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QUANTITATIVE CEREBRAL ANATOMY IN SCHIZOPHRENIC PATIENTS – A CONTROLLED COMPUTED TOMOGRAPHY IMAGING STUDY

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ABSTRACT. Despite significant support for abnormal brain morphology in individuals with schizophrenia, the precise nature of the abnormalities remains unclear. In the present study we used computed tomography imaging morphometric techniques to estimate volumes of specific cerebral structures. The study included 19 schizophrenic patients meeting the DSM IV criteria for schizophrenia, aged between 23 and 50 years. The control group included 24 age- and sex-matched mentally normal subjects. All subjects underwent CT examination without venous enhancement. Cortical atrophy was assessed using mean composite ratings for ventricles calculated: frontal horn index (FHI) and Huckmann digit (HZ). The schizophrenic patients showed mild to moderate decrease in the frontal horn index (Mean=3.27, SD=0.29) compared with the controls (4.08, SD=0.68) ($p<0.01$). The Huckmann digit was slightly increased in the patients (Mean=5.1, SD=0.42) compared with the controls (Mean=4.57, SD=0.55) ($p<0.05$). We hypothesize that the generalized decrease in the brain volume can be attributed to a process that affected the whole cerebrum over a time period exceeding beyond the early stages of brain development.

KEY WORDS. schizophrenia, computed tomography, brain ventricle

INTRODUCTION

It has been suggested that primary vulnerability to schizophrenia is established during early stages of brain development. Neuropathology and brain imaging studies have produced evidence of brain abnormalities in schizophrenic patients (1). Despite significant support for abnormal brain morphology in individuals with schizophrenia, the precise nature of the abnormalities remains unclear. The most consistent finding to date from computed tomography (CT) and magnetic resonance imaging (MRI) studies has been slightly enlarged lateral ventricles, possibly indicative of volumetric reduction of grey matter in the frontal and temporal regions, although the amygdala and hippocampus have also been implicated (2). Furthermore, it now appears that the ventricular enlargement is present at the beginning of the disease and is not progressive but is instead related to the degree of premorbid impairment (3,4).

There was no change in cerebral ventricular size or degree of cortical atrophy over this period. The stability of CT scan measures of cerebral atrophy in individual schizophrenic patients confirms the hypothesis of the early appearance of structural brain abnormalities in schizophrenia as formulated in previous cross-sectional studies. Furthermore, the pathological process responsible for the CT finding of cortical or central atrophy does not seem to progress nor to reverse itself in young schizophrenic patients.

Although MRI provides relatively precise information on volumetric measurements of specific regions of interest, the patient samples in studies of first-episode schizophrenic psychosis are generally small and selected mostly from hospital inpatients. However, CT studies can be conducted on larger samples of most new cases of first-episode psychosis within a defined population base (5,6). Results of such studies show an enlargement of the third ventricle in patients who receive a diagnosis of schizophrenia, but not in those with other psychotic disorders (5) and a significantly higher ventricular brain ratio (lateral ventricles) unrelated to any clinical symptoms (6).

In the present study we used computed tomography imaging morphometric techniques to estimate volumes of specific cerebral structures.

MATERIAL AND METHODS

The study included 19 schizophrenic patients of Bulgarian ancestry, who met the criteria of DSM IV for schizophrenia, aged between 23 and 50 years. The control group included 24 age- and sex-matched mentally normal subjects. All subjects underwent CT examination without venous enhancement at angle of examination + 15°-20° in relation to the orbitomeatal line. Potential subjects were excluded from the study if they had anamnesis of alcohol or drug abuse, neurological disorder or somatic disorder with neurological components. CT scans were rated by a neuroradiologist (V.G.) who was blind to the patients' demographic and symptom status but not to diagnosis.

Cortical atrophy was assessed using mean composite ratings for ventricles calculated as follows: frontal horn index (FHI), which is the ratio between the greatest external diameter of the skull (A) and the greatest distance between the frontal horns (B) and Huckmann digit (HZ), which is the sum of the greatest distance between the frontal horns (B) and the distance between the frontal horns at the level of caudate nucleus (C) (Figure 1). The measurements were done according to Meese and Grumme scheme (7), which graded the pathological changes of the examined variables as followed: 1. Frontal horn index – mild decrease 3.6-3.1 mm, moderate decrease 3.0-3.1 mm, marked decrease ≤ 2.5 mm. 2. Huckmann digit – mild increase 5.1-6.4 mm, moderate increase 6.5-7 mm, marked increase ≥ 8 mm.

RESULTS

The data obtained showed difference in the values of the examined variables between the schizophrenic patients compared with the control subjects. We found evidence of at least a mild degree of enlargement of brain ventricles.

The schizophrenic patients showed mild to moderate decrease in the frontal horn index (Mean=3.27, SD=0.29) compared with the controls (4.08, SD=0.68) ($p<0.01$) (Figure 2). The Huckmann digit was slightly increased in the patients (Mean=5.1, SD=0.42) compared with the controls (Mean=4.57, SD=0.55) ($p<0.05$) (Figure 3).

DISCUSSION

In accordance with other imaging planimetric studies of schizophrenic patients (8,9), our findings show increase in the ventricular space and decrease in the brain ventricular ratio indicating an overall loss of brain tissue. The observed evidence of cortical loss in schizophrenic patients reflects a pathological process operating before completion of the brain growth. The possible relevance of these findings of ventricular enlargement and brain volume loss to neurodevelopmental hypothesis of schizophrenia can be seen in some fundamental principles of normal neurodevelopment. Brain growth outward from the ventricles appears the main driving force of intracranial cavity growth. The intracranial cavity expansion is not reversible after skull sutures fuse. Hence, after brain growth reaches its maximum, intracranial size remains constant and any loss of brain volume leads to an equivalent increase in extracerebral and ventricular CSF volume.

Our data indicate, however, that ratings of lateral ventricles may show greater agreement between raters than ratings of third ventricle or some sulcal areas such as frontal and parietal sulci (10). This could be related to the size of the area and anatomical landmarks available (e.g., in the case of lateral ventricle) or the degree of difficulty demarcating the area to be rated (e.g., sylvian fissure v. frontal or parietal sulci). Improved image resolution on MRI would likely provide more reliable data on specific morphological changes.

Our CT scan measures of brain lateral ventricles in a sample of schizophrenia patients show mild enlargement of ventricles. These changes were mostly related to older age; there were no relations found between CT ratings and clinical syndromes, sex and length of illness.

However, results of a sample of chronic schizophrenia patients show correlation between schizophrenia subtype and brain tissue changes (11). Patients with schizophrenia who meet the criteria for catatonic subtype show more diffuse frontal, parietal and temporal enlargement of cerebrospinal fluid space than normal controls, whereas patients with hebephrenic and paranoid subtypes are more likely to show enlargement of mostly upper and lower temporal sulci including the sylvian fissure (11).

In conclusion, we hypothesize that the generalized decrease in the brain volume can be attributed to a process that affected the whole cerebrum over a time period exceeding beyond the early stages of brain development.

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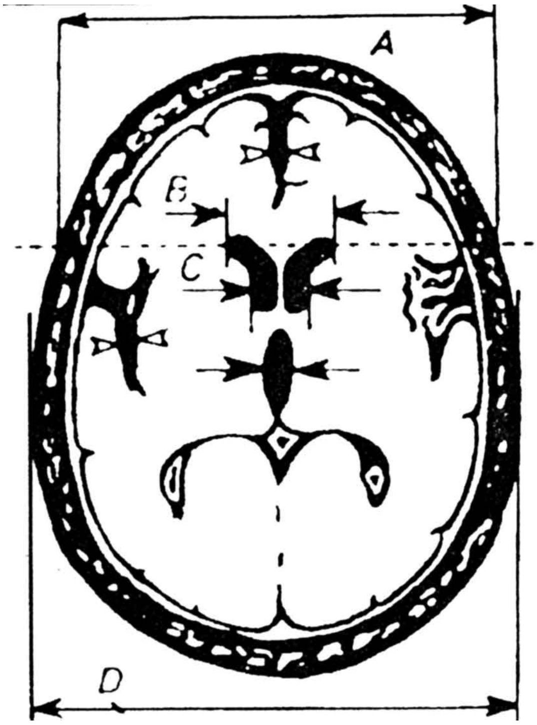

Figure 1. Frontal horn index (FHI) - the ratio between the greatest external diameter of the skull (A) and the greatest distance between the frontal horns (B) and Huckmann digit (HZ) - the sum of the greatest distance between the frontal horns (B) and the distance between the frontal horns at the level of caudate nucleus (C) (after Meese W., Groome T.).

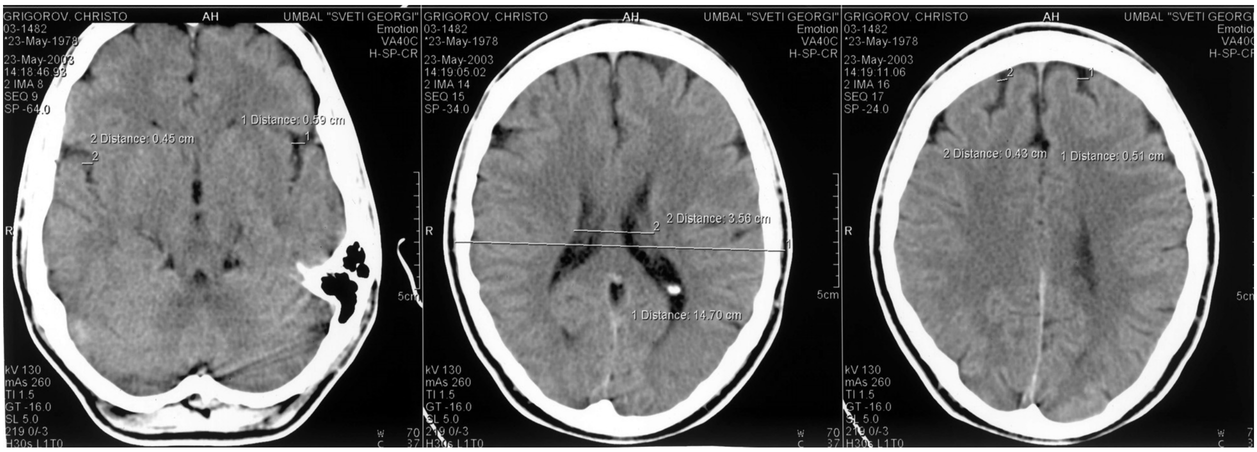

Figure 2. A 26-year-old man with one-year duration of the disease. Moderate widening of the lateral ventricles, decreased frontal horn index.

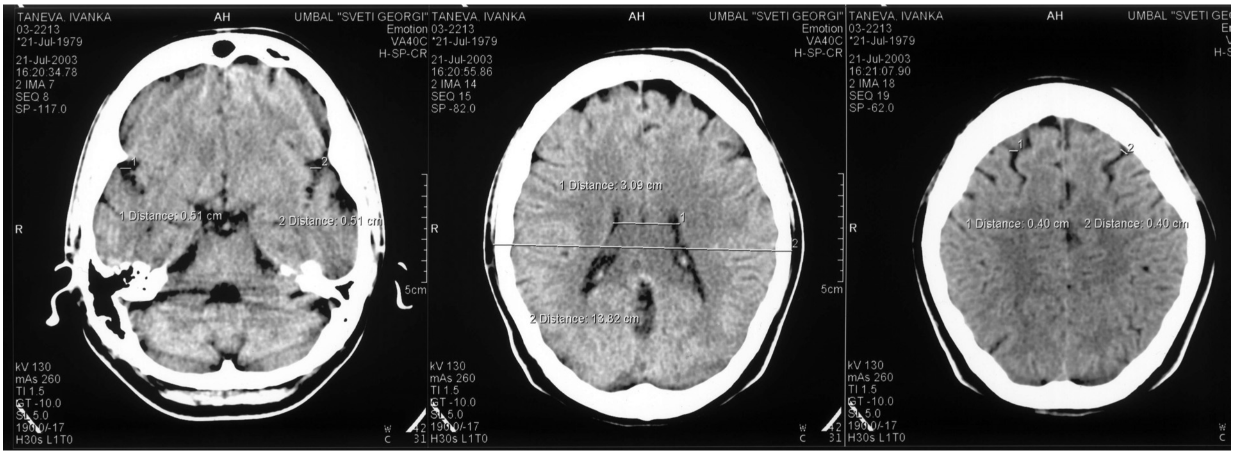

Figure 3. A 23-year-old woman with recently diagnosed schizophrenia. Widening of the lateral ventricles, increased Huckmann digit.