enlargement is a sensitive indicator of central nervous system pathology as it reflects volume of the ventricular system. Knowledge about ventricular enlargement associated with the course of schizophrenic illness could provide information about the nature, timing, and progression of structural brain abnormalities in schizophrenia. Findings in the literature are inconsistent as to whether ventricular enlargement is present at the onset of schizophrenia and whether it progresses during the course of the illness[14]. Ventricle size appears to be unrelated to duration and treatment of schizophrenic illness[15,16]. Data suggest that ventricular enlargement is probably not an ongoing process throughout the course of schizophrenic illness ; however, it is unclear whether or not progressive ventricular enlargement occurs during the initial years of illness.

We used the linear measures to determine ventricular size because of its simplicity, although the most widely used way is the ventricle : brain ratio (VBR)[17]. Our study confirmed that there was a difference in ventricular size between chronic schizophrenics and normal controls, which would seem to be an indisputable characteristic of schizophrdnia. Then this present preliminary study showed that larger ventricles were associated with water intoxication, raising three possibilities involving the occussence of ventricular enlargement and water intoxication in

schizophrenia. 1) If this ventricular enlargement is present at the onset of schizophrenia, there might be some organic vulnerability to develop to water intoxication. Hariprasad reported 20 psychotic patients with polydipsia and hyponatremia, who consisted of 14 schizophrenic patients and 6 patients with organic brain syndrome[18]. From a family history taken from schizophenic patients with self-induced water intoxication, Ripley et al suggested that some of the genetic factors that predispose to alcoholism might also predispose to water intoxication[19]. It is suggested that some developmental factors or organic vulnerability may predispose to water intoxication. 2) If ventricular enlargement progresses during the course of the illness in schizophrenics with water intoxication, this might be related to hyponatremic toxic damage resulting from repeated or chronic hyponatremia. 3) Whether or not progressive ventricular enlargement occurs during the course of illness, water intoxication , polydipsia and hyponatremia might be a sequela or one of the symptoms of the preterminal stage of psychosis. Vieweg et al placed the onset of water drinking in the preterminal stage of schizophrenia[20]. As described by Arieti in 1945, this stage occurs "5-15 years after the disease onset", and is characterized by disorganization, lack of emotional content, and compulsive behavior[21]. The ventricular enlargement, identified in this study, coincides with that of "type II" schizophrenia proposed by Crow[22]. He described type II schizophrenia as associated with chronic course, poor response to neuroleptics, intellectual impairment, and the presence of neurological signs and ventricular enlargement. Hyponatremia may be one of the neurological signs of type II schizophrenia.

With methodological consideration for determining the areas or volumes of brain structures and of the ventricles from CT or MRI scans, longitudinal studies of schizophrenic patients followed through various stages of illness will be necessary to test these hypotheses.

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